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2nd Innovations and State of the Art In Dementia Research

Jul 16 - 18, 2018 Valencia, Spain

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1 Monday

Hall Name - Flamenco Meeting Room

8:30-9:30 — **Registrations**

9:30-9:45 — **Opening Ceremony**

Moderator:
Susanne Aileen Funke,
Hochschule für Angewandte Wissenschaften Coburg, Germany

KEYNOTE FORUM

09:45-10:20 — **Title: The Role of Posttranslational Modifications of Amyloid-β for Neurotoxicity and Resulting Therapeutic Opportunities**
Hans-Ulrich Demuth, Fraunhofer IZI-MWT, Germany

10:20-10:55 — **Title: Multimode Optical Molecular Imaging for Early Neurodegeneration Detection**
Daniel Farkas, University of Southern California, USA

Coffee Break 10:55 -11:15 @ Terrace

Sessions:

Dementia Research | Alzheimer and Neuro Imaging

Session Chairs:

Michael Strong, Western University, Canada
Lora Appel, York University, Faculty of Health, Toronto, Canada

11:15-11:35 — **Title: Tau-specific D-enantiomeric peptides for therapeutic applications in Alzheimer's disease**
Susanne Aileen Funke, Hochschule für Angewandte Wissenschaften Coburg, Germany

11:35-11:55 — **Title: Cmax-based synergistic therapeutic effect on cognitive disability in mild Alzheimer's disease after 36 weeks treatment with baclofen and acamprosate**
Jacques Touchon, Montpellier School of Medecine INSERM U1061, France

1 Monday

11:55-12:15 —— **Title: Pathogenic tau protein phosphorylation in ALS, CTE and ALS/CTE: A unifying mechanism**
Michael Strong, Western University, Canada

12:15-12:35 —— **Title: Asymmetry of hippocampus and amygdala defect in Subjective cognitive decline among the community dwelling Chinese**
Ling Yue, Shanghai Mental Health Centre, Shanghai Jiao Tong University School of Medicine, Shanghai, China

12:35-12:55 —— **Title: Comparing fragility fracture burden in a high risk outpatient Movement Disorder service and a General Practice: Bridging the gap between research and clinical practice in osteoporosis using quality improvement initiatives**
Inderpal Singh, Aneurin Bevan University Health Board, UK

12:55-13:15 —— **Title: A potential tri-therapy for Alzheimer's disease**
Rodolphe Hajj, Pharnext Sa, France

Group Photo

Lunch Break 13:15 -14:15 @ Aeropuerto Meeting Room

Sessions:

Dementia Research | Pharmacological Treatment of Dementia | Dementia Care Practice | Physical Therapy

Session Chairs:

Daniel Farkas, University of southern california, USA
Hans-Ulrich Demuth, Fraunhofer IZI-MWT, Germany

14:15-14:35 —— **Title: A quantitative assay to measure human cerebrospinal fluid induced membrane permeabilization**
Suman De, University of Cambridge, UK

14:35-14:55 —— **Title: Algoplus® scale in older patients with dementia: A reliable pain assessment tool**
Fiammetta Monacelli, University of Genoa, Italy

14:55-15:15 —— **Title: Dementia among Indigenous populations in Ontario**
Laura Warren, University of Toronto, Canada

1 Monday

15:15-15:35 — **Title: Fixed-dose combination of donepezil hydrochloride and memantine hydrochloride for treatment of moderate to severe Alzheimer's disease**
Stevin Zung, Aché Laboratories, Brazil

Coffee Break 15:35 -15:50 @ Picasso

15:50-16:10 — **Title: A Multifunctional Biocompatible Drug Candidate Effectively Delays the Progression of Alzheimer's Disease in 5XFAD Mice**
Bilha Fischer, Bar-Ilan University, Israel

16:10-16:30 — **Title: A study on support for older adults with moderate to severe dementia following spousal death**
Akiko Watanabe, Miyagi University, School of Nursing, Japan

16:30-16:50 — **Title: The effect of navigational problems and assessment location on driving test performance for people with Alzheimer's disease**
Kay Russell, Austin Health, Australia

16:50-17:10 — **Title: The challenges of post-hip fracture rehabilitation among people with cognitive impairments**
Michal Elboim-Gabyzon, University of Haifa, Haifa, Israel

Panel Discussions

2 Tuesday

Hall Name - Flamenco Meeting Room

Sessions:

Diagnosing Dementia | Dementia Care Practice

Moderator:

Laura Warren, University of Toronto, Canada

KEYNOTE FORUM

09:35-10:10 — **Title: Optimizing Transport of Therapeutic Nanomedicines Across the Blood-Brain Barrier**
Silvia Muro, ICREA & University of Maryland, USA

10:10-10:45 — **Title: Personality traits and behavioural disturbances in dementia: Is there a link?**
Fiammetta Monacelli, DIMI, University of Genoa, Italy

Group Photo

Coffee Break 10:45 -11:00 @ Terrace

Session Chairs:

Rodolphe HAJJ, Pharnext Sa, France
Jacques Touchon, Montpellier School of Medecine INSERM U1061, France

11:00-11:20 — **Title: Impact of Hospital Design on Acutely Unwell Patients with Dementia**
Inderpal Singh, Aneurin Bevan University Health Board, UK

11:20-11:40 — **Title: Prescribing Virtual Reality (VRx): A novel therapy for people living with Dementia/ Cognitive Impairment - Preliminary results from a multi-site study**
Lora Appel, York University, Faculty of Health, Toronto, Canada

11:40-12:10 — **Title: Dual Control of Glutathione Regulation in Neuroprotection**
Chisato Kinoshita, Teikyo University School of Medicine, Japan

12:10-12:30 — **Title: Neurodegeneration study from a population of heroin dependent patients under methadone maintenance therapy**
Yu-Li Liu, National Health Research Institutes, Taiwan

2 Tuesday

12:30-12:50 — **Title: ADFlag, a diagnostic blood test for pre-dementia stages of Alzheimer's disease**
Beatice Blanc, ICDD, France

12:50-13:10 — **Title: Virtual Gene Panel For Whole Exome Sequencing Studies On Neurodegenerative Diseases**
Eva Bagyinszky, Gachon University, South Korea

Lunch Break 13:10 -14:00 @ Aeropuerto Meeting Room

Poster Presentations (13:50-14:40)

Sessions:

Neuropsychology & Neurophysiology

Session Chairs:

Laura Warren, University of Toronto, Canada
Weidong Le, Dalian Medical University, China

14:40-15:00 — **Title: Tau Protein in the Retina**
Umur Kayabasi, Bahcesehir University, Istanbul –TR, Turkey

15:00-15:20 — **Title: Electrophysiology as a Biomarker of Memory Impairment in Dementia**
Juicheng Chen, China Medical University Hospital, Taiwan

15:20-15:40 — **Title: Changes In Chemokines And Its Receptors In A Mouse Model Of Alzheimer's Disease**
Soraya Vallés Marti, Universidad de Valencia, Spain

15:40-16:00 — **Title: Urea-induced Unfolding Dynamics of RNA recognition motifs (RRMs) of TDP-43 Involve in Amyotrophic Lateral Sclerosis**
Amresh Prakash, Jawaharlal Nehru University, India

Coffee Break 16:00 -16:15 @ Picasso

16:15-16:35 — **Title: Chronic hypoxia/sleep disturbance and Alzheimer's disease**
Weidong Le, Dalian Medical University, China

16:35-16:55 — **Title: Harnessing Mass Spectra Data with KNN Principle; Alzheimer's Disease Diagnoses**
Oriehi Edisemi Destiny Anyaiwe, Lawrence Technological University, USA

Panel Discussions

Day-3 (18-07-2018) - Networking

Poster Presentations Day 2 (13:50-14:40)

ISADR201 —— **Title: Preoperative Dementia Screening and Postoperative Delirium in Older Surgical Patients**
Lucy Andrews, At Your Service Nursing and Home Care, USA

ISADR202 —— **Title: A screening tool for evaluating the semantic deterioration in Alzheimer's disease: The Mini SKQ (Semantic Knowledge Questionnaire)**
Laurent Lefebvre, University of Mons, Belgium

ISADR203 —— **Title: The rapid increase in violence by aged persons and its relationship with dementia**
Yoichiro Matsubara, Juntendo Tokyo Koto Geriatric Medical Centre, Japan

ISADR204 —— **Title: Group cognitive behavior therapy program for family caregivers of people with dementia: A single arm pilot study**
Ryo Shikimoto, Keio University, Japan

ISADR205 —— **Title: A probable case of frontotemporal lobar degeneration associated with atypical multiple system atrophy**
Mika Konishi, Keio University, Japan

ISADR206 —— **Title: Traffic-related air pollution and risk of dementia: A nationwide case-control study in Taiwan**
Pei-Chen Lee, National Taipei University of Nursing and Health Sciences, Taiwan

ISADR207 —— **Title: Early onset Alzheimer's disease patient with Amyloid Precursor Protein (V669L) mutation**
AhRa Cho, St Paul's hospital, Catholic University of Korea, South Korea

Panel Discussions

Thanks giving & Closing Ceremony

Innovinc
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Day-1
Keynote Sessions

2ND INNOVATIONS AND STATE OF THE ART IN DEMENTIA RESEARCH

Jul 16 - 18, 2018 Valencia, Spain

Hans-Ulrich Demuth

Fraunhofer Institute for Cell Therapy and Immunology, Dept. Drug Discovery and Target Validation, Germany

The Role of Posttranslational Modifications of Amyloid-β for Neurotoxicity and Resulting Therapeutic Opportunities

Alzheimer's disease (AD) and Parkinson disease (PD) are the two most common age-related neurodegenerative diseases. Both disorders characterized by misfolded proteins which form insoluble deposits in human brain. Since their discovery they were believed the reason for the progression of the disorders. In the last 20 years this view has changed. First there is increasing evidence that soluble oligomeric forms of the later deposited peptides, Abeta, Tau and alpha-Synuclein exhibit there neurotoxicity before they form fibrils and deposits.

Second many posttranslational modifications of these peptides have shown to be faster aggregating into oligomeric forms serving as seeds for aggregation of unmodified peptides. Accordingly, therapeutic approaches have been derived to reduce their neurotoxic capacity. We have developed inhibitors of Glutaminyl Cyclase to prevent the N-terminal pGlu-formation of Abeta molecules and therefore reducing their oligomeric and seeding capacity. This project has reached clinical phase 2.

Similar the reduction of already existing pGlu-Abeta molecules and spontaneously formed isoAspartate containing modified Abeta peptides using monoclonal antibodies have reached preclinical stage and demonstrated proof of concept in different mouse models.

Finally, we have recently demonstrated that Abeta molecules are able to cross-seed and accelerate the aggregation of alpha-Synuclein, opening another therapeutic avenue to treat Parkinson's disease.

Biography

Prof. Demuth has completed his PhD at the age of 28 years from Martin-Luther-University Halle/S. and did postdoctoral studies at University of Kansas and the University of Uppsala. He is one director of the Fraunhofer Institute of Cell Therapy and Immunology, a German non-profit translational research organization and heading two departments in Halle and in Potsdam, respectively. He has published more than 247 papers in reputed journals and co-authored more than 100 patents. He has been serving as an editorial board member of The Journal of Alzheimer's Disease.

2ND INNOVATIONS AND STATE OF THE ART IN DEMENTIA RESEARCH

Jul 16 - 18, 2018 Valencia, Spain

Daniel L. Farkas

Univ. of Southern California, Los Angeles CA The Brain Window, Inc., Sherman Oaks CA, USA

Multimode Optical Molecular Imaging for Early Neurodegeneration Detection

In order to see the bench-to-bedside dream of *translational* research become a reality, we need biophotonic approaches that, while technologically sophisticated, allow deployment into a clinical setting. Our focus area is where light and patient meet, and improvements that yield better outcomes, by identifying and addressing the obstacles preventing the timely clinical adoption of laboratory-based advances, not the least of which is the difficulty of detecting, characterizing and monitoring very small entities (molecules, cells) *within* the human body, especially quantitatively, dynamically, and preferably without contrast agents. *How and where we look* becomes critically important, especially if one targets (as one should) early diagnosis; for this, new tools and strategies are needed, with likely new outcomes. We proposed and implemented a multimode approach to biomedical optical imaging at all levels, featuring hyperspectral imaging, and optimized for earlier, more quantitative and reproducible detection of abnormalities and a tighter spatio-temporal coupling between such diagnosis and intervention. Addressing major areas of unmet need in the clinical realm with these new approaches could yield important improvements in disease management. Our work on neuroimaging (specifically highlighting very early detection of Alzheimer's Disease) will be described, with emphasis on the new technologies needed. We designed a multimode optical imaging confocal scanning laser ophthalmoscope, with some (needed) performance advantages over current commercial offerings, in all of the following: spatial resolution, imaging depth, imaging angle in the retina (and thus spatial coverage), sensitivity and specificity. It is aimed at non-invasive quantitative imaging of amyloid plaques (via both their autofluorescence and scattering), and of their relationships with important structures in the eye, such as blood vessels. Thoughts about better ways for academia, the clinical and the corporate world to work together for innovative biophotonic solutions and their use for addressing major disease will be briefly outlined.

Biography

Daniel L. Farkas, PhD, a former Fulbright scholar, directed a National Science & Technology Center at Carnegie Mellon Univ. that won the Smithsonian Award for Science. He was Professor of Bioengineering at U. of Pittsburgh, and Vice-chairman for Research and Professor of Surgery at Cedars-Sinai Medical Center. His scientific interests center on investigating the living state with light, for uses in biology, bioengineering, medicine and surgery, and yielded 200+ articles, 30 books edited and $80MM in academic funding. He chaired 32 international conferences, was on 11 editorial boards, and his work was recognized with prestigious awards. He (co)founded 11 startups, and is currently chairman of three of these, focusing on their development.

Day-1
Scientific Sessions

Tau-specific D-enantiomeric peptides for therapeutic applications in Alzheimer's disease

Susanne Aileen Funke

Institut fuer Bioanaytik, Hochschule fuer Angewandte Wissenschaften, Coburg, Germany

A variety of neurodegenerative disorders, including Alzheimer's disease, are associated with neurofibrillary tangles composed of the tau protein, as well as toxic tau oligomers, which can spread from cell to cell by a prion-like mechanism. Inhibitors of pathological tau aggregation might be useful for the development of therapeutics. Employing mirror-image phage display with a large peptide library (> 1 billion different peptides), we have identified tau-fibril binding peptides consisting of D-enantiomeric amino acids. D-enantiomeric peptides are extremely protease stable and not or less immunogenic than L-peptides, and the suitability of D-peptides for in vivo applications have already been demonstrated. Here, we report on D-enantiomeric peptides, which bind to aggregating tau variants, as well as to full length tau fibrils, and modulate the aggregation thereof. These peptides might be an interesting starting point for therapy development.

Biography

Dr. Susanne Aileen Funke is vice president for research and professor for molecular biology at the Coburg University of Applied Sciences and Arts. Before, she was group leader of the Alzheimer's research team of the Institute of Structural Biology and Biophysics of the Research Centre Jülich. She majored in Biology in Bochum, Germany and received a PhD in Biology at the University of Düsseldorf, Germany, after performing studies in Groningen, the Netherlands, and Marseille, France. She performed postdoctoral studies at the Institute for Physical Biology, Heinrich Heine University Düsseldorf, Germany.

Cmax-based synergistic therapeutic effect on cognitive disability in mild Alzheimer's disease after 36 weeks treatment with baclofen and acamprosate

Jacques Touchon, MD PhD[1], Jean-Marc Orgogozo, MD PhD[6], Pierre-Jean Ousset, MD[2], Florence Pasquir, MD PhD[3], Claude Guériot, MD[4], Philippe Robert, MD PhD[5], Sophie Auriacombe, MD[6], Jacques Hugon, MD, PhD[7], Peter Schmitt, PhD[8], Rodolphe Hajj, PhD[8], René Goedkoop, MD[8] and Daniel Cohen, MD PhD[8]

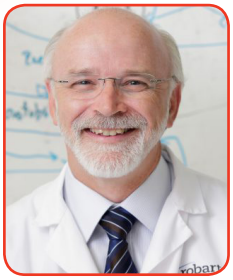
[1]Memory Research Resource Center for Alzheimer's disease, University Hospital Montpellier, France
[2]Alzheimer's Disease Clinical Research Centre, Gérontopôle, Toulouse University Hospital, France
[3]Memory Clinic, University Hospital Lille, France
[4]Memory Research Resource Center for Alzheimer's disease, University Hospital La Timone, Marseille, France
[5]Memory Center CHU -EA CobTeK, University of Nice Sophia Antipolis, Nice, France
[6]Memory Research Resource Center for Alzheimer's disease, University Hospital Pellegrin, Bordeaux, France
[7]Memory Clinical Center CMRR Paris Nord Ile-de-France, Saint Louis-Lariboisiere, Fernand Widal Hospital AP-HP, Paris, France
[8]Pharnext SA, Issy-les-Moulineaux, France

A fixed low-dose combination of baclofen and acamprosate (PXT864), deduced from a network pharmacology-based approach, is predicted to act by synergistically restoring inhibitory and excitatory imbalances present in Alzheimer's disease (AD). PXT864 restored cognitive ability in amyloid-ß intoxicated animals and prevented scopolamine-induced amnesia in rodents and humans (Chumakov 2015:9;78). A multicentre, 36-week single-blind, explorative study of PXT864 in anti-dementia treatment-naïve patients with mild AD was designed to assess safety and to evaluate efficacy. AD patients, aged over 60 years of either sex, with progressive cognitive decline (> 6 months), a MMSE score of 20-26, and without major or severe depressive disease were eligible for the 36-week study. Forty-five patients were evenly assigned to one of 3 doses of PXT864. PXT864 was administered orally (2x/day) and concomitant donepezil (5 mg/day) was allowed from week 24 onward. The efficacy of PXT864 alone was assessed through cognitive and behavioural tests for the per protocol dataset (n=32) by dose and compared to historical placebo-treated patients with mild AD (Thomas et al., 2016;12:598). The exposure to both drugs (Cmax) was measured at each visit evidencing various Cmax groups used to assess the synergy.On a composite score of 9 clinical endpoints, a synergistic profile using the various Cmax groups at 36 weeks was identified. From the higher Cmax group, an improvement on ADAS-Cog11 (1.16 point increase) was observed, whereas by dose, no improvement was observed. The mean change from baseline ADAS-Cog11 was significantly improved for D2 and D3 PXT864 alone vs historical placebo at W36 ($p<0.002$ and $p<0.014$, respectively) and improved

for the higher Cmax group vs D3 ($p<0.052$). PXT864 was safe and well tolerated and its proof-of-action in stabilising and even improving cognitive ability of patients with mild AD. Cmax-based approach could become a key methodology for the development of drug combinations.

Biography

Jacques Touchon, MD, PhD is a member of the neurology and brain aging INSERM UNIT 1061 in Montpellier, France he is the Editor in Chief of the Journal of Prevention of Alzheimer's disease (JPAD); co-organizer and founding member of the organizing committee of the Clinical Trials on Alzheimer's Disease (CtaD) conference. Jacques Touchon obtained his MD in 1979 at the Medical School of Montpellier, France, and his degree in neurology in 1992. Formerly, Jacques Touchon was the Chief of the Neurology Department of the Montpellier University Hospital (2004-2014), Dean of the Montpellier Medical School (2000-2010), Professor of Neurology at the Montpellier Medical School (1990-2014), Director of the CNRMAJ: National Referent Center for Young Adults with Alzheimer's Disease (2004-2014), Director of the Center for Memory Resources and Research (CMRR) for the Languedoc-Roussillon region (2004-2014). His areas of interest are Alzheimer's Disease, affections of the central nervous system, aging and neurodegenerative diseases. He was awarded in 1999 the academic palms for excellence in Alzheimer Disease Research, in 2000 the PINEL prize and in 2007 he was made chevalier de la légion d'honneur.



Pathogenic tau protein phosphorylation in ALS, CTE and ALS/CTE: A unifying mechanism

Michael J Strong, MD and Alexander J Moszczynski, PhD

Robarts Research Institute, Schulich School of Medicine & Dentistry, Western University, London, Ontario, Canada

Amyotrophic lateral sclerosis (ALS) is associated with frontotemporal dysfunction in 50 – 60% of cases, including frontotemporal dementia (ALS-FTD) and more subtle cognitive impairment (ALSci). In both, prominent frontotemporal lobar degeneration with DNA/RNA binding protein TDP-43 inclusion formation in addition to the presence of pathological neuronal and glial tau deposition in temporal and mesial frontal structures. Chronic traumatic encephalopathy (CTE) is an uncommon dementia marked by severe behavioural and frontotemporal dysfunction and which affects a subset of athletes who have had a traumatic brain injury. There is clinical or neuropathological evidence of a concomitant ALS (CTE-ALS) in approximately 8%. In each of these disorders (ALSci, CTE and CTE-ALS) tau is present as neuronal and glial inclusions, and when purified is observed in both soluble and insoluble fractions as both the 3R and 4R tau isoforms, is phosphatase resistant, and is pathologically phosphorylated at Thr175 (pThr^{175}tau). In vitro, human tau pseudophosphorylated at Thr^{175} (Thr^{175} Asp tau) forms pathological fibrils, the formation of which is driven by the unprimed phosphorylation by activated GSK-3b of Thr^{231} tau (pThr^{231}tau). In vivo, one year following rAAV9 somatic gene transfer with stereotactic inoculations into Sprague Dawley rat hippocampus, Thr^{175}-Asp tau immunoreactive glial and neuronal tau pathological inclusions are formed, largely within CA2 region. This pathology is associated with upregulation of Caspase-3 cleavage and pThr^{231}tau. This pathway of pThr^{175}tau/pGSK3b/pThr^{175}tau and oligomeric tau formation that underpins the pathogenic tau deposition has recently been observed across a wide range of tauopathies, including CTE and CTE-ALS. Others have shown that pathologically phosphorylated tau in CTE CTE-ALS is in an open hairpin structure exposing the N-terminus and C-terminus domains, thus both exposing the phosphatase activating domain (PAD) and promoting fibrillization. In conclusion, pathological phosphorylation of tau at Thr^{175} appears to be a common mechanism underlying a broad range of tauopathies.

Biography

Michael Strong completed his MD at Queen's University in 1982, Neurology fellowship training in 1987 at Western University, and a postdoctoral fellowship at the National Institutes of Health in 1990. He has been a clinician scientist at the Robarts Research Institute and a professor in the Department of Clinical Neurological Sciences at Western University since. He is currently a Distinguished University Professor and the Dean of the Schulich School of Medicine & Dentistry at Western University. He has published more than 180 peer-reviewed manuscripts, edited or co-edited 4 texts, and given more than 160 lectures on ALS.`

Asymmetry of hippocampus and amygdala defect in Subjective cognitive decline among the community dwelling Chinese

Ling Yue

Shanghai Mental Health Center, Shanghai Jiaotong University School of Medicine, Shanghai, China

Subjective cognitive decline (SCD) may be the first clinical sign of Alzheimer's disease (AD). SCD individuals with normal cognition may already have significant medial temporal lobe atrophy. However, few studies have been devoted to exploring the alteration of left-right asymmetry with hippocampus and amygdala in SCD. The aim of this study was to compare SCD individuals with amnestic mild cognitive impairment (MCI) patients and the normal population for volume and asymmetry of hippocampus, amygdala and temporal horn, and to assess their relationship with cognitive function in elderly population living in the community of China. 111 SCD, 30 MCI, and 67 health controls underwent a standard T1-weighted MRI and were compared with volume of hippocampus and amygdala. Moreover, we also evaluated the pattern and extent of asymmetry in hippocampus and amygdala of these samples. Then we investigated the relationship between the altered brain regions and cognitive function. Between the three groups, SCD had more depression symptom ($p<0.001$) and more percentage of heart disease (16.4% vs 35.1%, $p=0.007$) than controls. In terms of brain data, significant differences were found in the volume and asymmetry of both hippocampus and amygdala among three groups ($P<0.05$). In logistic analysis controlled for age, gender, educational level, depressive symptoms, anxiety symptom, somatic disease and lifestyle of smoke, both SCD and MCI individuals showed significant decreased right hippocampal and amygdala volumes than controls. For asymmetry pattern, a ladder-shaped difference of left-larger-than-right asymmetry was found in amygdala with MCI>SCD>HC, and an opposite asymmetry of left-less-than-right pattern was found with HC>SCD>MCI in hippocampus. Furthermore, correlation was found between the volume of right hippocampus and right amygdala with MMSE and MoCA in SCD group. Our result supported that SCD individuals are biologically distinguishable from health controls, may related to cognitive impairment which need further longitudinal investigation. Moreover, different extents of asymmetry in hippocampus and amygdala may be a potential dividing factor to differentiate clinical diagnosis.

Biography

Ling Yue is an attending doctor of geriatric psychiatry with more than 12 years experience in Shanghai Mental Health Center. She received her B.S and M.D. from Shanghai jiaotong University School of Medicine, and she is also a PhD candidate at SJTU now. Recently, she had a visting scholar experience at Universtiy College London for 6 months in 2017. She has published more than 10 papers in reputed journals.

Comparing fragility fracture burden in a high risk outpatient Movement Disorder service and a General Practice: Bridging the gap between research and clinical practice in osteoporosis using quality improvement initiatives.

Inderpal Singh, Chris Edwards, Rachel Fletcher, Linda Scanlon, Mandy Tyler, Anser Anwar, Aman Rasuly, AH Farooq, S Majeed, Nitu Singh, A Waheed and Shridhar Aithal

Aneurin Bevan University Health Board, UK

Background: Fragility fractures are the hallmark of osteoporosis and are particularly common in the vertebra, wrist, hip and pelvis. The incidence of osteoporotic fracture increases exponentially with age and after 50 years, the lifetime probability of sustaining an osteoporotic fracture is one in every 2 women and one in 5 men. The risk of falls is higher in people with Parkinsonism (PwP) compared to those without Parkinsonism, and leads to adverse outcomes including fragility fractures. Osteoporosis is under recognised in the General Practice, and the prevalence of fragility fractures in not well studied. The primary aim of this study was to compare the prevalence of fragility fractures in a high risk outpatient service for PwP and all patients above 50 years of age according to Quality and Outcomes Framework (QOF) of the General Medical Services (GMS) contract in a General Practice. The secondary aim was to develop and apply quality improvement methodology to bridge the gaps between research and clinical practice in osteoporosis.

Method/Description: This was a retrospective observational study. Routinely captured information regarding demographics and fragility fractures was extracted from the clinical workstation, clinic letters, and clinical coding for all PwP attending Movement Disorder (MD) clinic. Data was also collected for all known patients above age 50 years with diagnosed osteoporosis, known fragility fracture or prescribed osteoporosis treatment according to a General Practice database for comparison. A quality improvement (QI) methodology based on the model of improvement, Plan-Do-Study-Act (PDSA) cycles were used to develop strategies to test, improve osteoporosis care and spread the innovative learning from MD clinic to a General Practice.

Result/Outcome: There is a high prevalence of fragility fractures 22.6% (68/300) in patients attending MD clinic, and only 40% (27/68) of PwP received evidence based medical treatment for the underlying osteoporosis. Following the quality initiatives, a monthly multidisciplinary meeting for all PwP to assess falls and osteoporosis, more than 90% of PwP had underlying osteoporosis treated according to guidance: a 56% increase. In this study, we also found that prevalence of fragility fracture in the patients studied according to Quality and Outcomes Framework of the General Medical Services contract in a General Practice was 37%, which is 1.8 % (n=116/6300) of the whole practice population. One-third (34.5%, n=40/116) patients were not treated to guidance. Learnings from MD clinic were spread to community and as a part of quality initiative 24 patients were commenced on oral treatment and 6 were considered for Denosumab treatment, suggesting an overall improvement by 75% for those who were not on evidence-based treatment. Another

7.3% (23/314) patients in the whole practice cohort were prescribed osteoporosis drugs inappropriately, who were either stopped or considered for drug holiday as per guidance.

Conclusion: Prevalence of fragility fracture varies based on our services but one-third patients with osteoporosis may not be treated to guidance. Regular monitoring of osteoporosis burden in high risk outpatient services and general practice data is warranted. Implementing quality initiatives could streamline the process, maximizing osteoporosis understanding and an enhanced autonomous osteoporosis care by the hospital specialists and general practice doctors. Similar interventions are needed for our community services to improve osteoporosis care, prevent a fragility fracture, particularly a hip fracture. We propose virtual bone health clinics as an example to deliver better integrated service and promote culture of innovation

Biography

Dr Singh is a consultant geriatrician. His qualifications include MBBS (1997); MD (2002); MRCP UK (2006); MSc-Ageing, Health and Disease (2011) and FRCP (2015). He is a Training Programme Director (Wales Deanery) and also a Clinical Director for a hospital site. He received "Excellence in Clinical Leadership award" in the Health Board Staff Recognition Award (2014). Dr Singh has led many research projects and has published several scientific papers in the field of education, inpatient falls and dementia and was awarded "Research for patient benefit" award (2015). He led a quality improvement project on inpatient falls and received NHS Wales award (2017).

A potential tri-therapy for Alzheimer's disease

Rodolphe Hajj*, Anthony Brureau, Nathalie Cholet, Julie Foucquier and Daniel Cohen

Pharnext, 11 rue des Peupliers, 92130 Issy-Les-Moulineaux, France

Cognitive symptoms in Alzheimer's disease (AD) are currently managed by moderately acting standards of care which efficacy decreases fast over time and use is often accompanied by side effects. We previously showed that a combination of acamprosate and baclofen (PXT864) synergistically prevented cognitive impairments in AD mice. In this study, we investigated whether PXT864 could i) protect cognitive functions by synergizing with sub-therapeutic doses of donepezil (DNPz) to limit the occurrence of adverse events, or ii) rescue the efficacy of DNPz that is lost over time under therapeutic doses.

We used the Aβ25-35 intracerebroventricular (ICV) injection mouse model that mimics AD features. We tested first PXT864 in combination with sub-therapeutic doses of DNPz, both administered to mice before Aβ25-35 injection (prevention protocol). Second, we modelized the loss of activity of DNPz treatment over time when initiated after Aβ25-35 ICV injection (interventional protocol). Third, once DNPz effect was lost, we added PXT864 to DNPz and assessed the value of such tri-therapy. Efficacy was assessed by Y-maze and stepthrough passive avoidance behavioral cognitive tests.
When mice were treated before Aβ25-35 ICV injection, we found that combining.

PXT864 with sub-therapeutic doses of DNPz yielded synergistic protection against Aβ-induced cognitive deficits. Then we showed in AD mice comparable efficacy kinetics of DNPz to the one observed in AD patients, which is a cognitive decline over time at a later stage of the disease when treatment was started after Aβ25-35 ICV injection. Interestingly, adding PXT864 at that stage fully restored lost cognition in these animals that became all irresponsive to DNPz. These data highlight the importance of combinational strategies and suggest that PXT864 could be used either as a first line treatment or as a second line treatment with a safe sub-therapeutic or even a full therapeutic dose of DNPz in Alzheimer's patients.

Biography

Rodolphe Hajj is the Chief Pharmacology Officer of Pharnext. He has completed his PhD from the University of Reims. He has more than 15 years' experience in research & development in various areas, such as stem cells, respiratory research, cystic fibrosis, cancer and neurology in academia and industry. He oversaw the Cancer Stem Cell project at Sanofi, then led at Servier the High Content Cellular imaging platform for different disease areas.

A quantitative assay to measure human cerebrospinal fluid induced membrane permeabilization

Suman De

Marie curie Postdoctoral Fellow, Department of Chemistry, University of Cambridge, Cambridge, UK

The study of protein aggregates and how they damage neuronal cells is important in order to understand the initiation and progression of several neurodegenerative diseases - including Alzheimer's disease (AD). In the case of AD, conversion of monomeric amyloid beta (Aβ) into amyloid fibrils involves the formation of small soluble aggregates, namely oligomer, which are believed to be the cause of the disruption and dysfunction of neuronal networks that lead to the subsequent cognitive decline that has been associated with AD pathology. However due to short lifetime, low abundance and high morphological heterogeneity of these pathological amyloid aggregates, information about their structure and their role in different pathological events is limited. To quantify and characterize the toxic protein aggregates associated with neurodegenerative diseases, we have developed an ultra senstive assay to quantity the aggregate induced membrane permeabilization by measuring $Ca2^{+}$ influx into hundreds of nanosized lipid vesicles. We have demonstrated that CSF of humans can permeabilize membranes and induce $Ca2^{+}$ influx. We also have shown that an extracellular chaperone clusterin, a nanobody specific to the amyloid-β peptide (Aβ) and Bapineuzumab, a humanised monoclonal antibody raised against Aβ, could all reduce the $Ca2^{+}$ influx caused by synthetic Aβ oligomers but are less effective in CSF. The method can be applied directly to other proteins such as β-synuclein, tau etc. which are linked to neurodegenerative disease and also to other complex biofluids. Our in vitro assays provide a high-throughput platform to determine if a given antibody is able to reduce the membrane permeabilization and consequent $Ca2^{+}$ influx caused by protein aggregate as well as CSF, and the concentration that is required for it to be effective.

Biography

Suman De has completed his PhD from Indian Institute of Technology and did his first postdoctoral work from University of Tuebingen, Germany. He then moved to University of Cambridge and subsequently awarded 'Marie Curie Individual Fellow'. He is currently developing ultrasensitive biophysical method to determine the composition, structure and size of the disease relevant preotein aggregate present in human brain tissue and bio-fluids.

Algoplus® scale in older patients with dementia: A reliable pain assessment tool

Fiammetta Monacelli

Geriatric Clinic, DIMI, Department of Internal Medicine and Medical Specialties, University of Genoa, Viale Benedetto Xv, 6 16132, Genoa, Italy

Pain is still a neglected clinical issue in elderly people with dementia and/or communicative disorders, with an unacceptable higher rate of under diagnosis and under treatment. Cognitive deficit and emotional and psychological disturbances entangle pain symptoms, affecting patient self-report. So far, observational pain tools do not have fully adequate clinimetric properties and quality requirements for easy-to-use daily rating. Older patients with dementia represent a clinical challenge. The assessment of pain is important for improving clinical outcomes, such as functional status, frailty trajectories, comorbidity, and quality of life. The PAINAID scale appears to be the most accurate pain tool in people with dementia along with the Algoplus® scale, a recently developed tool to rapidly assess acute pain in hospitals settings. The present study aimed to assess the clinimetric properties of the Algoplus®, as compared to PAINAID, for detecting acute pain in a real-world cohort of hospitalized older patients with dementia. Namely, ninety-six patients admitted to the transitional care ward of the Policlinico San martino Hospital from January 2016 to June 2016 were consecutively enrolled in this study with a mean age of 84.80 ± 6 years. The Algoplus® score was correlated with PAINAD ($p<0.001$). Algoplus also showed adequate discriminant validity for depression ($p<0.001$) and behavioural disturbances ($p<0.044$). The reliability of Algoplus® scale was also meaningful after 4 hours and 24 hours (t4: SD 0.56,301 95% CI –0.28 to –0.05, IQR 0, range –2 to 1) (t24: SD 0.68,303 95% CI –0.23 to 0.04, IQR 0). The present study moves a step forwards in the development of sensitive tools for acute pain detection in non communicating patients. The present study must be confirmend using other validated version of Algoplus® translated in other languages and applied to wider populations samples.

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Biography

Fiammetta Monacelli has completed her PhD in 2008 and her 2 level Master in Geriatrics (EAMA) in 2009. She is chief medical doctor at the memory clinic at the Policlinico San Martin Hospital Geriatric Clinic Genoa, Italy. She has published more than 45 papers in reputed journals and has been serving as an associate editor for the Journal of Alzheimer's disease (JAD).

Dementia among Indigenous populations in Ontario

Laura Warren

University of Toronto, USA

Background: There is evidence to suggest the burden of dementia may be greater in Indigenous populations than it is in non-Indigenous populations. The objective of this study is to characterize the epidemiology of dementia diagnoses and care in off-reserve, community-dwelling, Ontario Indigenous populations using data from the Canadian Community Health Survey (CCHS) and provincial health insurance claims datasets housed at the Institute of Clinical and Evaluative Sciences (ICES).

Methods: We have established a Community Advisory Board (CAB) comprised of five members from a variety of research backgrounds, Indigenous communities and lived experiences to provide leadership, support and direction to all stages of our research. Indigenous and non-Indigenous populations will be identified using the CCHS. We will use a definition of dementia (including Alzheimer's disease) developed and previously validated by ICES. All analyses will be conducted using SAS 9.3. Differences in prevalence estimates and patterns of care and service usage for Indigenous and non-Indigenous participants will be compared using Chi-square tests for frequencies and t-tests for means. Risk factors for dementia will be identified using PROC GENMOD to build a multivariate logistic model for both Indigenous and non-Indigenous participants.

Results: Participant characteristics will be reported as frequencies and proportions for Indigenous and non-Indigenous respondents by sex. Age-specific dementia prevalence estimates will also be reported for each group. Odds ratios will be reported from the final multivariate model for Indigenous and non-Indigenous participants. Differences in frequencies of drug prescirption types (e.g. Donepezil, Galantamine, Memantine, Rivastigmine, Tacrine), hospital admissions, specialist care, home care, and physician visits will be will be identified using Chi-square tests between Indigenous and non-Indigenous participants.

Conclusions: This study will be the first of its kind in Ontario. By characterizing the epidemiology of dementia cases and care in community-dwelling, off-reserve, Indigenous populations we hope to identify risk factors, identify patterns of care for dementia health services, and increase awareness of dementia among Indigenous populations in Ontario.

Biography

Laura Warren began her doctoral studies in epidemiology at the University of Toronto in September 2012. Her doctoral research focus is on aging among Indigenous populations in Canada. Laura completed her honours Bachelor of Science degree at the University of Guelph with a major in biology and a minor in statistics. Her MSc degree in epidemiology was also completed at the University of Guelph. Her master's thesis focused on cattle transportation. She also holds a MA degree in statistics from York University. Laura has worked in pharmaceutical research and HIV research at Women's College Hospital and at the Ontario HIV Treatment Network.

Fixed-dose combination of donepezil hydrochloride and memantine hydrochloride for treatment of moderate to severe Alzheimer's disease

Stevin Zung

Head of Medical Affairs & Scientific Information, Aché Laboratórios, Brazil

Background: Alzheimer's disease (AD) accounts for approximately 75% of total dementia cases worldwide and the total number of people with dementia is projected to be 65.7 million in 2030 and 115.4 million in 2050. As the world's population is rapidly aging, AD will clearly pose a major health problem in the near future. Furthermore, people with dementia often have comorbid health conditions and are polymedicated patients. According to these facts and based on the need to facilitate Alzheimer's patients and their caregivers' lives, Aché Laboratórios Farmacêuticos S.A., a Brazilian Pharmaceutical Company, developed a fixed-dose combination (FDC) of donepezil and memantine (10 mg + 5 mg; 10 mg+ 10 mg; 10 mg + 15 mg e 10 mg + 20 mg) indicated for the treatment of moderate to severe stages of AD according to the latest American and Brazilian guidelines for AD treatment.

Methods: The FDC has been developed considering physical chemical parameters, including assay content, content uniformity and dissolution profile, as well as the relative bioavailability study of pharmacokinetic (PK) evaluation of memantine associated with donepezil to assess PK behaviour and PK interaction of the referred drugs. The study was conducted to compare bioavailability of FDC of memantine 20 mg and donepezil 10 mg coated tablet (Aché S.A.'s test formulation) to Ebix® 10 mg coated tablet (Lundbeck Brasil Ltda., reference formulation) and Eranz® 10 mg coated tablet (Wyeth Pharmaceutical Industry Ltd., reference formulation).

Results: Content, uniformity and dissolution results showed that FDC tablets meet all necessary standards and good manufacturing quality control practices. Regarding the relative bioavailability study, the evaluated parameters were within the range 80-125% proposed by FDA and ANVISA (National Agency of Sanitary Surveillance in Brazil), and it was concluded that the 20 mg tablet of memantine associated to 10 mg of donepezil was bioequivalent to the concomitant administration of 2 tablets of Ebix® 10 mg and 1 tablet of Eranz® 10 mg. Thus, the test result indicated that the FDC presented the same PK profile of isolated drugs. The results of the mentioned tests and study are attached.

Conclusions: The concomitant use of donepezil and memantine for moderate to severe Alzheimer´s Disease treatment is well stablished in the latest American and Brazilian guidelines for DA treatment and in clinical practice. It has been seen that this association does not interfere with both drugs´ efficacy and tolerability. As established in Guidelines, concomitant use of donepezil and memantine in patients with moderate to severe AD is more effective than the use of donepezil hydrochloride or memantine hydrochloride as monotherapy. A FDC facilitates dosing of these drugs and contributes to increased adherence to treatment, since it considers the elimination half-life of the components and permits a single daily dose. In conclusion, FDC of donepezil and memantine meets the recommendations of main guidelines of the disease in moderate to severe stages and aims to benefit patients and caregivers with its unique formulation.

Physical Chemical Tests	Donepezil Assay Content	Memantine Assay Content	Donepezil Assay Uniformity	Memantine Assay Uniformity	Donepezil Dissolution	Memantine Dissolution
Tablets	90% - 110%	90% - 110%	max. 15	max. 15	min. 80%	min. 75%
Donila Duo 10/5	99.6%	105.2%	3.1	1.8	102.0%	100.0%
Donila Duo 10/10	97.9%	99.4%	3.4	1.9	99.0%	103.0%
Donila Duo 10/15	99.1%	96.8%	6.9	5.0	96.0%	104.0%
Donila Duo 10/20	103.7%	98.2%	10.1	6.4	96.0%	103.0%

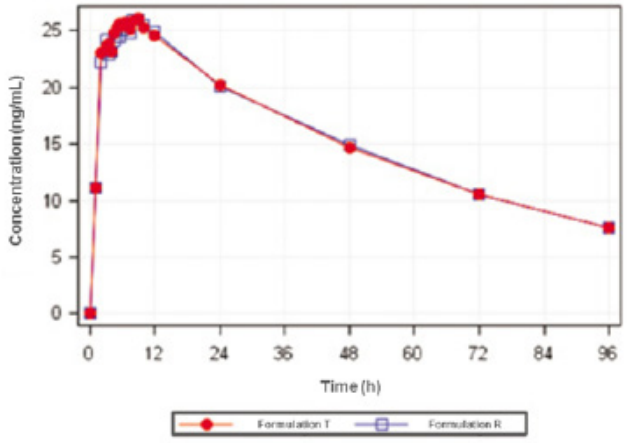

Figure 1: Mean plasma concentration versus time of memantine hydrochloride after administration of one tablet of the test formulation (memantine 20mg + donepezil 10mg) and two Ebix® 10mg tablets

A Multifunctional Biocompatible Drug Candidate Effectively Delays the Progression of Alzheimer's Disease in 5XFAD Mice

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Metal-ion-chelation was suggested to prevent zinc and copper ions-induced Amyloid beta (Aβ) aggregation and oxidative stress, both implicated in the pathophysiology of Alzheimer's disease (AD). In a quest for biocompatible metal-ion chelators potentially useful for AD therapy, we tested a series of nucleoside 5'-phosphorothioate derivatives as agents for decomposition of Cu(I)/Cu(II)/Zn(II)-Aβ-aggregates, and as inhibitors of OH radicals formation in Cu(I) or Fe(II) /H_2O_2 solution. We have identified 2-SMe-ADP(β-S), designated as SSA37A, as a most promising neuroprotectant. We evaluated SSA37A ability to decompose or inhibit the formation of $Aβ_{42}$-M(II) aggregates, and rescue primary neurons and astrocytes from $Aβ_{42}$ toxicity. Furthermore, we aimed at exploring the therapeutic effect of SSA37A on behavioral and cognitive deficits in the 5XFAD mouse model of AD. We found that SSA37A can rescue a primary culture of neurons and astrocytes from $Aβ_{42}$ toxicity and to inhibit the formation and dissolve $Aβ_{42}$-Zn(II)/Cu(II) aggregates. Furthermore, we show that SSA37A treatment at 1 mg/Kg can prevent behavioral disinhibition and ameliorate spatial working memory deficits in 5XFAD mice. Notably, the mice were treated at the age of 2 months, before the onset of AD symptoms, for duration of 2 months, while the effect was demonstrated at the age of 6 months. Our results indicate that SSA37A has the potential to delay progression of core pathological characteristics of AD in the 5XFAD mouse model.

Biography

Bilha Fischer has completed her PhD in the field of heterocyclic chemistry from Bar-Ilan University and postdoctoral studies from the NIH, Bethesda, MD, USA, in the field of medicinal chemistry (purinergic receptors and molecular modeling). She is a full Professor and the head of a medicinal chemistry laboratory at Bar-Ilan university. She has published ca. 110 papers in reputed journals in addition to 10 patents. She also serves as the vice dean of graduate school at BIU.

A study on support for older adults with moderate to severe dementia following spousal death

Akiko Watanabe*[1,2] and Sayuri Suwa[3]

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Background: Memory impairment can cause older adults with Alzheimer's disease (AD) to experience various difficulties and confusion, and the loss of a loved one is no exception. Thus, the purpose of this study was to characterise, from the perspective of professionals, the lifestyles of older adults with moderate to severe AD and the changes that occur following the loss of their spouse. This study also considered methods of providing support to older adults with AD following spousal death.

Methods: The study period was from July to December 2017. The research participants were professionals working in long-term care facilities in Japan. The subjects of analysis were older adults with moderate to severe AD whose spouses passed away within the last 5 years. Data were obtained from facility records and 60-minute semi-structured interviews using interview guides. Qualitative content analysis was conducted after the data collection.

Results: The results of the analysis for changes in the lifestyles of 4 older adults with AD before and after spousal death revealed the following. In the FAST6 case, the older adult seemed to encourage the spouse in situations that were easily understood. This subject also appeared to not recognize the spouse's passing in instances where she could not recall his death. However, in one instance where she was with her family, the subject asked about her spouse, 'Did my husband die?'

Conclusions: The results of this study indicate that it is important to provide support to older adults with moderate to severe AD before and after the death of their spouse by taking them to the hospital to visit their spouses to help them understand their situation, having the older adults attend their spouse's funerals, and explaining their situation in terms the older adults can easily understand.

Biography

Ms. WATANABE has completed her Master's degree from Graduate School of Nursing, Chiba University in 2016. She continues her research at Doctoral Program, Chiba University while teaching at Miyagi University, School of Nursing.

The effect of navigational problems and assessment location on driving test performance for people with Alzheimer's disease

Kay Russell, Professor Carolyn Unsworth, PhD[1], B.OccThy[2*], Robin Lovell, MOT[3], Associate Professor Michael Woodward[2] MD and Matthew Browne PhD[1]

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Background: An occupational therapy fitness-to-drive assessment may be required to determine if drivers in the early stages of dementia can continue to drive. Such assessments could be better tailored for clients with dementia if we had research evidence to support the location of assessment (open or local area), method (self-directed or directed) and whether repeat testing is required (opportunity to undertake a second test), or which combination of these factors is best for drivers with, and without navigational difficulties.

Objectives: To determine the effect of location of assessment (open or local area) and practice (undertaking more than one assessment) on pass or fail outcome for drivers both with, and without navigational problems.

Methods: 43 clients participated in a controlled trial in which the ordering and location of on-road driving tests have been randomised. Client driving assessment outcomes were recorded as pass, condition, or fail. Data were analysed using a generalized linear mixed effects model.

Results: The opportunity to have a second test (practice) had no effect on the probability of passing the on-road test (p=.514). 80% of drivers without navigational problems passed a local route self directed test, in comparison to 36% of drivers with navigational problems passing the same type of on road assessment, reflecting this group's difficulty with independent navigation. 63% of people without navigational problems passed an open route test, where directions are provided, compared to 45% of drivers with navigational problems passing this type of on road assessment. Drivers with navigational problems were less likely to pass the on road test than those without navigational problems (p=.032)

Conclusions: The difference in driver assessment performance is due to the characteristics of the driver, and not practice. Furthermore, whether the client undertakes a local area self directed test or an open route test (when instructions are given) is not pivotal to the outcome, but rather, whether the client has navigational problems or not. These findings will influence referral criteria, and the need to thoroughly assess navigational skills during driver assessment.

Biography

Kay is an Occupational Therapist at Austin Health and has been working as a Driver Assessor in the hospital's Memory Clinic for over 20 years. She has a keen interest in Alzheimer's disease, as well as other types of dementia, and the impact they have on driving ability. She teaches in the Driver Assessment and Rehabilitation Course at Swinburne University, and has co-authored several papers on this subject.

The challenges of post-hip fracture rehabilitation among people with cognitive impairments

Michal Elboim-Gayizon
University of Haifa, Israel

Hip fractures are the most serious outcomes of osteoporosis. The incidence increases exponentially with age. Hip fractures can have negative consequences. Elderly people with dementia are at higher risk for hip fractures. However, there is evidence that impaired cognitive status impedes the rehabilitation process and is related to higher incidence of complications, comorbidities, functional decline and mortality following hip fracture surgery, as compared to individuals matched for age, gender and type of fracture. Previous studies suggested that people with dementia are often poorly managed following hip fracture, with limited access to rehabilitation both as inpatients and in the community.

The relation between cognitive impairment and rehabilitation after hip fracture will be presented in terms of major barriers to encounters. Solutions to overcome them will be suggested. The current literature on the effectiveness of physical therapy interventions for this population and the person-centered care approach will also be discussed.

Biography

Michal Elboim-Gayizon is a lecturer and staff member at the physical therapy department of the University of Haifa (UOH). She completed her doctoral studies in physical therapy. She completed post-doctoral studies at the Biorobotics and Biomechanics Lab (BRML) at the Mechanical Engineering Faculty at the Technion-I.I.T, and at the Neuromuscular Research Laboratory, Schulthess Clinic, Zurich, Switzerland. Primary research areas include Electrical Stimulation in rehabilitation, Balance and gait capabilities of elderly individuals, Acute Orthopedic Rehabilitation and Ethics. She has a clinical experience that was acquired during her work as a senior physical therapist in an inpatient acute orthopedic and geriatric setting. She is an editor of the Outcome-measure column in the Israel Journal of Physical Therapy.

Day-2
Keynote Sessions

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2ND INNOVATIONS AND STATE OF THE ART IN DEMENTIA RESEARCH

Jul 16 - 18, 2018 Valencia, Spain

Silvia Muro
ICREA & University of Maryland, USA

Optimizing Transport of Therapeutic Nanomedicines Across the Blood-Brain Barrier

Background: Accessing the brain is key to study its function and pathology, and for diagnostic and therapeutic purposes. Yet, this remains a great challenge due to the blood-brain barrier (BBB). To overcome this, novel nanovehicles are being designed to cross this interface, without much translational success. A prime obstacle is the lack of knowledge on the "biological regulation" of these devices, as most efforts have been devoted to controling their chemical and physical properties.Research in our group focused on bridging this gap of knowledge.

Methods: We designed nanovehicles targeted to receptors of the main routes of transcytosis across endothelial barriers, i.e. clathrin-, caveolar, and cell adhesion molecule (CAM)-mediated pathways (the latter, identified in our lab). We then compared their properties and BBB transport ability in cellular and animal models, using fluorescent and radioactive tracers.

Results: Engagement of receptors of the three routes by drug nanocarriers coated with targeting antibodies resulted in vesicular transport across the endothelial lining. The CAM pathway, in contrast to clathrin and caveolar routes, was effective across a broad spectrum of carrier sizes and targeting valencies. This is reminiscent of the CAM function, which contributes to transcellular leukocyte migration. We observed this is because the CAM routes associates with a deep remodeling of the lipid composition of the endothelial plasmalemma and reorganization of the actin cytoskeleton. As a result, cargoes such as enzyme therapeutics for inherited neurodegenerative conditions were delivered in an active form in the brain after intravenous administration in mouse models. We also studied the influence exerted by carrier design parameters and those intrinsic to the physiological system on the transport outcome.

Conclusions: Improved delivery of therapeutics across the BBB in vivo illustrates the potential of nanodevices addressed to transcytosis routes as translational tools to improve CNS treatment.

Biography

Dr. Silvia Muro obtained her PhD in Sciences - Molecular Biology from Universidad Autónoma de Madrid (Spain), where she studied molecular pathology of inherited enzyme deficiencies. She then trained as a postdoctoral assistant in targeted drug delivery at the University of Pennsylvania Medical School where, thereafter, she held a Research Assistant Professor position in the Department of Pharmacology. In 2008 she joined the Department of Bioengineering and the Institute for Bioscience and Biotechnology Research at the University of Maryland (UMD), where she is a tenured Associate Professor since 2012. Since November 2017, she also holds a Research Professor position in the Catalan Institute for Research and Advanced Studies (ICREA) and the Catalan Institute for Bioengineering (IBEC) of the Barcelona Institute of Science and Technology (BIST). Dr. Muro's research focuses on ligand-mediated targeting and vesicular transport of nanomedicines into and across cells in the body, with emphasis on delivery of biological therapeutics for treatment of enzyme deficiencies affecting peripheral tissues and the central nervous systems. She has published over 80 articles and book chapters in this field, which have received recognitions by the Controlled Release Society, the American Society for Nanomedicine, the World Organization for Rare Lysosomal Disorders, and others. She received the UMD Outstanding Life Sciences Invention of the Year award in 2011 and the Junior Faculty Outstanding Engineering Research award in 2012. Dr. Muro served in the organizing committee for the International Conference on Nanotechnology and Nanomedicine in 2012, is an editor for several journals in this field, and from July 2014 she serves as a standing member of the NIH Nanotechnology (NANO) Study Section.

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2ND INNOVATIONS AND STATE OF THE ART IN DEMENTIA RESEARCH

Jul 16 - 18, 2018 Valencia, Spain

Fiammetta Monacelli

Geriatric Clinic, DIMI, Department of Internal Medicine and Medical Specialties, University of Genoa, Viale Benedetto Xv, 6 16132, Genoa, Italy

Personality traits and behavioural disturbances in dementia: Is there a link?

Accumulating evidence indicates that premorbid personality traits can predict behavioral disturbances in dementia. To date, some retrospective analyses have demonstrated that premorbid personality traits may exert a role in the onset of behavioral disturbances in dementia .Given this background, our research group conducted a cross-sectional analysis on a sample of older patients affected by dementia and followed at the Memory Clinics of IRCSS AUO San Martino Hospital Genoa(Italy) in order to investigate the eventual relationship between premorbid personality traits and BPSD in dementia.

Patients were included if they were aged 65 years or older, had a diagnosis of Alzheimer's Disease had a reliable caregiver, and BPSD. Patients were excluded whether they were clinically unstable, had concurrent pain or any change in the medication regimen. A written informed consent was obtained by the patients or their proxies. The study was approved by the local Ethical Committee.

Forty-one consecutive patients were recruited between January and June 2016. All patients received an abbreviated comprehensive geriatric assessment (e.g., MMSE, CIRS, Barthel index) and the polypharmacy was carefully collected. BPSD were assessed by the Neuropsychiatric Inventory (NPI). Patients were censored at the time of their last clinical evaluation. Personality traits were assessed by *Big Five Questionnaire-2* (BFQ-2), a 134-item questionnaire that assesses five major dimensions of personality (conscientiousness, energy/extroversion, openness, agreeableness and emotional stability) and includes 10 sub items for each main dimensions to obtain a composite score.The BFQ-2 is assessed through a caregiver interview and the Caregiver Burden Inventory (CBI) was also performed to assess caregiver's burden

The patients' clinical characteristics were the following: 28 (70%) females, mean age 85.3 years (SD: 5.3; Range: 72-95 years); mean disease duration: 4.5 years (SD: 2.2); mean MMSE score 15.6 (SD: 7.3); median ADL score: 4 (Range: 0-6); mean CIRS IS: 2.1 (SD: 0.34); mean CIRS IC: 5.1 (SD: 2); mean NPI 23.3 (SD: 12.7); CBI mean score was 31 (SD: 15.4; range: 0-62).

The results showed a significant correlation between emotional stability (both for sub items emotional control; n=41; r=-0.46, p=0.003 and impulse control n=41; r=-0.34, p=0.032) and decreased NPI (Figure 1) as well as a trend correlation between extroversion/energy total score and increased NPI (n=41; r= 0.29; p=0.074). The step wise regression analysis confirmed a significant correlation between emotional stability (emotional control sub item) and NPI (p<0.001) along with a significant trend between energy\extroversion and increased NPI (p=0.04), adjusting for age (p=0.017). Disease duration wasn't significantly associated with the outcome. The present study supported the existence of an association between higher emotional stability, as a negative affect over emotional experience, and decreased BPSD. Among the strengths of the present study, both the use of clinometric robust and detailed patients' personality traits (BFOQ2) and behavioral assessment may be reported. Conversely, the cross sectional study design and the limited sample of patients are the main limitations.

Eventually, further additional studies are requested to test the potential mechanisms underlying this association in order to include personality traits as risk factor for BPSD in dementia.

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Biography

Fiammetta Monacelli has completed her PhD in 2008 and her 2 level Master in Geriatrics (EAMA) in 2009. She is chief medical doctor at the memory clinic at the Policlinico San Martin Hospital Geriatric Clinic Genoa, Italy. She has published more than 45 papers in reputed journals and has been serving as an associate editor for the Journal of Alzheimer's disease (JAD).

Day-2
Scientific Sessions

Impact of Hospital Design on Acutely Unwell Patients with Dementia

Inderpal Singh, Chris Edwards, Rachel Fletcher, Anser Anwar, Caitlin Young, Sophie Knight and Justin Okeke

Aneurin Bevan University Health Board, UK

Introduction: Hospitalisation is hazardous for frail older people and particularly for those with dementia. Dementia friendly environments have been proposed to promote patient well-being, mobility and engagement with staff/family; however, there has been little emphasis on hospital design. Single room previously have been associated with increased risk of inpatient falls and adverse outcomes, particularly in those with dementia. However following quality initiatives, the incidence of the inpatient falls has shown sustained reduction.

Aim: The objective of this study was to profile the inpatient falls in single-rooms and compare the clinical outcomes of acutely unwell patients with dementia admitted to two different hospital environments before and after quality initiatives. The study also aim to report the trends in recorded inpatient falls related mortality over five years in single-rooms (2012–2016).

Methods: This prospective observation study was conducted for all patients admitted to single-rooms who have sustained an inpatient fall between January 2012 and December 2016. In addition, one-hundred acutely unwell patients with dementia admitted at Ysbyty Ystrad Fawr (hospital with 100% single rooms) and Royal Gwent Hospital (traditional multi-bedded wards - MBW) under the same University Health Board were observed prospectively in year 2015 and 2016 before after quality initiatives. All the DATIX incident reports which are filled for each inpatient falls were studied and the clinical information was extracted from Clinical Work station. Mortality data were also collected on all patients for up to a minimum of six months and a maximum of up to one year following the first incident of IF and also discharge from the hospital.

Results: 1704 patients had experienced 3408 incidents of falls over 5 years in single-rooms. 95% patients were admitted from their homes. Mean age of females (82.61±10.34 years) was significantly higher than males (79.36±10.14 years). Mean falls/patient=2.0±2.16, range 1-33). Mean hospital stay was 45.43±41.42 days. Mean hospital stay to first fall was 14.5±20.79 days and mean days to first fall prior to discharge was 30.8±34.33 days. There was no significant difference between the baseline characteristics of the two cohorts admitted to single rooms or MB-W as suggested by mean age, sex, functional capabilities, co-morbidity burden, polypharmacy or care needs for the acutely unwell dementia patients in 2015 or 2016. In 2015, Fifty-three IF were sustained by 16 patients

in SR compared to 23 incidents by 15 patients in MB-W. Mean IF/patient treated in SR were 3.3 (range=1-9) and this was significantly higher than those treated in MB-W (mean=1.5; range=1-3, p=0.035). In 2016, following quality initiatives, there was no significant difference in the incidence of inpatient falls (single rooms = 12, MBW = 8, p=0.175). There were no significant differences in the number of recurrent fallers (p=0.629). There was no significant difference in terms of falls-related injury, discharge to a new care home, 30-day readmission or mortality.

The results also shown a sustained reduction in the incidence of inpatient falls. There is downward trend with the incidence of hip fracture over the last two years. There is no significant different in the inpatient and 30-days mortality over the last five years. However, mortality trends appear to show a significant downward trend with six-month and one-year mortality over the last two years.

Conclusion: We have observed a significant reduction in the incidence of inpatient falls following quality initiatives initially, followed by a downward trend in the hip fracture. We have started to observe a significant reduction in the 6-month and one-year mortality in 2015-16. The single room environment appears to influence LoS but following the introduction of quality improvement initiatives to prevent inpatient falls, single-rooms do not appear to be associated with higher inpatient falls incidence. We propose more research to understand the relationship between single rooms and LoS. We propose that we must continue with every possible quality initiative to prevent 'first in-patient fall' which will surely result in sustained improved clinical outcomes.

Biography

Dr Singh is a consultant geriatrician. His qualifications include MBBS (1997); MD (2002); MRCP UK (2006); MSc-Ageing, Health and Disease (2011) and FRCP (2015). He is a Training Programme Director (Wales Deanery) and also a Clinical Director for a hospital site. He received "Excellence in Clinical Leadership award" in the Health Board Staff Recognition Award (2014). Dr Singh has led many research projects and has published several scientific papers in the field of education, inpatient falls and dementia and was awarded "Research for patient benefit" award (2015). He led a quality improvement project on inpatient falls and received NHS Wales award (2017).

Prescribing Virtual Reality (VRx): A novel therapy for people living with Dementia/ Cognitive Impairment - Preliminary results from a multi-site study

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Background: Depression and anxiety are common in people living with dementia/cognitive impairment (D/CI). Exposure to natural environments and social settings can help, but as D/CI progresses, people become increasingly confined indoors and isolated. As Virtual Reality (VR) technology becomes more accessible and affordable, there is a unique opportunity to expose people living with D/CI to simulated natural settings (green forest, calm beach). VR therapy may prove to be a more ethically desirable, less expensive means of relaxing, and engaging patients, without the negative side-effects of current approaches (e.g. psychotic medication, physical restrains).

Objectives: Determine 1) If VR is safe for people with D/CI, 2) The optimal characteristics of VR experiences for this population, and 3) If VR-therapy can decrease depression and anxiety, and increase relaxation.

Methods: Sixty-five seniors with D/CI were recruited at four sites in a non-randomized intervention pilot study. Data collection included pre/ post-intervention survey and interview, standardized observation during intervention, and cognitive scores (CPS/MoCA/MMSE). The intervention: watching 5 -15 minutes (3 -5 clips) of 360° footage from natural settings displayed on commercially available VR-headsets.

Preliminary Results: It is feasible to administer VR as therapy for people with D/CI. Participants had positive feedback, reported feeling more relaxed and adventurous, and less lonely. Participants tolerated the VR-headset well, and none reported feeling dizzy or disoriented. We found that enhancing image focus and enriching the narrative content would improve the VR experiences.

Conclusion: Immersive VR technology is increasingly present in healthcare, but its use as therapy for dementia is a novel solution for an old problem, where innovation, including breakthrough discoveries and new approaches to improve quality of life, is sorely needed. Given the positive findings and learnings form our pilot study, we will conduct a larger Randomized Controlled Trial with improved VR experiences and measure bio-physiological and clinical outcomes.

Figure i: Participant with VR Head Mounted Display

The VRx study was funded through the SPARK grant generously provided by the Centre for Aging and Brain Health Innovation (CABHI)

Biography

Dr. Lora Appel is an Assistant Professor of Health Informatics at the Faculty of Health at York University, and a Research Scientist at OpenLab, and innovation Centre housed at University Health Network, the largest medical research organization in Canada. She leads "Prescribing Virtual Reality (VRx)" a collection of studies that introduce and evaluate AR/VR/MR interventions for patients, caregivers, and healthcare providers. She received several grants from the Centre for Aging in Brain Health innovation to pursue this work in aging and dementia care. Her expertise is in applying design thinking and science methodologies to healthcare innovation; she is passionate about designing new technological interventions that provide care in the pursuit of a cure.

Dual Control of Glutathione Regulation in Neuroprotection

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Glutathione (GSH) is a key antioxidant that plays an important neuroprotective role in the brain. Decreased GSH levels are associated with neurodegenerative diseases (NDs) such as Alzheimer's disease, Parkinson's disease and Multiple system atrophy (MSA). In patient with these NDs, they are known to reveal abnormalities in circadian rhythms from early stage of disease progression. We found that diurnal fluctuation of GSH levels, which is correlated with neuroprotective activity against oxidative stress, is observed in the mouse brain and cultured dopaminergic cells. Further, the uptake of neuronal cysteine, the rate-limiting substrate for GSH biosynthesis, is controlled by cysteine transporter excitatory amino acid carrier 1 (EAAC1) and its negative regulator GTRAP3-18; both reveal circadian rhythmicity. Interestingly, circadian rhythms of these proteins are regulated by identical microRNA-miR-96-5p which also have circadian rhythm; but surprisingly opposite direction. MiR-96-5p negatively regulates EAAC1 expression whereas up-regulates GTRAP3-18 level.

Recent a line of evidence indicate deregulation of microRNA is emerging as a contributor to neurodegeneration. In the brain in patient with MSA, the expressions of miR-96-5p and its target EAAC1 are deregulated. Our results show that blocking miR-96-5p by intracerebroventricular administration of an inhibitor increased the level of EAAC1 as well as that of GSH and had a neuroprotective effect against oxidative stress in the mouse brain. These findings imply that dysregulation of miR-96-5p cause MSA through down-regulation of EAAC1 and reduction in GSH levels. GSH depletion is an early event in neurodegeneration and is related to disease progression in patients. A strategy to increase neuronal GSH levels by inhibitor of miR-96-5p would be a promising treatment for patients with NDs.

Biography

Chisato Kinoshita has completed her PhD at the age of 26 years from Tokyo Institute of Technology and postdoctoral studies from University of California, Irvine. She is an assistant professor in Teikyo University School of Medicine.

Neurodegeneration study from a population of heroin dependent patients under methadone maintenance therapy

Yu-Li Liu, Ph D

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Heroin dependence has been reported with prediposition to accelerate Alzheimer-related changes in the brain. Degeneration of central neurons and fibers has been observed in postmortem brains of heroin dependent patients. In order to understand the neurodegeneration status and to search for peripheral biomarkers, several chemokines of C-C motif chemokine ligand 2 (CCL2; also called monocyte chemoattractant protein-1, MCP-1), ligand 11 (CCL11; eotaxin-1), ligand 22 (CCL22; also called macrophage-derived chemokine, MDC), and fibroblast growth factor 2 (FGF-2) were screened in a population of 344 heroin dependent patients under methadone maintenance treatment (MMT). 87 normal controls subjects were also recruited for comparison. Using receiver operating characteristics curve analyses, CCL11 showed the strongest sensitivity and specificity in correlation with age by a cut-off at 45 years (AUC=0.69, P<0.0001) in MMT patients but not normal controls. Patients of 45 years or older had significant higher plasma levels of CCL11, fibroblast growth factor 2 (FGF-2), nicotine metabolite cotinine, and a longer duration of addiction. Using linear correlation analyses between the plasma CCL11 level and age of both MMT patients and normal controls, only the MMT patients showed a significant correlation (r=0.27, slope=1.21, P<0.0001), but not the normal controls (r=0.074, slope=0.36, P=0.51). Plasma level of CCL11 was correlated with that of FGF-2 (partial r2=0.24, P<0.0001), but not with plasma methadone concentrations or urine morphine test results in multiple regression analyses. Further comparison of plasma CCL11 between a small group of age and gender-matched of the medication free former heroin user and the MMT patients, the plasma CCL11 is reversible after obstinence. The results suggest possible novel mechanisms mediated through CCL11 involving neurotoxicity in heroin dependent patients.

Biography

Yu-Li Liu has completed her Ph.D. at the Department of Pharmacology from East Tennessee State University, U.S.A. and postdoctoral studies from the Department of Psychiatry, National Taiwan University Hospital. She is the investigator of Center for Neuropsychiatric Research, National Health Research Institutes, TAIWAN, a clinical researcher. She has published more than 50 papers in the field of neuropsychiatric illness including schizophrenia, major depressive disorder, and heroin dependence. She is serving as an editorial board member mainly in the addiction medicine.

ADFlag, a diagnostic blood test for pre-dementia stages of Alzheimer's disease

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Alzheimer's disease AD affects 47.5 millions people worldwide. Despite its prevalence, and year of research, there are still currently no treatments to cure or prevent AD, in large part due to a lack of appropriate diagnostic tools. ADFlag® is a diagnostic tool able to identify 5 subgroups of patients based on their immunological profile, generating a 1-5 scale at pre-dementia stages of the disease. It is non-invasive and uses validated analytical techniques to facilitate its adoption in clinical reference laboratories. To date, 388 patients were analyzed through ADFlag®, in two independent cohorts constituted of SCI, MCI and early-AD patients. The level of expression of the proteins constitutive of the ADFlag® panel was measured in all blood samples, and patients were classified on a scale from 1 to 5. The ADFlag® classification was coherent with neuropsychological assessments, including cognitive tests, verbal fluency tests and memory scales such as CANTAB paired-associated learning RAVLT with 82-92% accuracy. It also enables to pre-screen for amyloid positivity as measured by CSF biomarkers. Analysis of variance showed that an ADFlag® score of 5 was present at a higher frequency in patients with low Abeta/high tau Chisq=0.0195 or pTau Chisq=0.0224. Moreover, we found that an ADFlag® score of 4 significantly increased the odds for conversion by 4.00-fold compared to patients scoring 1 p=0.0035 and 6.36-fold compared to patients scoring 3 on the ADFlag® scale p=0.0030. A generalized regression predictive model confirmed the association between conversion to AD and scoring 4 on the ADFlag® scale. The positive predictive value for ADFlag® scores corrected by age, presence of ApoE4 allele and amyloid beta status was 0.84. Hence, using ADFlag® as stratification tool to pre-screen MCI patients into preventive or therapeutic trials may enhance their chance of success.

Biography

Beatrice Blanc holds a Ph.D. in Biochemistry from the University of Notre Dame IN, USA. She specializes in recombinant protein production. Before joining ICDD, she was a post-doctorate fellow at the CEA in Grenoble, where her work focused on enzyme kinetics and protein characterization that reinforced her skills in protein chemistry. Beatrice has a solid interdisciplinary scientific background with a main focus on protein expression and characterization. Since joining ICDD in 2014 as project manager, she has been involved in the development and operation of diagnostic production & processing, and participates in assay development and validation.

Virtual gene panel for whole exome sequencing studies on neurodegenerative diseases

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[4]Department of Neurology, Chung-Ang University School of Medicine, Chung-Ang University Hospital, Korea

Pathological similarities overlap among the different types of neurodegenerative diseases, such as Alzheimer's disease (AD), Parkinson's disease (PD), amyotrophic lateral sclerosis (ALS) and frontotemporal dementia (FTD). Since above diseases have complex genetic background, a genetic profiling would be essential for the precise diagnosis, estimating the future risks. Recently, the next generation sequencing technologies (NGS) were developed. Whole genome sequencing (WGS) and whole exome sequencing (WES) using NGS could provide a cheaper, quicker and complex approach in genetic studies of neurodegenerative diseases. Majority of pathogenic mutations were found in the coding regions or splicing sites. Since WES would cover only exons with higher depth analyses, it would provide accurate data and be cost-effective than WGS. However, all variants should be validated. Initially, a gene panel of 50 disease-causing or risk factor genes were designed and performed the targeted NGS. All mutations were analyzed by in silico tools and pathway analysis by ClueGo. Here, WES was performed for complex analysis of dementia patients. WES would generate a big data, a virtual panel of 100 genes was selected. The big data analysis is in progress, and several novel genetic candidates could be anticipated in association with AD, PD, FTD, or ALS. Beside APP, PSEN1 and PSEN2, several novel candidates were suggested to be involved in early onset AD, such as SORL1, ABCA7 or CLU.

Biography

I started my PhD in 2010, at Gachon University (Seongnam, Republic of Korea), and graduated in 2014. After graduation, I continued working the same university as assistant professor. During my PhD years I started to work on the genetics of early onset Alzheimer's disease. In our research, found several EOAD-associated mutations in patients from South-East Asia. We have broad domestic and international collaborations. Recently, we are performing whole exome sequencing on patients with neurodegenerative disease, which facilitates the extensive genetic analyses. We have several publications on Alzheimer's disease and other neurodegenerative diseases.

Tau Protein in the Retina

Umur Kayabasi, MD

Bahcesehir University , Istanbul –TR and John Rose Sr. John Rose Eye Center, London- United Kingdom

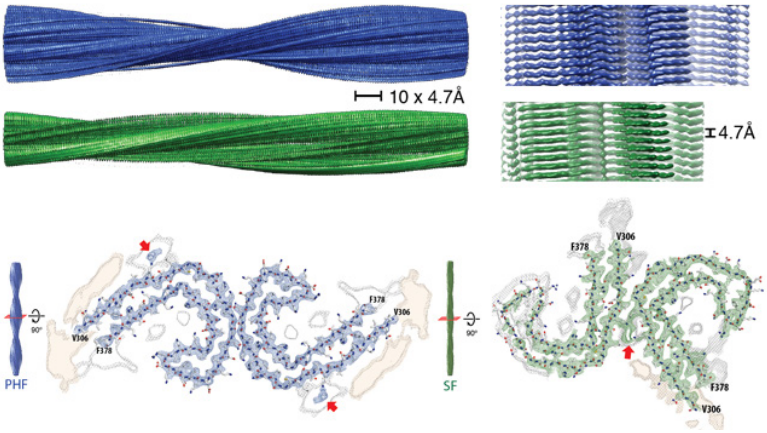
Background: Recent research suggests that Tau is the culprit lesion along with neuroinflammation in the etiology of Alzheimer's Disease (AD). Retina is the extention of the brain and is the most easily approachable part of the central nervous system. Detection of the pathological protein accumulations may be possible by using spectral domain optical coherescent tomography (SD-OCT) and fundus autofluorescein (FAF). There is evidence showing that retinal plaques start accumulating even earlier than the ones in the brain. Most recent Tau protein images in the brain consist of normal or reverse C-shaped paired hellical filaments.

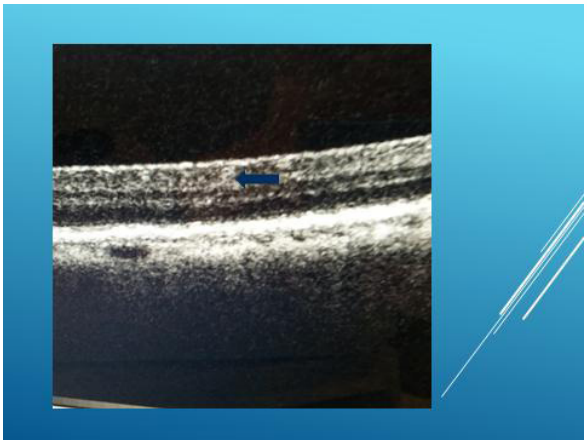
Methods: 20 patients with PET proven AD were examined by SD-OCT and FAF. Mean age was 72. Hypo or hyperfluorescent retinal lesions were scanned by SD-OCT and C shaped paired hellical filaments were investigated in a masked fashion. The researchers agreed on the shape of the lesions. Both C-shaped (normal or reverse) filaments and thinner fibrillary structures were taken into consideration.

Results: In all the patients, paired hellical filaments that exactly corresponded with the histopathologic and cryo-EM images of Tau (Figure 1) in terms of shape and dimension were detected along with thin fibrils and lesions similar to amyloid beta. The number of the retinal filaments and other abnormal proteins was in concordance with the severity of the disease process. The advanced retinal filaments had normal or reverse paired C shapes (Figure 2) and thin fibrils had the shape of histopathologic images seen in early developmental stages of the disease.

Conclusions: Retinal images of Tau were disclosed for the first time in live AD patients. Retinal neuroimaging is a trustable biomarker and tool for monitoring the disease.

Tables and Figures:





Biography

Umur Kayabasi is a graduate of Istanbul Medical Faculty. After working as a resident in Ophthalmology, he completed his clinical fellowship program of Neuroophthalmology and electrophysiology at Michigan State University in 1995. After working as a consultant neuro- ophthalmologist in Istanbul, he worked at Wills Eye Hospital for 3 months as an observer. He has been working at World Eye Hospital since 2000. He has chapters in different neuro- ophthalmology books, arranged international symposiums, attended TV programs to advertise the neuro- ophthalmology subspecialty. He has also given lectures at local and international meetings, plus published papers in neuro-ophthalmology. He became an assistant professor at Uskudar University- Istanbul in 2015.

Electrophysiology as a Biomarker of Memory Impairment in Dementia

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Background: Mismatch negativity (MMN) is an event related potential recorded via EEG reflecting the ability of automatic novel detection by the brain. NMDA receptors is involved in the genesis of this ERP. Previously, abnormal MMN in Alzheimer disease (AD) and Parkinson disease with dementia (PDD) have been found and this abnormality related to glutamatergic mechanism is suggested. Here, we tried to investigate the ability of novel detection in AD and PDD with MMN paradigm by NMDA receptor dysregulation-related electrophysiology for the monitoring of clinical condition in PDD.

Method: We recruited AD and PD patients with normal aged controls. We recorded auditory MMN with a novel frequency paradigm and traditional paradigm. The inter-trial interval was 500 ms and 500 trials were collected with a 32-channel EEG. We further processed the data with 500ms epoch while the baseline set 50 ms before the stimuli and rejected the artefact with absolute 100 microvolt. The mean amplitude and peak latency of Fz between 150-250 ms of MMN were measured for further Statistics.

Result: We recruited 15 PDD patients with 30 AD patients and age matched controls. In the protocol 1000-2000Hz, the amplitude of controls significantly larger than PDD patients (mean=-2.43μV, SD=1.13 V.S. mean=-0.93 μV, SD=1.92, p=.021). Additionally, in AD patients, independent t-test for MMN data showed a smaller MMN amplitude ratio in AD patients (Protocol 3: p=0.00, protocol 4: p=0.04). We also showed a AUC=0.75 in ROC curve in protocol 3 (p=o.o3).

Conclusion: MMN amplitudes in Parkinson disease dementia patients and AD are impaired. It could be related to the underlying abnormal NMDA related plasticity change. This result suggested MMN could be a useful biomarker in the monitoring of PDD and AD.

Biography

Jui-Cheng Chen, MD, PhD, is a neurologist of the China Medical University Hospital, and trustee of Taiwan Neurophysiology Society. Dr. Chen directs a multidisciplinary research program focused on the neurological diseases, such as Parkinson's disease and Alzheimer's disease by non-invasive recording and stimulation. Dr. Chen is interested in how these regulatory mechanisms contribute to both neurophysiological and pathological motility, and in leveraging this information for the development of therapeutics that target neurodegenerative diseases. Work of Dr. Chen has been supported by several grants from the dystonia UK foundation, Ministry of Science Technology, Taiwan, Ministry of Education, Taiwan and DAAD, Germany.

Dr. Chen earned his bachelor's degree in Medicine from the China Medical University and his Ph.D. in Neurology in University College London. After completing postdoctoral visiting at Oxford University in clinical neuroscience, he joined China Medical University.

Changes in chemokines and its receptors in a mouse model of alzheimer's disease

Soraya L. Valles and Adrian Jorda

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The amyloid precursor protein plus presenilin-1 (APP/PS1) mice are a frequently model for Alzheimer's disease studies (AD) but the inflammatory proteins involved are not sufficiently study in that mice. Using behavior studies, quantitative RT-PCR and western-blot techniques, significant findings were determined by the expression of proteins involved in inflammation comparing APP/PS1 and Wild type mice. Increased GFAP expression was associated with elevation in number of reactive astrocytes. IL-3 involved in inflammation and ABDF1 up-regulated transport across cell membranes in APP/PS1 mice occurred. Furthermore, CCR5 expression decrease and both CCL3 and CCL4 chemokines were highly expressed indicating increase in chemotaxis lymphocytes and T cell generation. We also noted for the first time, a CCR8 increase expression with diminution of its CCL1 chemokine, both involved in protection from bacterial infection and demyelination. Control of inflammation proteins will be the next step to understand progression of AD and also to determine the mechanisms that can development this disease.

Biography

Dr. Soraya L. Vallés was born in Valencia, Spain. In 1990 she finished her degree in Biology at University of Valencia and in 1996 obtained her PhD with honour at the same University. After Three years working in inflammation, in the Hallamshire Hospital, Sheffield, UK, she won a senior lecture position in the Department of Physiology, School of Medicine, U. of Valencia. She has published more than 45 journals some of them with high impact factor, assisted to about 90 congresses and obtained more than 25 research projects. She is working now in brain toxicity during development and in neurodegenerative diseases.

Urea-induced Unfolding Dynamics of RNA recognition motifs (RRMs) of TDP-43 Involve in Amyotrophic Lateral Sclerosis

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Protein folding is an impulsive method of gathering a polypeptide chain into a unique biologically active conformation. Although, it is quite hard to understand and differentiate the types of forces that trigger the protein folding, as the process follows through the wide range of conformational states of the unfolded ensemble to achieve the native fold. Here, we examine the conformational dynamics of RNA recognition motifs (RRM1 and RRM2) of TDP-43 protein aggregation mediates the pathological condition of amyotrophic lateral sclerosis (ALS). Multiple all-atoms simulations were carried out in the aqueous mixture of 8M urea for the period of 500ns at different temperatures (300-450 K). Results display that unfolding of RRMs occurred through the wide range of conformational states, stable and meta-stable intermediates (I_N) states at 450K. Free-energy landscape shows the three distinct minima that are largely confined to native (N) and native-like intermediate (I_N) and unfolded population as U state. These results suggested that conditional dependent intermediate may leads to misfolding or aggregation associated with pathological conditions of neurodegenerative diseases.

Biography

Amresh Prakash earned his Ph.D. degree in Biomedical Sciences at Dr. B. R. Ambedkar Centre for Biomedical Research, University of Delhi, India. He determined intrinsic dynamics and propensity of interfacial residues of A2AR-D2R belonging to GPCR protein using the computational biology approach that are an important targets for Parkinson's disease while doing his thesis work. He expanded his skills on computational biophysics to study the biophysical behaviors of proteins (FUS, SOD1, and TDP-43) involved in neurodegenerative diseases as Young Scientist (SERB, India) at Jawaharlal Nehru University. Presently, he is involve in identifying the RNA binding pockets and understanding the molecular mechanisms for the disease phenotypes.

Chronic hypoxia/sleep disturbance and Alzheimer's disease

Weidong Le, MD, PhD

Professor and Director of Center for Translational Research on Neurological diseases, and Vice President of 1st Affiliated Hospital, Dalian Medical University, China

Alzheimer's disease (AD) is the most common neurodegenerative disease mainly caused by genetic and environmental perturbation. Our previous studies have documented that chronic hypoxia/sleep disturbance is one of the important environmental factors that may trigger the AD development and aggravate the disease progression. Recently, we have conducted a series of investigations to determine the pathological effects of chronic hypoxia/sleep disturbance on the onset and development of AD and identify the possible molecule mechanisms underlying the chronic hypoxia/sleep disturbance-mediated AD pathogenesis. Based on our studies we have found that chronic hypoxia/sleep disturbance can cause long-lasting altered Aβ metabolism, specific tau phosphorylation, mitochondrial disruption and chronic inflammation in the brain, and epigenetic modulation of DNA methylation might be the key player in the chronic hypoxia/sleep disturbance-mediated neurodegeneration in AD. Our findings may represent a new research direction to uncover the disease mechanisms and provide a renovational therapeutic intervention of this devastating disease.

Biography

Weidong Le, MD, PhD is a neurologist/neuroscientist with the major research interest in neurodegenerative disorders. He has been served as a Professor of Neurology in Baylor College of Medicine, and Professor and Director of Institute of Neurology, Shanghai Jiao Tong University School of Medicine, and Professor and Director of Neurogenomic Laboratory, Institute of Health Sciences, SIBS, Chinese Academy of Sciences. Since 2013 he has been appointed as a Director of Center for Clinical Research on Neurology Disease, and Vice President of 1st Affiliated Hospital, Dalian Medical University. He has published over 240 SCI papers in peer review journals with a citation over 10000s. He is a board member or associate editor for 8 international journals. He has been selected by Elsivier as one of the most influenced neuroscientist in China from 2014-2017.

Harnessing Mass Spectra Data with KNN Principle; Alzheimer's Disease Diagnoses

Destiny E. O. Anyaiwe[1*], George D. Wilson[2], Timothy J. Geddes[3] and Gautam B. Singh[4]

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A high level of expertise, rigorous algorithms and methods are needed to adequately mine and harness Mass Spectrometer generated data due to its unique nature and structure. Hitherto, peptide ions are matched with theoretical results and/or public databases in order to identify expressed proteins in analyzed protein source samples, but this is done on a spectrum by spectrum basis. In this study, we present a mechanism that extends the principle of K-nearest neighbor algorithm for mining pools of mass spectrometer saliva data towards discovering and characterizing patterns for diagnosing Alzheimer's disease. The methodology discusses feature selection by correlation matrix, matrix to vector decomposition, an extension of Euclidean distance formula, and successfully classifies donor samples into the three stages of Alzheimer's disease with over 85% accuracy without collaborating clinical records.

Biography

Oriehi Destiny Anyaiwe, Ph.D.: Currently, Oriehi is an Adjunct Professor in the department of mathematics and computer science, Lawrence Technical University. He will be joining the department full time as an Assistant Professor this Fall. He obtained his PhD in Computer Science and Informatics from Oakland University. His research interest spans divers areas, such as, Bioinformatics, Data Science, Big Data Mining and Pattern Recognition in Health Care, Artificial Intelligence, and development of Classification Algorithms for Matrix Data Points

Poster Presentations

Preoperative Dementia Screening and Postoperative Delirium in Older Surgical Patients

Dr. Lucy Andrews
At Your Service Nursing and Hme Care, United States

People 65 years or older are having surgery later in life and are at risk of developing a major postoperative complication, delirium., The Montreal Cognitive Assessment, is a preoperative cognitive screening tool which was used to screen thirty-three older orthopedic surgical patients to reduce the incidence of this serious postoperative complications. Patients who scored below normal were identified *as at risk*, and monitored to ascertain if identification and monitoring influenced their postoperative course. At the first postoperative visit each patient was evaluated for falls, confusion, and the ability to follow the required postoperative home exercise program to identify an undetected episode of delirium after discharge. Of the patients screened, 34.1% (n = 14) of patients fell below the cutoff for normal cognition. Subsequent monitoring and nursing interventions may have influenced their postoperative course as there were no reported episodes of delirium in the 90-day period.Thus, preoperative screening with the Montreal Cognitive Assessment tool provides a baseline cognitive assessment and early identification of patients at higher risk for postoperative delirium, and therefore, identification of patients at risk for postoperative delirium may allow for early interventions and decrease postoperative delirium. Implementation and meaningful follow up of these ar risk patients can decrese risks associated wtih postoperative delirium as well as initiate a doiolog of discussion when a patient is found to be at risk wehn they did not know they had a potential reisk or deficiet. Early detection of risk can influence both decision making and the course of a progreessive degenerative disease and assist the patient and their famiy in determing the course of action for the best care of the patient.

Biography

Dr. Lucy Andrews received her Doctorate in Nurisng with a focus on Dementia, after a long career as a nurse leader in the field of dementia and aging. She is the CEO of At Your Service Nursing and Home Care Services providing inovative care to aging patients with Dementia and other neurological diseases. She presents here work across th Unitd States and recently at the International Alzheimere's Association Conference in London,United Kindom. She has publihed her research and advocates for dementia rsearch at state and national levels and serves on numerous boards associated with aging and the issues of the aging polulation around the world.

A screening tool for evaluating the semantic deterioration in Alzheimer's disease: The Mini SKQ (Semantic Knowledge Questionnaire)

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Background: It is now well-accepted that semantic memory disturbance is one of the first symptom in Alzheimer 'disease (AD). However, this ability is not always investigated in the traditional neuropsychological assessment and is rather evaluated through non-specific semantic measurements. The objective of the Semantic Knowledge Questionnaire (SKQ) was to explore semantic impairment in AD patients. Proposed by Laiacona et al.[1], revised in a French version by Simoes Loureiro and Lefebvre[2], SKQ assesses some levels of hierarchy and attributes in semantic memory by the mean of 120 questions about 30 objects. The score for each question is 1 (expected answer) or 0 (error). The objective of this work is to create a brief version of our SKQ, with the most discriminant questions to AD, in order to be easily used in clinical environment.

Method and Results: We administered SKQ to 39 healthy senior (MMSE > or = 28) and 35 mild AD (MMSE>20). An item by item analysis were conducted to compare our groups in order to pick up the most differentiated items. 12 items discriminating both group at a level of significance of p=.001 (by a khi-square analysis) were selected (4 questions about intracategorical aspects; 4 questions about perceptual attributes and 4 questions about thematical/functional attributes). We also performed correlational analyses for non-parametric data (Kendall's Tau correlation) to ensure that the failure to these 12 items are well correlated with AD (p=.001). Finally, a Bravais-Pearson correlation analysis confirms the correlation between the score at mini-SKQ and the full version of SKQ (r=.992; p=.001).

Conclusion: The Mini-SKQ is a fast and easily administered questionnaire, adapted for screening semantic knowledge. The failure to the items of the mini-SKQ is highly correlated to AD. These first observations underline that mini-SKQ could potentially be attractive for screening semantic memory deterioration in a clinical use.

[1]Laiacona M, Barbarotto R, Trivelli C, Capitani E. Dissociazoni semantiche intercategoriali descrizione di una batteria standardizzata e dati normativi. Archivio di Psicología, Neurología e Psichiatria, 1993 ; 54 : 209-48.

[2]Simoes Loureiro, I., & Lefebvre, L. Le QCS : questionnaire de connaissances sémantiques pour déterminer le stade de détérioration sémantique chez les patients atteints de la maladie d'Alzheimer. Gériatrie et Psychologie Neuropsychiatrie Du Vieillissement, 2015 ; 13(2), 225–33.

Biography

Laurent Lefebvre has acquired an expertise in the study of language and executive functioning deficits encountered by patients with neurodegenerative diseases (Alzheimer's disease, Primary Progressive Aphasia, Vascular Dementia). He is at the head of the UMONS department of Cognitive Psychology and Neuropsychology since 2012. He created some neuropsychological tests (e.g. GREMOTS, DTLA) and cognitive interventions (e.g. Logaatome) specifically dedicated for aged patients with cognitive deficits. Laurent Lefebvre is a member of several scientific and patients' groups committees in neuropsychology and dementia. He is Full Professor at the University of Mons and Dean of the Faculty of Psychology and Education.

The rapid increase in violence by aged persons and its relationship with dementia

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Background: In 2016, the Japanese Ministry of Justice reported that for the age group of over 65, there was a 49-fold increase in the number of arrests in cases of violence, compared to 20 years before. While Japan indeed does have one of the highest rates of aging in the world, the increase in arrests for violent acts cannot be explained only by the increasing population of this age group, as the total number of arrests (not limited to violent acts) in the same age group has reached a plateau in 2008. If this development is in any way due to the increasing cases of dementia, a system that takes the possibility of dementia into consideration and protects the rights of patients to live well with dementia is needed urgently. In order to look into the relationship between violent behavior and dementia, and also the nature of dementia-related violence, we have conducted detailed interviews with patients and their families, analyzing the various dimensions of their violent behavior.

Methods: We have surveyed the details of violent acts by 210 consecutive new dementia out-patients in our Medical Centre, between January 2017 and December 2017. Data was collected on the following points: Nature and Background of violent acts, the patient's Age, Gender, Diagnosis, Brain image, Medical history, MMSE scores, Educational level Alcohol consumption level, Medication.

Results: Of 210 new outpatients, 14.3% (n=30) exhibited physical violence, and 33.3%□n=70□ exhibited verbal violence. These accounted for 36 of 99 patients (36.4%) with AD, 8 of 41 patients (19.5%) with MCI, 17 of 36 patients (47.2%) with VD, 5 of 9 patients (55.6%) with□DLB. One patient with bvFTD exhibited verbal violence while none of 8 patients (0.00%) within normal cognitive aging did.

Conclusions: Problems of violent behavior could arise before dementia can be diagnosed, as is clear from the fact that a certain percentage of MCI patients exhibit verbal violence. Most occurrences of violent behavior did not involve serious violence, and were entered into impulsively. The impulsive nature of these acts is more likely to be connected to vulnerability in the frontal lobe in dementia. This further suggests the possibility that much of the violent behavior for which persons over 65 are arrested is also similarly impulsive in nature, and includes acts by patients of undiagnosed dementia or MCI. If dementia patients are being arrested for violent behaviour without sufficient understanding of their condition, this is a serious problem from the viewpoint of dementia care. This suggests an urgent need for a system that protects the rights and interests of these individuals.

Group cognitive behavior therapy program for family caregivers of people with dementia: A single arm pilot study

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Objective: To develop a group program which aims to reduce psychological distress and care burden of family caregivers of people with dementia, and to evaluate feasibility of the program.

Methods: With reference to the UK START program (Livingston G. 2013), we developed a group cognitive behavior therapy (CBT) program, consisting of biweekly six sessions. The program had three elements; (1) psychoeducation of dementia, (2) communication skills training based on applied behavior analysis theory, and (3) stress management strategies of the caregivers based on CBT and positive psychology. We conducted a single arm pilot study.

Results: Twelve caregivers of people with dementia were enrolled. The participants' mean age was 64.5 (standard deviation (SD) = 11.0). Six of them were male. The care-recipients' mean age was 87.2 (SD = 4.0), and their type of dementia were Alzheimer type (n = 3), vascular type (n = 2), mixed type (n = 1), Lewy bodies disease (n = 2) and others (n = 2). Three participants dropped out during the program and nine completed the program. In the analysis of all participants (LOCF method), the Hospital Anxiety and Depression Scale's anxiety subscale score decreased from 10.4 (SD = 3.8) to 8.0 (SD = 4.2), depressive subscale score decreased from 8.9 (SD = 4.1) to 6.3 (SD = 4.4), short version of the Zarit caregiver burden scale (J-ZBI-8) decreased from 19.9 (SD = 6.2) to 16.7 (SD = 6.6). All the variables showed significant improvement (paired t-test; $p<0.05$). Neuropsychiatric Inventory scores showed a tendency to improve.

Discussion: Our group CBT program for caregivers of people with dementia appears feasible and can be efficacious to reduce psychological distress and burden of caregivers, and behavioral and psychological symptoms of people with dementia. A future randomized controlled trial is warranted to examine its effectiveness.

A probable case of frontotemporal lobar degeneration associated with atypical multiple system atrophy

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Background: Spinocerebellar degeneration (SCD) is a neurodegenerative diseas that shows mainly ataxia, but symptoms of behavioral variant fronto-temporal dementia (bvFTD) are not common in SCD. Recently, there have been case reports of atypical multiple system atrophy (MSA) with frontotemporal lobar degeneration (FTLD) (Aoki N, et al. Acta Neuropathologica, 2015).

Case Report: A 60-year-old right-handed male was referred to our Memory Clinic at Keio University due to difficulties in speech and, paper work and cash transfer at work. He showed cerebellar ataxia in the right side of body dominantlly at the initial examination, and SCD was suspected based on the atrophy of the brainstem and the the cerebellum in the brain MRI. On the neuropsychological examination, he scored 26/30 on the Mini-Mental State Examination and his performance on verbal episodic memory, visuoconstraction tests and verbal fluency were below on the age-matched average . One year later, his dysarthria and cognitive dysfunctions became worse, and he started to show incontinence of urine and feces. He began to ritualistically follow a daily routine with going to work and eating the same food, and the cerebral blood flow in the bilateral frontal and temporal regions was reduced in the SPECT images. Neurological findings showed as follwed: saccadic and horizontal nystagmus(+), muscle tonue: rigidity U/E(+-), L/E(-/+-), truncal rigidity(-), muscle atrophy(-), fasciculation(-), Barre(-), coordination: dysmtria(-), heel-shin test; bilaterally slightly impaired, knee-tapping test; bilaterally slightly impaired, sensory: intact, gait: wide-base and unstable, autonomic function: intact, extrapyramidal sign: masked face(+), tremor(-), diadokokinesis(+); bradykinetic, retropulsion(+), micrographia, apraxia(-), Myerson(+), palmomental reflex(+), sucking reflex(+), forced grasp(-).

Conclusion: The patient presented cerebellar ataxia at initial stage and developed symptoms of bvFTD. These symptoms met the diagnositc criteria for both probable MSA (Gilman S, et al. Neurology, 2008) and bvFTD (Raskovsky K, et al. Brain, 2011). Our case could be variant of FTLD-synuclein.

Biography

Mika Konishi PhD is a speech pathologist and neuropsychologist. Graduated from University of Wales, Bangor (Department of Psychology) in 2001 and Graduate school of Keio University (Department of Neuropsychiatry) in 2009. Working at Keio University Hospital, as carrying out clinical assessment and rehabilitation and research on developmental disorders (such as autism spectrum disorder and learning disorders) and neurodegenerative disorders.

Traffic-related air pollution and risk of dementia: A nationwide case-control study in Taiwan

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Background/Aim: In recent years, a growing body of research has linked cognitive effects to ambient air pollution, but most of previous studies were based on cross-sectional design with a smaller sample size. Here, we investigated the influence of traffic-related air pollution on dementia in a nationwide population-based case-control study in Taiwan.

Methods: We identified 45,067 dementia patients with a first hospital or outpatient clinic contact for dementia (ICD-9 codes 2900-2904, 2941, and 3310) between 2007 and 2009 from the Taiwanese National Health Insurance Research Database and randomly selected four controls matched to cases on age, sex, and year of diagnosis from the longitudinal health insurance database. Daily concentration for NOx and CO from 1998 through the onset of dementia were estimated using quantile-based Bayesian Maximum Entropy models. Based on logistic regression models we estimated odds ratios (ORs) and 95% confidence intervals (CIs) of traffic-related pollutant exposures and dementia risk.

Results: The mean age of dementia cases at the first diagnosis in the registry system was 77.7 years, and 54% of cases were female. For NOx and CO, when models that also adjusted other pollutants (i.e., SO2, O3, PM10), the adjusted odds ratio were 1.09 (95% CI=1.02-1.16) and 1.08 (95% CI=1.02-1.14) for above the top quartile of NOx and CO compared with the lowest quartile, respectively.

Conclusions: This large population-based case-control study suggests that traffic related pollutants like NOx and CO increase dementia risk in the Taiwanese population.

Biography

I have a broad background in epidemiology, with extensive training and expertise in environmental epidemiology and nationwide claims data analyses. During my study at the University of Pittsburgh, I was trained as an environmental epidemiologist and heavily involved in research related to the health effects of air pollution on birth outcomes. After joining Dr. Ritz's research group at UCLA as a postdoc, I received genetic statistical training and began working on genetics of Parkinson's disease. After returning to Taiwan, I started to analyze Taiwanese nationwide claim data again with a focus on birth outcomes and Parkinson's disease.

Early onset Alzheimer's disease patient with Amyloid Precursor Protein (V669L) mutation

AhRa Cho

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Background & Case Report : A 56-year-old woman with 12 years of education presented to the memory disorder clinic reporting progressive memory difficulties for the past 2 years. Cognitive testing the patient scored 25 out of 30 on the Mini-Mental State Examination (MMSE). Her initial investigations including routine dementia blood workup was normal. The patient's MRI revealed mild global atrophy with medial temporal lobe predominance and hippocampal atrophy. A iagnosis of mild cognitive impairment was made. The patient was started on donepezil. One year later, her memory deficits were most noticeable when she recalled recent events as opposed to events from the distant past. And she was unable to perform her activities of daily living. Her MMSE score was 13. MRI revealed severe global atrophy with pronounced hippocampal atrophy. A fluorodeoxyglucose positron emission tomography scan was ordered and revealed bilateral temporoparietal hypometabolism. Two years later, she showed Parkinsonian features (bradykinesia, limb rigidity with cogwheel, short-stepped gait, anterior flexed posturing etc.). The next year, she experienced myoclonic jerk and generalized tonic clonic seizure. Finally she became bed-ridden state and her MMSE score was 0. Diffusion weighted imaging revealed more aggravated diffuse brain atrophy and small vessel ischemic lesion, but not detected CJD evidence.

Results: We performed genetic analysis to rule out early onset Alzheimer's disease. Direct sequencing analysis of the amyloid precursor protein (APP), presenilin 1 (PSEN1), and presenilin 2 (PSEN2), genes revealed mutation of the APP gene (V669L). A diagnosis of early onset Alzheimer's disease with APP mutation (V669L) was made. In addition, we identified that her two daughters have the same mutation. This is the 1st Korean mutation in the APP exon 16-17 region. It's unclear, whether this mutation could be pathogenic. However, it is located relatively near to the beta secretase cleavage site.

Conclusion: Cell studies may be helpful to evaluate the role of mutation in AD progression.

Biography

AhRa Cho , M.D. is a clinical fellow in department of physical medicine & rehabilitation of the Catholic University of Korea. She is acting in the field of neurological rehabilitation for adults and children and involved in genetic studies and neuroimage studies in neuroscience.

Notes:

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