대한치매학회
Korean Dementia Association

IC-KDA 2023

International Conference of the Korean Dementia Association

November 24-25, 2023 | BEXCO, Busan, Republic of Korea

ABSTRACTS

IC-KDA 2023

International Conference of the Korean Dementia Association

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Daily Program

Friday, November 24

09:00-10:30	**Session 1 : Gut-Brain Axis and Neuroinflammation in Dementia** **Chairpersons** Won-Seok Choi (Chonnam National University, Republic of Korea) Hoo Won Kim (Chosun University, Republic of Korea)	301 Grand Ballroom
09:00-09:30	Modern Koch's Postulates Applied to Bacterial Pathogenesis of Alzheimer's Disease Jan Potempa (Jagiellonian University, University of Louisville School of Dentistry, Poland/USA)	
09:30-10:00	Fecal Microbiota Transplantation in Patients with Dementia Seong Hye Choi (Inha University College of Medicine, Republic of Korea)	
10:00-10:30	ApoE Isoform-and Microbiota-Dependent Progression of Neurodegeneration in a Mouse Model of Tauopathy Dong-oh Seo (Washington University in St.Louis, USA)	
10:30-10:50	**Opening Ceremony**	301 Grand Ballroom
10:50-11:30	**Plenary Session I** **Chairperson** Kunho Lee (Chosun University, Republic of Korea)	301 Grand Ballroom
10:50-11:30	Pathogenesis and Early Diagnosis of Neurodegenerative Disease Keqiang Ye (Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS), China)	
11:30-12:10	**Plenary Session II** **Chairperson** Dong Won Yang (The Catholic University of Korea, Republic of Korea)	301 Grand Ballroom
11:30-12:10	Update on Plasma Biomarkers in Alzheimer's Disease Kaj Blennow (University of Gothenburg, Sweden)	
12:10-13:00	**Luncheon Symposium 1** **Chairperson** Jae-Hong Lee (Asan Medical Center, Republic of Korea)	301 Grand Ballroom
12:10-12:35	Alzheimer's Disease Biomarkers Towards a New Era in the Diagnosis and Treatment of AD (Supported by Eisai) Jaeho Kim (Hallym University College of Medicine, Republic of Korea)	

12:35-13:00	Neurotrophic Approaches in Dementia: A Closer Look at Cerebrolysin (Supported by Daewoongbio) Chi-Hun Kim (Hallym University Sacred Heart Hospital, Republic of Korea)	
13:00-14:00	**Poster Session 1**	201-204
14:00-15:30	**Session 2 : Blood-based Biomarkers for AD in Clinical Practice** **Chairpersons** SangYun Kim (Seoul National University Bundang Hospital, Republic of Korea) Seong-Ho Koh (Hanyang University Guri Hospital, Republic of Korea)	301 Grand Ballroom
14:00-14:30	Implementation of High Performance Blood Biomarkers in Routine Clinical Care for the Evaluation of Individuals with Cognitive Impairment Joel Braunstein (C2N, USA)	
14:30-15:00	Plasma Biomarkers of Neurodegenerative Diseases toward Clinical Practice(MagQu) Charles Shieh-Yueh Yang (MagQu, Taiwan)	
15:00-15:30	AlzOn: The Real World Example of Blood-based Biomarker Test Utility in Clinical Practice Sungmin Kang (PeopleBio, Republic of Korea)	
15:50-17:20	**Session 3 : Update in Treatment of Dementia** **Chairpersons** Kee Hyung Park (Gachon University College of Medicine, Republic of Korea) Sang Won Seo (Sungkyunkwan University, Republic of Korea)	301 Grand Ballroom
15:50-16:20	Advances in AD Experimental Therapeutics Alireza Atri (Banner Sun Health Research Institute (AZ) & Harvard Medical School (MA), USA)	
16:20-16:50	Gene Therapy for Neurodegenerative Diseases Jae young Lee (ToolGen, Republic of Korea)	
16:50-17:20	Neuromodulation for Gliopathy in Alzheimer's Disease Tae Kim (GIST, Republic of Korea)	
17:20 -	**Presidential Dinner** (Invited Only)	Nurimaru

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Saturday, November 25

08:25-08:30	**Korea-Taiwan Joint Symposium Opening Remark** Dong Won Yang (The Catholic University of Korea, Republic of Korea)	205 Summit Hall
08:30-09:30	**Korea-Taiwan Joint Symposium 1** **Chairpersons** SangYun Kim (Seoul National University Bundang Hospital, Republic of Korea) Jong-Ling Fuh (National Yang Ming Chiao Tung University, Taiwan)	205 Summit Hall
08:30-08:50	Can Fluid Biomarker Testings Change the Diagnosis and Management of Dementia? Yung Shuan Lin (Taipei Veterans General Hospital, Taiwan)	
08:50-09:10	Alzheimer's Disease Biomarkers: Towards a New Era in the Diagnosis and Treatment of AD Based on Blood Biomarkers Seong-Ho Koh (Hanyang University Guri Hospital, Republic of Korea)	
09:10-09:30	What is the Role of Brain Imaging in the Diagnosis of Dementia? Jung Lung Hsu (New Taipei Municipal TuCheng Hospital, Taiwan)	
09:30-10:30	**Korea-Taiwan Joint Symposium 2** **Chairpersons** Dong Won Yang (The Catholic University of Korea, Republic of Korea) Chaur-Jong Hu (Taipei Medical University, Taiwan)	205 Summit Hall
09:30-09:50	What is the Appropriate Use of Amyloid Imaging Under the Situations that DMT Drugs Have Been Developed? Kee Hyung Park (Gachon University College of Medicine, Republic of Korea)	
09:50-10:10	How Can I Choose the Right Pharmacological Therapy for Alzheimer's Disease? Li-Kai Huang (Taipei Medical University Shuang-Ho Hospital, Taiwan)	
10:10-10:30	South Korean Study to Prevent Cognitive Impairment and Protect BRAIN Health through Lifestyle Intervention (SUPERBRAIN) Seong Hye Choi (Inha University College of Medicine, Republic of Korea)	
10:30-10:40	**Korea-Taiwan MOU** Dong Won Yang (The Catholic University of Korea, Republic of Korea) Young Chul Youn (Chung-Ang University, Republic of Korea) Cheng-Sheng Chen (Kaohsiung Medical University, Taiwan) Ming-Chyi Pai (National Cheng Kung University, Taiwan)	205 Summit Hall
10:40-10:45	**Korea-Taiwan Joint Symposium Closing Remark** Cheng-Sheng Chen (Kaohsiung Medical University, Taiwan)	205 Summit Hall

9:00-10:30	**Session 4 : The Recent Issues in Clinical Neuropsychology** **Chairpersons** So Young Moon (Ajou University, Republic of Korea) Ju Hee Chin (Sungkyunkwan University, Republic of Korea)	301 Grand Ballroom
09:00-09:30	Unsupervised Remote Memory Assessments in Early Stages of Alzheimer's Disease David Berron (German Center for Neurodegenerative Diseases (DZNE), Germany)	
09:30-10:00	Predictive Utility of Machine Learning Approach with Neuropsychological Test in AD Spectrum Seyul Kwak (Pusan National University, Republic of Korea)	
10:00-10:30	Digital Neuropsychological Assessments for Frontotemporal Dementia Adam Staffaroni (University of California, San Francisco, USA)	
10:50-11:30	**Plenary Session III** **Chairperson** Kun-Woo Park (Korea University, Republic of Korea)	301 Grand Ballroom
10:50-11:30	Social Cognition in Neurodegenerative Diseases Katherine P. Rankin (University of California San Francisco, USA)	
11:30-12:10	**Plenary Session IV** **Chairperson** Jee Hyang Jeong (Ewha Womans University, Republic of Korea)	301 Grand Ballroom
11:30-12:10	Creating a Worldwide platform Trial for Genetic Frontotemporal Dementia - The FTD Prevention Initiative Jonathan Rohrer (University College London, UK)	
12:10-13:00	**Luncheon Symposium 2** **Chairperson** Yong Soo Shim (The Catholic University of Korea, Republic of Korea)	301 Grand Ballroom
12:10-12:35	Advancing Dementia Care: The Innovative Donepezil Patch and its Influence on Enhancing Compliance (Supported by Celltrion) Geon Ha Kim (Ewha Womans University College of Medicine, Republic of Korea)	
12:35-13:00	Optimizing Treatment Strategies: Focusing on Donepezil's Role in Neuroprotection and Early-Stage Alzheimer's Disease (Supported by Eisai) Hyemin Jang (Seoul National University Hospital, Republic of Korea)	
13:00-14:00	**Poster Session 2**	201-204

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14:00-15:30	**Session 5 : Update in FTD (Including FTD Cohort Study)** **Chairpersons** Jonathan Rohrer (University College London, UK) Eun Joo Kim (Pusan National University Hospital, Republic of Korea)	301 Grand Ballroom
14:00-14:30	North American FTD Registry (ALLFTD) Howard Rosen (University of California San Francisco, USA)	
14:30-15:00	Korean FTD Registry (LEAF-FTD) Eun Joo Kim (Pusan National University Hospital, Republic of Korea)	
15:00-15:30	Familial FTD in China: Progress and Prospects Qin Chen (West China Hospital of Sichuan University, China)	
15:50-17:20	**Session 6 : Pathogenesis of non-AD dementia** **Chairpersons** Yong Jeong (KAIST, Republic of Korea) Yun Kyung Kim (KIST, Republic of Korea)	301 Grand Ballroom
15:50-16:20	Molecular Neuropathology of Chronic Traumatic Encephalopathy (CTE) Reveals Alzheimer's Disease-like Signatures Hoon Ryu (KIST, Republic of Korea)	
16:20-16:50	Molecular Mechanism of α-Synuclein in Non-AD Dementia Seung-Jae Lee (Seoul National University, Republic of Korea)	
16:50-17:20	Identifying the Early Events in ALS Pathogenesis Jeehye Park (University of Toronto, Canada)	
17:20 -	**Closing Ceremony**	301 Grand Ballroom

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International Conference of the Korean Dementia Association

Session 1
Gut-Brain Axis and Neuroinflammation in Dementia

Nov 24 (Fri) 09:00-10:30 I 301 Grand Ballroom

CHAIRPERSONS

Won-Seok Choi (Chonnam National University, Republic of Korea)

Hoo Won Kim (Chosun University, Republic of Korea)

09:00 – 09:30 **Modern Koch's Postulates Applied to Bacterial Pathogenesis of Alzheimer's Disease**
Jan Potempa (Jagiellonian University, University of Louisville School of Dentistry, Poland/USA)

09:30 – 10:00 **Fecal Microbiota Transplantation in Patients with Dementia**
Seong Hye Choi (Inha University College of Medicine, Republic of Korea)

10:00 – 10:30 **ApoE Isoform-and Microbiota-Dependent Progression of Neurodegeneration in a Mouse Model of Tauopathy**
Dong-oh Seo (Washington University in St.Louis, USA)

SESSION 1 09:00 – 09:30 | 301 Grand Ballroom

Jan Potempa

Jagiellonian University, University of Louisville School of Dentistry, Poland/USA

Educational Background & Experience

CURRENT	JAGIELLONIAN UNIVERSITY - Kraków, Poland	Research Professor
1998	PRESIDENT OF THE REPUBLIC OF POLAND	Professor
1993	JAGIELLONIAN UNIVERSITY - Kraków, Poland	D.Sc.
1982	JAGIELLONIAN UNIVERSITY - Kraków, Poland	Ph.D.
1979	JAGIELLONIAN UNIVERSITY - Kraków, Poland	M.S.

Modern Koch's Postulates Applied to Bacterial Pathogenesis of Alzheimer's Disease

In the 19th century Robert Koch established rigorous guidelines to evaluate causation in infectious disease. These postulates have been updated to reflect modern scientific methods including DNA sequencing and immunohistochemical techniques. First, a DNA/protein belonging to a putative pathogen should be present in most cases of an infectious disease; second, lower level, or none pathogen-associated DNA/antigens should occur in hosts or tissues without disease; third, with effective treatment, the level of pathogen-associated factors should decrease. Applying these postulates to Porphyromonas gingivalis revealed that this bacterium may contribute to pathogenesis of Alzheimer's disease (AD) through activity of gingipains, its main virulence factors. First, both P. gingivalis derived DNA and gingipain antigens were identified in the brain of AD patients. Notably, a level of gingipains in the brain of AD patients correlated with tau and ubiquitin pathology. Second, although gingipains were found in the brain of age-matched controls, they occurred at a significantly lower level. Third, oral infection of mice with wild-type P. gingivalis, but not gingipains-null strains, resulted in brain colonization and increased deposition of Aβ1-42 plaques. Fourth, gingipains were neurotoxic in vivo and in vitro. Fifth, targeting gingipains by small-molecule inhibitors in a murine model diminished the bacterial load of an established P. gingivalis brain infection, blocked Aβ1-42 production, reduced neuroinflammation and rescued neurons in the hippocampus. Together these results revealed the potentially causative relation between chronic periodontitis and AD and suggested that gingipain inhibitors could be valuable for treating P. gingivalis brain colonization and neurodegeneration in Alzheimer's disease.

SESSION 1 09:30 – 10:00 | 301 Grand Ballroom

Seong Hye Choi

Inha University College of Medicine, Republic of Korea

Educational Background & Experience

2022 - Now	Society for Cognitive Intervention	Chairman
1999 - Now	College of Medicine, Inha University	Professor
2006	University of Pittsburg	Research scholar
2003	PhD at College of Medicine, Seoul National University	
1993	Master degree at College of Medicine, Seoul National University	

Fecal Microbiota Transplantation in Patients with Dementia

Cognitive improvements are noticeable after fecal microbiota transplantation (FMT) to treat Clostridioides difficile infection (CDI), suggesting an essential link between the gut microbiome and brain function. Even though the gut microbiome has been associated with cognitive function, it remains to be elucidated whether fecal microbiota transplantation can improve cognition in patients with cognitive decline. This study included ten patients with dementia and severe CDI (age range, 63–90 years; female, 80%) who received FMT. Additionally, ten patients with dementia and severe CDI (age range, 62–91; female, 80%) who did not receive FMT were included as controls. They were evaluated using the Mini-Mental State Examination (MMSE) and Clinical Dementia Rating scale-Sum of Boxes (CDR-SB) before and 1 month after FMT or antibiotic treatment (control group). The fecal samples from the patients were analyzed to compare the composition of the gut microbiota before and 3 weeks after FMT or antibiotic treatment. Ten patients who received FMT had significant improvements in clinical symptoms and cognitive function compared to the control group. The MMSE and CDR-SB scores of the FMT group were significantly improved compared to the control group with antibiotic treatment (MMSE: 16.00, median, 13.00–18.00 [IQR] vs. 10.0, median, 9.8–15.3 [IQR]); CDR-SB: 5.50, median, 4.00–8.00 [IQR]) vs. 8.0, median, 7.9–12.5, [IQR]). FMT resulted in changes in the gut microbiota composition of recipients, with enrichment of Proteobacteria and Bacteroidetes. Alanine, aspartate, and glutamate metabolic pathways were also significantly increased after FMT. This study revealed important interactions between the gut microbiome and cognitive function. There are indicators that FMT may delay cognitive decline in patients with dementia.

SESSION 1 10:00 – 10:30 | 301 Grand Ballroom

Dong-oh Seo

Washington University in St.Louis, USA

Educational Background & Experience

2020-Present	Department of Neurology, Washington University in St. Louis, Missouri, USA	Instructor
2018-2020	Department of Neurology, Washington University in St. Louis, Missouri, USA	Postdoctoral Research Associate
2015-2018	Department of Anesthesiology, Washington University in St. Louis, Missouri, USA	Postdoctoral Research Associate
2015	Behavioral Neuroscience, The University of Texas at Austin, Texas, USA	Ph.D.
2010-2015	Department of Psychology, The University of Texas at Austin, Texas, USA	Predoctoral Research Assistant
2007-2009	Department of Aging and Geriatrics, The University of Florida, Gainesville, Florida, USA	Research Technician
2006	Biological Psychology, Department of Psychology, Korea University, South Korea	B.A; M.A

ApoE Isoform-and Microbiota-Dependent Progression of Neurodegeneration in a Mouse Model of Tauopathy

Tau-mediated neurodegeneration is a hallmark of Alzheimer's disease. Primary tauopathies are characterized by pathological tau accumulation and neuronal and synaptic loss. Apolipoprotein E (ApoE)–mediated neuroinflammation is involved in the progression of tau-mediated neurodegeneration, and emerging evidence suggests that the gut microbiota regulates neuroinflammation in an APOE genotype–dependent manner. However, evidence of a causal link between the microbiota and tau-mediated neurodegeneration is lacking. In this study, we characterized a genetically engineered mouse model of tauopathy expressing human ApoE isoforms reared under germ-free conditions or after perturbation of their gut microbiota with antibiotics. Both of these manipulations reduced gliosis, tau pathology, and neurodegeneration in a sex- and ApoE isoform–dependent manner. The findings reveal mechanistic and translationally relevant interrelationships between the microbiota, neuroinflammation, and tau-mediated neurodegeneration.

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Plenary Session I

Nov 24 (Fri) 10:50-11:30 I 301 Grand Ballroom

CHAIRPERSON

Kunho Lee (Chosun University, Republic of Korea)

10:50 – 11:30 **Pathogenesis and Early Diagnosis of Neurodegenerative Disease**
Keqiang Ye (Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS), China)

PLENARY SESSION I 10:50 – 11:30 | 301 Grand Ballroom

Keqiang Ye

Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS), China

Educational Background & Experience

2021-Present	Shenzhen Institute of Advanced Technology (SIAT), Chinese Academy of Sciences (CAS)	Endowed Chair Professor and Department Chair
2010-2021	Emory University School of Medicine, Department of Pathology and Laboratory Medicine	Tenured Full Professor
2007-2010	Emory University School of Medicine, Department of Pathology and Laboratory Medicine	Tenured Associate Professor
2001-2007	Emory University School of Medicine, Department of Pathology and Laboratory Medicine	Assistant Professor
1993-1998	Biochemistry and Cell Biology Department, Emory University	Ph.D.
1990-1993	Chemistry Department, Peking University, Beijing, China	M.S.
1986-1990	Chemistry Department,Jilin University, Changchun, China	B.S.

Pathogenesis and Early Diagnosis of Neurodegenerative Disease

Aging is the key risk factor for neurodegenerative diseases. Accumulating evidence suggests that C/EBPβ/AEP signaling drives both Alzheimer's disease (AD) and Parkinson's disease (PD) onset and progression. C/EBPβ acts as a major transcription factor for AEP (asparagine endopeptidase, also called legumain), and neuronal C/EBPβ transgenic mice display gene dose-dependent short lifespan. Deletion of AEP from Thy1-C/EBPβ Tg mice extends the lifespan. AEP levels are escalated in the brain in an age-dependent manner, cleaving APP, Tau and a-Synuclein (a-Syn) at N585, N368 and N103, respectively, and triggering Aβ amyloids and Tau aggregation and a-Syn inclusions. Knockout of AEP substantially ameliorates AD and PD pathologies in their mouse models, restoring the behavioral functions. Thus, AEP proteolytic cleavage acts upstream of senile plaques and NFT and Lewy body pathologies, laying foundation for the early diagnosis of these devastating diseases. Quantitative SIMOA (single molecule array) methods have been developed for determining serum APP N585, C586 and Tau N368 levels. Early diagnosis of these neurodegenerative diseases will allow us to therapeutically treat or cure these devastating diseases in the future.

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Plenary Session II

Nov 24 (Fri) 11:30-12:10 I 301 Grand Ballroom

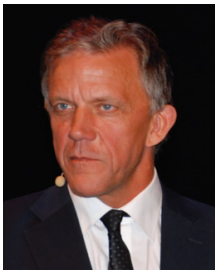
CHAIRPERSON

Dong Won Yang (The Catholic University of Korea, Republic of Korea)

11:30 – 12:10 **Update on Plasma Biomarkers in Alzheimer's Disease**

Kaj Blennow (University of Gothenburg, Sweden)

PLENARY SESSION II 11:30 – 12:10 | 301 Grand Ballroom



Kaj Blennow

University of Gothenburg, Sweden

Educational Background & Experience

2003 -	University of Gothenburg	Professor and Academic Chair in Clinical Neurochemistry
1995 -	Sahlgrenska University Hospital	Head and senior consultant
1994	Sweden	Specialist competence in clinical chemistry
1993	Sweden	Specialist competence in general psychiatry
1990	University of Gothenburg	PhD
1984	Lund University	MD

Update on Plasma Biomarkers in Alzheimer's Disease

Alzheimer's disease (AD) fluid biomarkers, including blood tests for screening and cerebrospinal fluid (CSF) tests for confirming the diagnosis, will be of great importance for management of patients with suspected AD, especially when amyloid immunotherapies or other disease-modifying drugs will be available for clinical use.

The CSF tests were developed as initial ELISA methods to measure and monitor β-amyloid (Aβ)metabolism and deposition (A), tau phosphorylation and tau pathology (T), and neurodegeneration (N). These biomarkers show excellent performance for diagnostics, have been extensively clinically validated, and are now available on CLIA certified and FDA approved fully automated high-precision instruments.

Importantly, these core AD biomarkers can today also be measured in blood samples. While the CSF Aβ42/40 ratio (reflecting amyloid deposition), show a marked reduction in AD, when measured in plasma, using either immunoassays or immunoprecipitation - mass spectrometry (IP-MS) methods, the fold change is small despite that the concordance with brain amyloidosis evaluated by PET is high (AUCs of 80-90%). A drawback with plasma measurements is therefore a marked overlap between patients and controls, which makes the robustness low and will introduce difficulties if the test would be introduced in clinical practice.

For tau pathology biomarkers, very promising data have been reported for several phosphorylated tau species (P-tau181, P-tau205, P-tau212, P-tau217, and P-tau231) in blood. Plasma P-tau shows a specific increase in AD (levels are normal in other cognitive disorders) and a high concordance with tau PET. P-tau levels in plasma increase with more extensive tau pathology, but still, P-tau is increased in cognitively unimpaired elderly who have evidence of brain amyloidosis on PET, but negative tau PET scans.

Non-phosphorylated tau (also called total tau, T-tau) is an established CSF biomarker to monitor the intensity of neurodegeneration and severity of neuronal damage. CSF T-tau is increased in AD, but even higher in disorders with more rapid neurodegeneration such as Creutzfeldt-Jakob disease (CJD). Current assays for plasma T-tau does not work as an AD biomarker, probably because tau is also produced in peripheral tissues and secreted to plasma. For that reason, a new plasma test, called brain-derived tau (BD-tau), based on antibodies only reacting with tau isoforms produced in the brain. Plasma BD-tau is high in AD and show great promise as a new test to monitor neurodegeneration.

Neurofilament light (NFL) levels are increased in both CSF and blood in AD, but NFL is a general neurodegeneration (N) biomarker showing high levels in many other neurodegenerative disorders, such as amyotrophic lateral sclerosis and progressive supranuclear palsy. AD.

High plasma GFAP is found in AD, also in the very early phases of the disease. Plasma GFAP has been found to be associated with presence of brain amyloidosis and shows promise as a biomarker for glial activation (G) and neuroinflammation.

To sum up, blood biomarkers show great promise as easily accessible and cheap screening tools to for AD pathophysiology, that will be very useful in the clinical setting.

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Luncheon Symposium 1

Nov 24 (Fri) 12:10-13:00 I 301 Grand Ballroom

CHAIRPERSON

Jae-Hong Lee (Asan Medical Center, Republic of Korea)

12:10 – 12:35 **Alzheimer's Disease Biomarkers Towards a New Era in the Diagnosis and Treatment of AD**
(Supported by Eisai)
Jaeho Kim (Hallym University College of Medicine, Republic of Korea)

12:35 – 13:00 **Neurotrophic Approaches in Dementia: A Closer Look at Cerebrolysin**
(Supported by Daewoongbio)
Chi-Hun Kim (Hallym University Sacred Heart Hospital, Republic of Korea)

LUNCHEON SYMPOSIUM 1 12:10 – 12:35 | 301 Grand Ballroom

Jaeho Kim

Hallym University College of Medicine, Republic of Korea

Educational Background & Experience

2022-	Department of Neurology, Hallym University Dongtan Sacred Heart Hospital, Hallym University College of Medicine, Hwaseong-si, Gyeonggi-do, Korea	Assistant Professor
2021-2022	Department of Neurology, Hallym Universi Dongtan Sacred Heart Hospital, Hwaseong-si, Gyeonggi-do, Korea	Clinical Assistant Professor
2020-2021	Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, US	Research Fellow
2019-2020	Department of Neurology, Samsung Medical Center, Seoul, Korea	Clinical Fellow, Ph.D.
2015-2019	Department of Neurology, Samsung Medical Center, Seoul, Korea	Resident
2006-2010	Pusan National University, School of Medicine, Busan, Korea	M.D., M.S.
2002-2006	Department of Bio and Brain Engineering, Korea Advanced Institute of Science and Technology (KAIST), Daejeon, Korea	B.S.

Alzheimer's Disease Biomarkers Towards a New Era in the Diagnosis and Treatment of AD

As it is currently accepted that AD starts decades before clinical symptoms could be diagnosed, the opportunity to detect biological alterations prior to clinical symptoms is important in the prodromal stage to allow early diagnosis or even perhaps change treatment possibilities. This presentation concentrates on the expectations and the effects of using biomarkers in the prediction of risk of dementia in prodromal AD.

LUNCHEON SYMPOSIUM 1 12:35 – 13:00 | 301 Grand Ballroom

Chi-Hun Kim

Hallym University Sacred Heart Hospital, Republic of Korea

Educational Background & Experience

2023-	Department of Neurology, Hallym University Sacred Heart Hospital, Anyang, Korea	Clinical Associate Professor
2019-2023	Department of Neurology, Hallym University Sacred Heart Hospital, Anyang, Korea Department of Neurology, Kyungpook National University Chilgok Hospital, Daegu, Korea	Clinical Assistant Professor
2015-2019	Department of Psychiatry, University of Oxford, UK	Postdoctoral Researcher
2012-2015	Pembroke College, University of Cambridge, UK	PhD in (Experimental) Psychology
2004-2012	Department of Neurology, Samsung Medical Center, Seoul, Korea	Intern, Resident, Clinical Fellow
2007-2011	Sungkyunkwan University School of Medicine, Korea	Master of Science in Medicine
1998-2004	Sungkyunkwan University School of Medicine, Korea	Bachelor of Medicine

Neurotrophic Approaches in Dementia: A Closer Look at Cerebrolysin

Dementia poses a significant global healthcare challenge, and finding effective therapeutic strategies is of paramount importance. Among these approaches, neurotrophic therapies have been a topic of interest. This presentation aims to provide scientific foundations of the neurotrophic approaches in dementia care, with particular attention to Cerebrolysin.

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Session 2
Blood-based Biomarkers for AD in Clinical Practice

Nov 24 (Fri) 14:00-15:30 l 301 Grand Ballroom

CHAIRPERSONS

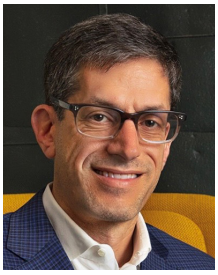
SangYun Kim (Seoul National University Bundang Hospital, Republic of Korea)
Seong-Ho Koh (Hanyang University Guri Hospital, Republic of Korea)

14:00 – 14:30 **Implementation of High Performance Blood Biomarkers in Routine Clinical Care for the Evaluation of Individuals with Cognitive Impairment**
Joel Braunstein (C2N, USA)

14:30 – 15:00 **Plasma Biomarkers of Neurodegenerative Diseases toward Clinical Practice(MagQu)**
Charles Shieh-Yueh Yang (MagQu, Taiwan)

15:00 – 15:30 **AlzOn: The Real World Example of Blood-based Biomarker Test Utility in Clinical Practice**
Sungmin Kang (PeopleBio, Republic of Korea)

SESSION 2 14:00 – 14:30 | 301 Grand Ballroom



Joel Braunstein

C2N, USA

Educational Background & Experience

2007 –	C2N Diagnostics, LLC	Co-Founder, CEO
2001-2003	Johns Hopkins University, Baltimore, MD	M.B.A.
2001-2003	Johns Hopkins Medical Institutions, Baltimore, MD	M.D.
1999-2003	Johns Hopkins Medical Institutions, Baltimore, MD	M.D.
1996-1999	Brigham & Women's Hospital, Harvard Medical School, Boston, MA	MA
1996	Northwestern University, Chicago, IL	M.D.

Implementation of High Performance Blood Biomarkers in Routine Clinical Care for the Evaluation of Individuals with Cognitive Impairment

The World Health Organization estimates that 55.2 million people globally have dementia. Alzheimer's disease (AD) accounts for many of these dementia cases. Despite high prevalence, a rising incidence, and poor quality of life implications, dementia caused by underlying AD pathology is underdiagnosed in approximately 40% of adults >65 years old. As disease-modifying therapies (DMTs) that can specifically treat the underlying causes of AD become available, an urgent medical need exists for accurate, cost-effective, and widely accessible diagnostic tools that can both aid in the early diagnosis of AD and help identify the presence of amyloid pathology to facilitate timely anti-amyloid treatment. The PrecivityAD2™ commercial blood test by C_2N Diagnostics is an analytically and clinically validated multianalyte assay with algorithmic assessment (MAAA) that has potential to help address these unmet medical needs. This test relies upon high-throughput, mass spectrometry to precisely and accurately quantitate key biomarkers implicated in AD pathology, including the Aβ42 and Aβ40 peptides (expressed as Aβ42/40 ratio), and the phosphorylated and non-phosphorylated tau peptides that contain Threonine-217 (expressed as p-tau217/np-tau217 ratio, or %p-tau217). The rationale for developing the PrecivityAD2™ test as well as the original PrecivityAD® blood test – each designed as an aid to the diagnosis of AD and to help identify the likely presence or absence of brain amyloid plaques among individuals aged 55 years and older with cognitive impairment – will be shared during the discussion. Integration of these blood tests into routine clinical care relies upon not only high diagnostic accuracy but also evidence of clinical usefulness and economic usefulness. These factors and other factors impacting the future role of blood biomarkers in cognitive care and management will also be discussed.

SESSION 2 14:30 – 15:00 | 301 Grand Ballroom

Charles Shieh-Yueh Yang

MagQu, Taiwan

Educational Background & Experience

2018-present	MagQu LLC	President
2008-present	MagQu Co., Ltd.	President
2010-2015	National Taiwan Normal University	Adjunct Professor
2007-2008	National Taiwan Normal University	Associate Professor
2003-2007	National Taiwan Normal University	Assistant Professor
2000-2003	Academia Sinica	Postdoctoral fellow
1999	National Taiwan Normal University	PhD in Physics

Plasma Biomarkers of Neurodegenerative Diseases toward Clinical Practice(MagQu)

Objective

MagQu commercialized the novel technology, so-called immunomagnetic reduction (IMR), for assaying plasma biomarkers associated Alzheimer's diseases (AD). The clinical trials for assaying plasma amyloid β peptides and total tau proteins using IMR for the comparisons with clinical diagnosis, brain atrophy, amyloid positron emission (PET) and amyloid neuropathology at autopsy have been successfully finished.

Methods

International multi-centered clinical trails and studies using IMR plasma biomarker assay for validations of clinical practices are investigated.

Results

The results reveal the assessments of plasma Aβ1-42/Aβ¬1-40 or Aβ1-42xT-Tau levels highly agree with clinical diagnosis for discriminating normal controls (NC) form patients with amnesic mild cognitive impairment (aMCI) or AD. Negatively moderated correlation between plasma T-Tau levels and brain volumes was obtained. Plasma Aβ1-42/Aβ1-40 levels moderately correlates with SUVRs in amyloid PET. Plasma Aβ1-42xT-Tau levels predict amyloid neuropathology at autopsy. The following studies evidence the predicting power for the progression of cognitive decline using plasma Aβ1-42 and T-Tau at baseline. Furthermore, the plasma p-Tau181 levels were found to be significantly correlated to SUVRs of Tau PET. Since 2020, the IMR

assay for AD biomarkers in plasma has been approved for clinical practices in Taiwan. In addition to the assistant diagnosis of aMCI and AD, IMR assay combined with ApoE genotypes helps doctors for determining the examinations of amyloid PET in prodromal AD, who are the target patients treated with drugs. Medical doctors also are using IMR assay to monitor the effects of disease managements or interventions for patients in clinic.

Conclusion

IMR assay of AD biomarkers in plasma is entering IVD markets in Taiwan, Korea, Middle, China and US.

SESSION 2 15:00 - 15:30 | 301 Grand Ballroom

Sungmin Kang

PeopleBio, Republic of Korea

Educational Background & Experience

2002-Present	PeopleBio, Inc.	Founder & CEO
2000-2002	University of Akron	Business (MBA)
1992-1996	Yonsei University	Biology (B.S.)

AlzOn: The Real World Example of Blood-based Biomarker Test Utility in Clinical Practice

Since its incorporation in 2002, PeopleBio has aimed for blood diagnosis of protein misfolding diseases based on its proprietary technology, Multimer Detection System, realizing development of the first-ever commercial blood test for Alzheimer's disease (AD) after receival of product approval from Ministry of Food and Drug Safety (MFDS) in 2018 and come-through on new Health Technology Assessment (nHTA) in 2021, country's unique accreditation process to become implementable for the clinical practice.

AlzOn, an enzyme-linked immunosorbent assay based on MDS, is an AD blood-based biomarker test which detects and measures in chemiluminescence the plasma level of beta-amyloid (Aβ) oligomerization, the core and earliest pathologic change of the disease.

With its approved intended use as an aid to AD diagnosis as well as its ability to detect the ongoing AD pathology with over 85% accuracy validated in more than 20 published clinical studies, the test service of AlzOn is being provided in over 500 hospitals including 35 tertiary hospitals and major medical checkup centers in Korea.

In primary care providers, so-called 'go-to' clinics for diagnosis and prescription for AD, AlzOn is a first-line blood test utilizable along with simple neuropsychological tests such as MMSE and MoCA. They can play a compatible duo detecting the ongoing pathology and impairment in cognition. In secondary and tertiary hospitals, while its clinical utility as a first-line test stands, AlzOn also lends clinicians with the original clinical utility as an aid to the enrichment of AD diagnosis. Given that final AD diagnosis is made by clinician's judgement based on a series of diagnostic measures and that so-called 'golden-standard' biomarkers, namely amyloid PET and CSF biomarker tests are not practical for routine clinical use due to high cost and invasiveness, respectively, AlzOn, as a simple, inexpensive AD biomarker can be used along with brain imaging in differential diagnosis for cause of dementia. Additionally, its characteristic of reflecting peripheral amyloidosis secures its clinical utility as a test that detects the ongoing amyloid pathology, a desirable option for those finding the cost of amyloid PET unaffordable.

AlzOn is also being used in medical check-up centers as an AD risk factor test for those who concerned about memory loss or subjectively complaining memory decline. With results of high Aβ oligomerization tendency level, people can proactively head-start on early intervention followed by consultation with clinicians.

IC-KDA 2023

International Conference of the Korean Dementia Association

Session 3
Update in Treatment of Dementia

Nov 24 (Fri) 15:50-17:20 I 301 Grand Ballroom

CHAIRPERSONS

Kee Hyung Park (Gachon University College of Medicine, Republic of Korea)

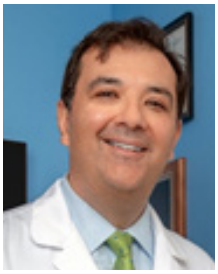
Sang Won Seo (Sungkyunkwan University, Republic of Korea)

15:50 – 16:20 **Advances in AD Experimental Therapeutics**
Alireza Atri (Banner Sun Health Research Institute (AZ) & Harvard Medical School (MA), USA)

16:20 – 16:50 **Gene Therapy for Neurodegenerative Diseases**
Jae young Lee (ToolGen, Republic of Korea)

16:50 – 17:20 **Neuromodulation for Gliopathy in Alzheimer's Disease**
Tae Kim (GIST, Republic of Korea)

SESSION 3 15:50 – 16:20 | 301 Grand Ballroom



Alireza Atri

Banner Sun Health Research Institute (AZ) & Harvard Medical School (MA), USA

Educational Background & Experience

Present	Banner Sun Health Research Institute, Sun City	Director
Present	NIA/NIH-funded Arizona Alzheimer's Disease Research Center	Associate Director
Present	Harvard Medical School (HMS), Boston, MA, USA	Part-time faculty
	Massachusetts General Hospital-Brigham	Internship, Residency
	MGH/HMS (Cognitive Neurology)	Fellowships

Advances in AD Experimental Therapeutics

This lecture will provide an overview of the most recent developments in AD experimental therapeutics, including the current AD drug development pipeline, and with a focus on the latest data (efficacy, safety) and considerations (e.g. patient selection; risk assessment; ARIA detection, monitoring and management) regarding amyloid plaque lowering monoclonal antibodies (e.g. lecanemab, aducanumab, donanemab) from clinical trials to clinical practice.

SESSION 3 16:20 – 16:50 | 301 Grand Ballroom

Jae young Lee

ToolGen, Republic of Korea

Educational Background & Experience

2018-Now	ToolGen	Director
2016-2018	ToolGen	Senior Researcher
2015-2016	Monash University	Postdoctoral Research Fellow
2011-2015	Monash University	PhD in Medicine
2007-2010	University of Melbourne	B. Eng (Biocellular)

Gene Therapy for Neurodegenerative Diseases

Despite advances in therapeutic developments in dementia field including Alzheimer's disease, there are significant unmet needs. Gene therapy has become one of the important therapeutic modalities to various diseases. Here I review recent progress on gene therapy approach for neurodegenerative diseases including Alzheimer's disease. The opportunities and potential hurdles that needs to be addressed for gene therapy development for neurological diseases will also be discussed.

SESSION 3 16:50 – 17:20 | 301 Grand Ballroom

Tae Kim

GIST, Republic of Korea

Educational Background & Experience

2016-Present	GIST	Associate Professor
2014-2016	Kyung Hee University Hospital at Gangdong	Clinical Professor
2013-2014	Seoul National University Bundang Hospital Department of Psychiatry	Clinical Fellow & Clinical Instructor
2008-2013	Harvard Medical School Department of Psychiatry	Postdoc Fellow & Instructor
2009	Kyung Hee University College of Medicine	PhD
2004	Kyung Hee University College of Medicine	MS
1999-2004	Kyung Hee Medical Center Department of Psychiatry	Internship & Psychiatry residency
1999	Kyung Hee University College of Medicine	MD

Neuromodulation for Gliopathy in Alzheimer's Disease

The pathophysiology of Alzheimer's disease (AD) remains incompletely understood, although emerging evidence suggests that glial cells contribute to disease progression. In recent years, non-invasive neuromodulation techniques have been proposed as potential therapeutic interventions to modulate glial pathophysiology. One such avenue is gamma entrainment, which has shown promise in reducing AD pathology. In this symposium, we present our novel research findings centered on astrocytic GABA in AD. Firstly, we identify the presence of astrocytic GABA in sleep-promoting areas in AD models. Secondly, we demonstrate that 40Hz acoustic stimulation leads to a reduction in astrocytic GABA levels. Thirdly, we establish a correlation between sleep disturbances and altered astrocytic GABA levels. We further probe the underlying mechanisms, revealing that neuronal activity induces astrocytic volume expansion, leading to a secondary increase in calcium influx—changes that potentially exert a protective effect on brain pathology. These findings hint at the intriguing possibility that the benefits of gamma entrainment may be mediated through a cascade of secondary responses initiated by changes in astrocytes. In conclusion, our research suggests that 40Hz acoustic neuromodulation could trigger glial alterations, thereby offering a promising therapeutic avenue for ameliorating AD pathology.

IC-KDA 2023

International Conference of the Korean Dementia Association

Korea-Taiwan Joint Symposium 1

Nov 25 (Sat) 08:30-09:30 l 205 Summit Hall

CHAIRPERSONS

SangYun Kim (Seoul National University Bundang Hospital, Republic of Korea)

Jong-Ling Fuh (National Yang Ming Chiao Tung University, Taiwan)

08:30 – 08:50 **Can Fluid Biomarker Testings Change the Diagnosis and Management of Dementia?**
Yung Shuan Lin (Taipei Veterans General Hospital, Taiwan)

08:50 – 09:10 **Alzheimer's Disease Biomarkers: Towards a New Era in the Diagnosis and Treatment of AD Based on Blood Biomarkers**
Seong-Ho Koh (Hanyang University Guri Hospital, Republic of Korea)

09:10 – 09:30 **What is the Role of Brain Imaging in the Diagnosis of Dementia?**
Yung Shuan Lin (New Taipei Municipal TuCheng Hospital, Taiwan)

KOREA-TAIWAN JOINT SYMPOSIUM 1 08:30 – 08:50 | 205 Summit Hall

Yung Shuan Lin

Taipei Veterans General Hospital, Taiwan

Educational Background & Experience

2022-Present	Neurological institute, Taipei Veterans General Hospital	Attending physician
2020-2022	Neurological institute, Taipei Veterans General Hospital	Fellow
2017-2020	Neurological institute, Taipei Veterans General Hospital	Resident

Can Fluid Biomarker Testings Change the Diagnosis and Management of Dementia?

Considerable efforts have been directed towards redefining Alzheimer's disease (AD) from a biological standpoint rather than relying solely on clinical syndromes. This transformative perspective views AD as a continuous spectrum, encompassing the progression from asymptomatic brain pathology to overt clinical symptoms.

Other than CSF assays, blood-based biomarkers have been developed and clinically studied; with some demonstrated excellent diagnostic performance. The draft of the updated criteria had incorporated blood-based biomarkers (BBB) for disease diagnosis and staging. Seemingly, BBB could work alongside CSF-based and imaging biomarkers or even being a stand-alone approach, offering a more cost-effective and less invasive avenue for diagnosing AD.

Altogether, the paradigm of diagnosing Alzheimer's disease (AD) has been changed from clinical to biological diagnosis. As the landscape of AD diagnosis continues to evolve, these biological markers serve as promising tools for achieving more accurate, timely, and cost-effective diagnoses, ultimately enhancing our understanding and management of this intricate condition.

KOREA-TAIWAN JOINT SYMPOSIUM 1 08:50 – 09:10 | 205 Summit Hall

Seong-Ho Koh

Hanyang University Guri Hospital, Republic of Korea

Educational Background & Experience

2016-2016	Immunology, Genetics and Pathology, Uppsala University, Uppsala, Sweden	Visiting Scholar and researcher
2013-2014	Neurology and Radiology, Harvard Universtity College of Medicine, Boston, MA, USA	Visiting Scholar and research fellow
2005-2007	Department of Neurology, Hanyang University College of Medicine, Seoul, Korea	Doctor of Philosophy (Ph.D.)
2002-2005	Department of Neurotoxicology, National Institute of Toxicological Research, Korea Food and Drug Administration, Seoul, Korea	Researcher
1998-2002	Department of Neurology, Hanyang University Hospital, Seoul, Korea	Residency
1991-1997	Hanyang University College of Medicine, Seoul, Korea	Bachelor of Medicine

Alzheimer's Disease Biomarkers: Towards a New Era in the Diagnosis and Treatment of AD Based on Blood Biomarkers

Alzheimer's disease (AD) is a prevalent brain disorder leading to the most common form of dementia, marked by a progressive decline in memory and cognitive abilities. As the global population ages, AD cases are on the rise. While a detailed medical history and neurological examination remain essential for AD diagnosis, recent technological advancements have significantly improved diagnostic precision. Modern imaging techniques, including amyloid and tau PET scans, illuminate the pathological changes in the brains of dementia patients. Leveraging these techniques, we can diagnose or exclude AD in those with mild cognitive impairment and early-stage dementia. This precision allows us to select the most suitable AD patients for clinical trials and assess the diagnostic potential of fluid biomarkers from cerebrospinal fluid (CSF) and blood. Thanks to cutting-edge methods, we now understand that fluid biomarkers can rival the accuracy of imaging markers. Numerous fluid indicators, including amyloid beta 42, 40, their ratios, pTau217, 181, and 231, GFAP, neurofilament light chain, among others, sourced from CSF and blood, are under investigation for their diagnostic and monitoring capabilities in AD. Multiple phase-3 clinical trials have corroborated the potential of these fluid biomarkers in AD patient pre-screening, screening, and monitoring. These revelations have spurred the National Institute on Aging and the Alzheimer's Association (NIA-AA) to propose a revision of AD diagnostic criteria, incorporating many of these fluid biomarkers. Given these advancements, it's evident that we are on the cusp of a transformative phase in AD diagnosis that pivots on fluid biomarkers. Consequently, my presentation will delve into the pivotal role of fluid biomarkers in diagnosing and tracking AD progress.

KOREA-TAIWAN JOINT SYMPOSIUM 1 09:10 – 09:30 | 205 Summit Hall

Jung Lung Hsu

New Taipei Municipal TuCheng Hospital, Taiwan

Educational Background & Experience

2020-now	New Taipei Municipal TuCheng Hospital	Chief
2014-2020	Chang Gung Memorial Hospital, Linkou	Attending
1996-2014	SHIN KONG WHS MEMORIAL HOSPITAL	Attending
2004-2005	University of California San Diego	Clinical research fellow

What is the Role of Brain Imaging in the Diagnosis of Dementia?

Brain imaging plays an important role in the diagnosis of dementia. The following are some of the advantages of brain imaging in the diagnosis of dementia:

1. Identification of structural changes: Brain imaging techniques such as computed tomography (CT) and magnetic resonance imaging (MRI) can identify structural changes in the brain that may be associated with dementia, such as cortical atrophy and ventricular enlargement
2. Detection of other causes of cognitive impairment: Brain imaging can help rule out other causes of cognitive impairment, such as tumors, stroke, and hydrocephalus
3. Identification of biomarkers: Brain imaging can identify biomarkers associated with dementia, such as amyloid plaques and tau protein, which can help with early diagnosis and treatment
4. Monitoring disease progression: Brain imaging can be used to monitor disease progression and treatment response in patients with dementia
5. Research: Brain imaging is important in dementia research, as it can help identify changes in brain structure and function associated with dementia and aid in the development of new treatments

In summary, brain imaging plays a crucial role in the diagnosis of dementia by identifying structural changes, detecting other causes of cognitive impairment, identifying biomarkers, monitoring disease progression, and aiding in research.

IC-KDA 2023

International Conference of the Korean Dementia Association

Korea-Taiwan Joint Symposium 2

Nov 25 (Sat) 09:30-10:30 l 205 Summit Hall

CHAIRPERSONS

Dong Won Yang (The Catholic University of Korea, Republic of Korea)

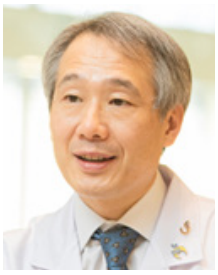
Chaur-Jong Hu (Taipei Medical University, Taiwan)

09:30 – 09:50 **What is the Appropriate Use of Amyloid Imaging Under the Situations that DMT Drugs Have Been Developed?**
Kee Hyung Park (Gachon University College of Medicine, Republic of Korea)

09:50 – 10:10 **How Can I Choose the Right Pharmacological Therapy for Alzheimer's Disease?**
Li-Kai Huang (Taipei Medical University Shuang-Ho Hospital, Taiwan)

10:10 – 10:30 **South Korean Study to Prevent Cognitive Impairment and Protect BRAIN Health through Lifestyle Intervention (SUPERBRAIN)**
Seong Hye Choi (Inha University College of Medicine, Republic of Korea)

KOREA-TAIWAN JOINT SYMPOSIUM 2 09:30 – 09:50 | 205 Summit Hall



Kee Hyung Park

Gachon University College of Medicine, Republic of Korea

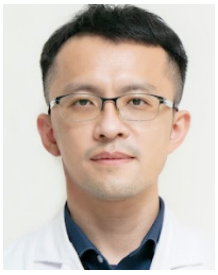
Educational Background & Experience

Present	Dept of Neurology, College of Medicine, Gachon University	Professor
Present	Gachon Brain Health Center, Gachon University Gil Hospital	Director
Present	Sleep Medicine Center, Gachon University Gil Hospital	Director
2010-2013	Dementia Prevention & Management Agency of Incheon City Government	Director
2010-2011	UC San Francisco	Visiting professor
2008-2009	national-wide education program of dementia specialist for nurses, supported by Korean Ministry of Health & Welfare	Director

What is the Appropriate Use of Amyloid Imaging Under the Situations that DMT Drugs Have Been Developed?

Amyloid positron emission tomography (PET) is an important and increasingly used, reliable, in vivo tool for the detection of amyloid plaques in Alzheimer's disease (AD), differential diagnosis of dementia and for guiding changes in clinical management. The introduction and approval of anti-amyloid disease-modifying therapy for mild cognitive impairment (MCI) and early AD is likely to impact the use of amyloid PET. Based on existing international guidelines and results of a commissioned survey of Korean physicians specializing in dementia (n =59), we developed consensus Korean guidelines for the appropriate use of amyloid PET in AD. Key recommendations include the use of amyloid PET for individuals who meet the following preconditions: 1) A cognitive complaint with objectively confirmed impairment; 2) When knowledge of the presence or absence of β-amyloid (Aβ) pathology is expected to increase diagnostic certainty and alter management. Amyloid PET is generally recommended for use in most cases, regardless of age, with only a few exceptions, and its use is particularly emphasized for `MCI due to AD', `mild stage of probable AD dementia', and `increasing the certainty of differential diagnosis of AD'.

KOREA-TAIWAN JOINT SYMPOSIUM 2 09:50 – 10:10 | 205 Summit Hall



Li-Kai Huang

Taipei Medical University Shuang-Ho Hospital, Taiwan

Educational Background & Experience

2014-Present	Department of Neurology, Taipei Medical University Shuang-Ho Hospital	Attending Physician
2019-Present	Taiwan Dementia Society	Vice Secretary
2009-2013	Department of Neurology, Taipei Medical University Shuang-Ho Hospital	Resident
2000-2008	China Medical University, Taiwan	

How Can I Choose the Right Pharmacological Therapy for Alzheimer's Disease?

Effective pharmacological treatments for Alzheimer's Disease (AD) depend significantly on accurate diagnosis, with a growing emphasis on biomarkers such as amyloid-β (Aβ), tau pathology, and other indicators for qualitative and quantitative assessment. The US FDA has granted accelerated approval to ADUHELM® and traditional approval to LEQEMBI® for AD management, but these treatments present several challenges, including administration methods, financial costs, imaging requirements, and specialized healthcare facilities. Appropriate Use Recommendations (AURs) stress the importance of meticulous patient selection, continuous monitoring, and healthcare provider readiness for the proper use of lecanemab and aducanumab. Cholinesterase inhibitor (ChEI) drugs like donepezil, galantamine, or rivastigmine are the standard AD treatments, commonly licensed and reimbursed by National Health Systems in many countries. However, clinical practice reveals that only 30 to 60 percent of patients exhibit a modest clinical response. Predicting a patient's response before treatment initiation would be valuable. Gray matter brain age can predict long-term cognitive outcomes of ChEI treatment in patients with a Clinical Dementia Rating (CDR) of 0.5, aiding in distinguishing between ChEI-responsive and ChEI-unresponsive individuals.

KOREA-TAIWAN JOINT SYMPOSIUM 2 10:10 – 10:30 | 205 Summit Hall

Seong Hye Choi

Inha University College of Medicine, Republic of Korea

Educational Background & Experience

2022 - Now	Society for Cognitive Intervention	Chairman
1999 - Now	College of Medicine, Inha University	Professor
2006	University of Pittsburg	Research scholar
2003	PhD at College of Medicine, Seoul National University	
1993	Master degree at College of Medicine, Seoul National University	

South Korean Study to Prevent Cognitive Impairment and Protect BRAIN Health through Lifestyle Intervention (SUPERBRAIN)

In the South Korean study to Prevent cognitive impairment and protect BRAIN health through lifestyle intervention in at-risk elderly people (SUPERBRAIN), participants without dementia and with one or more modifiable dementia risk factors, aged 60-79 years, were randomly assigned to the facility-based multidomain intervention (MI) (FMI; n=51), the home-based MI (HMI; n=51), or the control group receiving general health advice (n=50). The 24-week intervention comprised vascular risk management, cognitive training, social activity, physical exercise, nutrition guidance, and motivational enhancement using Tablet PC app. The FMI participants performed all intervention programs at a facility three times a week. The HMI participants performed some programs at a facility once every 1-2 weeks and performed others at home. In the FMI and HMI groups, the retention rates were 88.2% and 96.1%, and adherence to the intervention was 94.5% and 96.8%, respectively. The Repeatable Battery for the Assessment of Neuropsychological Status (RBANS) total scale index score improved significantly in the FMI (5.46 ± 7.50, P = 0.004) and HMI (5.50 ± 8.14, P = 0.004) groups compared to the control group (-0.74 ± 11.51). Serum brain-derived neurotrophic factor (BDNF) levels were significantly increased in the FMI group compared to the control group. Compared to the control group, plasma cortisol levels were significantly decreased in both the FMI and HMI groups at the study endpoint. Compared to the control group, body fat mass was significantly decreased in each of FMI and HMI groups, respectively. Compared with the control group, the mean global cortical thickness increased in the FMI group (0.033 ± 0.070 vs. − 0.003 ± 0.040, p = 0.013); particularly, cortical thickness of the bilateral frontotemporal lobes, cingulate gyri, and insula increased. Regional homogeneity value in the left medial orbitofrontal gyrus was increased and correlated positively with serum BDNF changes.

In SUPERBRAIN-Alzheimer's disease (AD) study, SUPERBRAIN-based multidomain intervention with nutritional supplements improved cognition and gut microbiota in patients with early symptomatic AD who were amyloid-positive by positron emission tomography.

In conclusion, the SUPERBRAIN are feasible and likely to delay cognitive impairment in at-risk older people and early symptomatic AD. Multidomain lifestyle interventions may influence the brain through inactivation of the HPA axis and enhanced brain plasticity.

IC-KDA 2023

International Conference of the Korean Dementia Association

Session 4
The Recent Issues in Clinical Neuropsychology

Nov 25 (Sat) 09:00-10:30 l 301 Grand Ballroom

CHAIRPERSONS

So Young Moon (Ajou University, Republic of Korea)

Ju Hee Chin (Sungkyunkwan University, Republic of Korea)

09:00 – 09:30 **Unsupervised Remote Memory Assessments in Early Stages of Alzheimer's Disease**
David Berron (German Center for Neurodegenerative Diseases (DZNE), Germany)

09:30 – 10:00 **Predictive Utility of Machine Learning Approach with Neuropsychological Test in AD Spectrum**
Seyul Kwak (Pusan National University, Republic of Korea)

10:00 – 10:30 **Digital Neuropsychological Assessments for Frontotemporal Dementia**
Adam Staffaroni (University of California, San Francisco, USA)

SESSION 4 09:00 – 09:30 | 301 Grand Ballroom

David Berron

German Center for Neurodegenerative Diseases (DZNE), Germany

Educational Background & Experience

Since 2021	German Center for Neurodegenerative Diseases (DZNE), Magdeburg, Germany	Research Group Leader
2018-2021	Clinical Memory Research Unit, Lund University, Sweden	Postdoctoral Researcher
2017-2018	Institute of Cognitive Neurology and Dementia Research, Otto-von-Guericke University, Magdeburg, Germany	Postdoctoral Researcher
2012-2017	Institute of Cognitive Neurology and Dementia Research, Otto-von-Guericke University, Magdeburg, Germany	PhD in Cognitive Neuroscience
2006-2011	University of Bremen, Germany	Diploma in Psychology

Unsupervised Remote Memory Assessments in Early Stages of Alzheimer's Disease

Remote and unsupervised cognitive assessments via mobile devices such as smartphones and tablets hold the promise to facilitate case-finding and the individual detection of cognitive impairment in clinical and research settings. Here I will discuss how a suite of digital remote and unsupervised memory assessments can be used in Alzheimer's disease to detect mild cognitive impairment, how longitudinal digital remote memory assessments across an entire year capture memory change in MCI patients and how this relates to cognitive change in established in-clinic cognitive assessments.

SESSION 4 09:30 – 10:00 | 301 Grand Ballroom

Seyul Kwak

Pusan National University, Republic of Korea

Educational Background & Experience

2021-	Pusan National University	Assistant Professor
2020-2021	Boramae Medical Center, Psychiatry	Postdoctoral Associates
2020-2021	Boramae Medical Center, Psychiatry	Clinical Internship (Korean Clinical Psychological Association Accredited)
2016-2020	Psychology (Clinical) Seoul National University	Ph.D.
2014-2016	Psychology (Clinical) Seoul National University	M.A
2007-2015	Education and Psychology Yonsei University	B.A

Predictive Utility of Machine Learning Approach with Neuropsychological Test in AD Spectrum

Background: In assessing the levels of clinical impairment in dementia, a summary index of neuropsychological batteries has been widely used in describing the overall functional status.

Objective: It remains unexamined how complex patterns of the test performances can be utilized to have specific predictive meaning when the machine learning approach is applied.

Method: In this study, the neuropsychological battery (CERAD-K) and assessment of functioning level (Clinical Dementia Rating scale and Instrumental Activities of Daily Living) were administered to 2,642 older adults with no impairment (n = 285), mild cognitive impairment (n = 1,057), and Alzheimer's disease (n = 1,300). Predictive accuracy on functional impairment level with the linear models of the single total score or multiple subtest scores (Model 1, 2) and support vector regression with low or high complexity (Model 3, 4) were compared across different sample sizes.

Results: The linear models (Model 1, 2) showed superior performance with relatively smaller sample size, while nonlinear models with low and high complexity (Model 3, 4) showed an improved accuracy with a larger dataset. Unlike linear models, the nonlinear models showed a gradual increase in the predictive accuracy with a larger sample size (n > 500), especially when the model training is allowed to exploit complex patterns of the dataset.

Conclusions: Our finding suggests that nonlinear models can predict levels of functional impairment with a sufficient dataset. The summary index of the neuropsychological battery can be augmented for specific purposes, especially in estimating the functional status of dementia.

SESSION 4 10:00 – 10:30 | 301 Grand Ballroom

Adam Staffaroni

University of California, San Francisco, USA

Educational Background & Experience

2018-present	UCSF	Assistant Professor
2016-2018	UCSF	Postdoctoral Fellow
2016	Palo Alto University	PhD, Clinical Psychology

Digital Neuropsychological Assessments for Frontotemporal Dementia

Frontotemporal dementia (FTD) is a neurodegenerative disease that manifests with impairments in cognition, behavior, language, or motor functioning. Digital tools are being developed to quantify impairments in the domains affected by FTD. In addition to improving clinical care, these tools can enable remote assessments that can be useful for addressing barriers to recruitment for observational research and clinical trials in FTD. This presentation will review existing digital technologies for the assessment of FTD, including tablet-based testing solutions and smartphone application.

IC-KDA 2023

International Conference of the Korean Dementia Association

Plenary Session III

Nov 25 (Sat) 10:50-11:30 l 301 Grand Ballroom

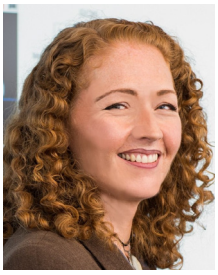
CHAIRPERSON

Kun-Woo Park (Korea University, Republic of Korea)

10:50 – 11:30 **Social Cognition in Neurodegenerative Diseases**

Katherine P. Rankin (University of California San Francisco, USA)

PLENARY SESSION III 10:50 – 11:30 | 301 Grand Ballroom



Katherine P. Rankin

University of California San Francisco, USA

Educational Background & Experience

2020 - present	UCSF Bakar Computational Health Sciences Institute	Professor
2020 - present	UCSF Global Brain Health Institute	Professor
2014 - present	University of California San Francisco	Professor in Residence
2008 - 2014	University of California San Francisco	Associate Professor in Residence
2008 - 2010	University of California San Francisco	Associate Adjunct Professor

Social Cognition in Neurodegenerative Diseases

The dementia field has come to consensus on how to evaluate patients with neurodegenerative disease in traditional domains of cognitive functioning such as memory, visuospatial, language, and executive functioning; however, neuropsychological evaluation of socioemotional cognition remains overlooked in research and clinic. Significant advances in social cognitive neuroscience have provided important insights into the neural circuits underpinning socioemotional behaviors such as empathy, self-awareness, warmth, and reading others' intentions, and these findings help explain why these behaviors change in syndromes like behavioral variant frontotemporal dementia, semantic variant primary progressive aphasia, and right temporal lobe degeneration. We will examine how the intrinsically connected functional networks for salience and semantic appraisal normally function to support social behavior, and will show how changes to the functioning in these networks leads to behavioral dysfunction in neurodegenerative disease. We will also examine neuropsychological tests that can be used in research and clinical settings to evaluate social cognition in patients with dementia, and discuss international efforts to develop and validate these tests across languages and cultures.

IC-KDA 2023

International Conference of the Korean Dementia Association

Plenary Session IV

Nov 25 (Sat) 11:30-12:10 l 301 Grand Ballroom

CHAIRPERSON

Jee Hyang Jeong (Ewha Womans University, Republic of Korea)

11:30 – 12:10 **Creating a Worldwide Platform Trial for Genetic Frontotemporal Dementia - The FTD Prevention Initiative**

Jonathan Rohrer (University College London, UK)

PLENARY SESSION IV 11:30 – 12:10 | 301 Grand Ballroom

Jonathan Rohrer

University College London, UK

Educational Background & Experience

2021-Present	Neurology at the Dementia Research Centre, UCL Institute of Neurology	Professor
2014-Present	National Hospital for Neurology and Neurosurgery	Honorary Consultant Neurologist
2018	Royal College of Physicians	Fellow
2010	Neuroscience at UCL Queen Square Institute of Neurology	Ph.D.

Creating a Worldwide Platform Trial for Genetic Frontotemporal Dementia - The FTD Prevention Initiative

The Frontotemporal dementia Prevention Initiative (FPI) is a worldwide study of FTD with a focus on the familial forms. It brings together a number of ongoing cohort studies around the world including ALLFTD in the US, GENFI in Europe and Canada, DINAD in Australia, FTDGeNZ in New Zealand, ReDLat in South America, South East Asia FTD consortium, FTLD-J in Japan and networks in India and China as well as the LEAF-FTD study in Korea. The aim is to promote clinical trials of new therapies in FTD with the key goals of creating uniform standards for the conduct of trials, creating an international database of FTD research participants eligible for trials, and promoting responsible data sharing in both observational and pharma-led trials. Particular highlights of the FPI so far include the development of clinical rating scales, validation of multimodal biomarkers that could be used as outcome measures in trials, and the validation of fluid biomarkers including plasma neurofilament light chain. Further studies are ongoing in genomics and digital biomarkers. The culmination of these studies will be the development of a worldwide platform trial for testing novel therapies in FTD. The first of these will be focused on people with mutations in the MAPT gene and planning is already underway. Future studies are needed to refine the outcome measures being used and to expand trials across all forms of FTD.

IC-KDA 2023

International Conference of the Korean Dementia Association

Luncheon Symposium 2

Nov 25 (Sat) 12:10-13:00 l 301 Grand Ballroom

CHAIRPERSON

Yong Soo Shim (The Catholic University of Korea, Republic of Korea)

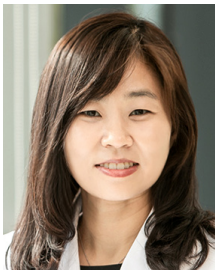
12:10 – 12:35 **Advancing Dementia Care: The Innovative Donepezil Patch and its Influence on Enhancing Compliance (Supported by Celltrion)**

Geon Ha Kim (Ewha Womans University College of Medicine, Republic of Korea)

12:35 – 13:00 **Optimizing Treatment Strategies: Focusing on Donepezil's Role in Neuroprotection and Early-Stage Alzheimer's Disease (Supported by Eisai)**

Hyemin Jang (Seoul National University Hospital, Republic of Korea)

LUNCHEON SYMPOSIUM 2 12:10 – 12:35 | 301 Grand Ballroom



Geon Ha Kim

Ewha Womans University College of Medicine, Republic of Korea

Educational Background & Experience

2021-Present	Department of Neurology, Ewha W. University College of Medicine, Ewha W. University Mokdong Hospital, Seoul, South Korea	Associate Professor
2019-2021	Department of Neurology, Ewha W. University College of Medicine, Ewha W. University Mokdong Hospital, Seoul, South Korea	Clinical Associate Professor
2013-2019	Department of Neurology, Ewha W. University College of Medicine, Ewha W. University Mokdong Hospital, Seoul, South Korea	Clinical Assistant Professor
2009-2012	Department of Neurology, Samsung Medical Center, Seoul, South Korea	Fellow
2015	Ewha W. University, School of Medicine, Seoul, South Korea	Ph.D

Advancing Dementia Care: The Innovative Donepezil Patch and its Influence on Enhancing Compliance

The global prevalence of dementia continues to rise, necessitating the development of a variety of therapeutic approaches to improve patient outcomes and alleviate the burden on caregivers and healthcare systems. Donepezil, an established cholinesterase inhibitor, has demonstrated efficacy in ameliorating cognitive decline associated with Alzheimer's disease. However, oral administration often presents challenges, including adherence issues and gastrointestinal side effects. The development of the transdermal Donepezil Patch offers a promising alternative, delivering controlled dosing and circumventing oral administration challenges. This lecture introduces the influence of the Donepezil Patch on enhancing treatment compliance in patients with dementia.

LUNCHEON SYMPOSIUM 2 12:35– 13:00 | 301 Grand Ballroom

Hyemin Jang

Seoul National University Hospital, Republic of Korea

Educational Background & Experience

2023.9-	Seoul National University hospital	Clinical Assistant Professor
2020.3-	Samsung Medical Center	Research Assistant professor
2022.8-2023.8	Samsung Advanced Institute for Health Sciences & Technology	Professor
	Samsung Advanced Institute for Health Sciences & Technology	

Optimizing Treatment Strategies: Focusing on Donepezil's Role in Neuroprotection and Early-Stage Alzheimer's Disease

1. Neuroprotective mechanisms of donepezil
- Donepezil has shown neuroprotective effects against Aβ42-induced neuronal toxicity, glutamate excitotoxicity and cholinergic depletion, alluding to it's potentially disease-modifying effect.

2. The Benefits of Early Treatment in Alzheimer's Disease
- In clinical trials, early and continuous donepezil preserves function, specifically cognitive function more effectively than delayed treatment
- Removal of false-positives from clinical trials which targeted MCI patients allowed unmasking of the beneficial effects of donepezil to the full extent.

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Session 5
Update in FTD (Including FTD Cohort Study)

Nov 25 (Sat) 14:00-15:30 l 301 Grand Ballroom

CHAIRPERSONS

Jonathan Rohrer (University College London, UK)

Eun Joo Kim (Pusan National University Hospital, Republic of Korea)

14:00 – 14:30 **North American FTD Registry (ALLFTD)**
Howard Rosen (University of California San Francisco, USA)

14:30 – 15:00 **Korean FTD Registry (LEAF-FTD)**
Eun Joo Kim (Pusan National University Hospital, Republic of Korea)

15:00 – 15:30 **Familial FTD in China: Progress and Prospects**
Qin Chen (West China Hospital of Sichuan University, China)

SESSION 5 14:00 – 14:30 | 301 Grand Ballroom

Howard Rosen

University of California San Francisco, USA

Educational Background & Experience

2004 - Present	UCSF Alzheimer's Disease Research Center	Director of Education
1996 - 1999	Washington University School of Medicine	Fellow
1993 - 1996	University of California, San Francisco	Resident
1989 - 1992	Albert Einstein College of Medicine	Intern
1983 - 1989	Boston University School of Medicine	M.D.
1983 - 1989	Boston University College of Liberal Arts Six-Year BA/MD Program; Minor: Philosophy	B.A.

North American FTD Registry (ALLFTD)

Advances in the scientific understanding of frontotemporal lobar degeneration (FTLD) have brought closer the possibility of disease modifying treatments this devastating disorder. The ARTFL-LEFFTDS Longitudinal Frontotemporal Lobar Degeneration (ALLFTD) consortium was established in 2014 to accelerate the development of disease modifying treatments (DMTs) for FTLD. The project has made remarkable progress, conducting over 4,000 visits with more than 2,500 participants with familial and sporadic FTLD across 28 North American sites. Major achievements include establishing the value of clinical rating scales, cognitive tests, MRI-based volumetrics and Neurofilament Light Chain (NfL) as important markers of disease evolution, and assembling these measures into mutation-specific multimodal models that can define an individual's status on the path toward symptoms and dramatically improve efficiency in clinical trials. ALLFTD has also identified new clinical and fluid based measures that may track with disease over time, and may mediate individual variation in vulnerability to neurodegeneration. Lastly, the consortium has piloted the use of mobile-phone-based applications that could further increase efficiency for clinical trials and expand opportunities for research participation.

SESSION 5 14:30 – 15:00 | 301 Grand Ballroom

Eun Joo Kim

Pusan National University Hospital, Republic of Korea

Educational Background & Experience

May. 2021 - present	Department of Neurology, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea	Professor
Sep. 2015 - Aug. 2017	Department of Neurology, University of California, Memory and Aging Center, Seeley lab, San Francisco, California, USA,	Visiting assistant professor
May. 2015 – Apr. 2021	Department of Neurology, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea	Associate professor
May. 2011 - Apr. 2015	Department of Neurology, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea	Assistant professor
Mar. 2008 – Apr. 2011	Department of Neurology, Pusan National University Hospital, Pusan National University School of Medicine, Busan, Korea	Clinical Instructor
Nov. 2005 – Feb. 2008	Memory and aging center, Department of Neurology, University of California, San Francisco, San Francisco, California, USA	Postdoc Scholar
Mar. 2003 – Oct. 2005	in Behavioral Neurology, Department of Neurology, Sungkyunkwan University School of Medicine, Seoul, Korea	Fellowship

Korean FTD Registry (LEAF-FTD)

LEAF (Longitudinal study of early onset dementia and family members) is a Korean early onset dementia cohort which started from Apr. 2021 and 31 centers across Korea participated in the LEAF. LEAF-FTD is one of sub-studies of LEAF (LEAF-AD, LEAF-FTD, and LEAF-Other early onset dementia) and recruits patients with bvFTD, svPPA, nfvPA, FTD-MND, CBS and PSPS. Almost 80 patients with sporadic and familial FTD have been enrolled in LEAF-FTD.

SESSION 5 15:00 – 15:30 | 301 Grand Ballroom

Qin Chen

West China Hospital of Sichuan University, China

Educational Background & Experience

2022-Present	Department of Neurology, West China Hospital of Sichuan University	Professor of Neurology
2019-2020	Center for Advanced imaging research, Mayo Clinic	Research Fellow
2017-2019	Center for Advanced imaging research, Mayo Clinic	Visiting Scientist
2013-2022	Department of Neurology, West China Hospital of Sichuan University	Associate Professor of Neurology
2012-2013	Department of Neurology, West China Hospital of Sichuan University	Chief resident of Neurology
2010-2012	Department of Neurology, West China Hospital of Sichuan University	Postdoc Research Fellow
2009-2010	Martino's Biomedical Image Center, Massachusetts General Hospital, Harvard Medical School, Harvard University	Research Fellow
2006-2010	Department of Neurology, West China Hospital of Sichuan University	Ph.D.
1999-2006	Department of Neurology, West China Hospital of Sichuan University	M.D.

Familial FTD in China: Progress and Prospects

Background: Frontotemporal dementia (FTD) is a set of clinical syndromes characterized by progressive abnormalities in behavior, executive function, language, with a strong genetic background. However, the familiar FTD studies were rare in China. Here we aim to review the previous cross-sectional reports of Chinese FTD patients with gene mutations, as well as the update status of the longitudinal familiar FTD study by the Chinese Familial Frontotemporal Lobar Degeneration Consortium (CFFC).

Method: We performed a comprehensive electronic searches to review current status of Chinese FTD patients with gene **mutations.** To start a multi-center longitudinal cohort of familiar FTD, we established the CFFC in October 2022 by involving 7 top teaching hospitals across China, and are expanding to more than 20 centers in the future. Patients with MAPT, GRN and C9orf72 mutations were enrolled and followed up according the designed framework.

Result: Based on the previous reports, genetic mutations accounted for 5.13%-27.9% as reported in a few cross-sectional cohort of Chinese FTD patients. Mostly reported pathogenic variants were MAPT, followed by GRN, TBK1, CHCHD10, C9orf72 repeat expansions, VCP, and SQSTM1. Up till now, there were 26 pedigrees with MAPT mutations, 11 pedigrees with GRN mutations and 9 pedigrees with C9orf72 repeat expansions mutations have been enrolled in the longitudinal multi-center cohort study by the CFFC. Furthermore, the CFFC aimed to set up social behavioral assessment scale suitable for Chinese patients with bvFTD, develop voice-based digital biomarkers for different types of PPA, and participant in international Phase III clinical trials for familial FTD.

Conclusion: The high prevalence of MAPT mutations in Chinese patients with FTD, may implies a genetic heterogeneity between Chinese and other ethnics. Longitudinal studies with larger sample size to modeling the trajectory of biomarkers in genetic mutation carriers for earlier diagnosis and intervention are needed in the future.

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Session 6
Pathogenesis of non-AD dementia

Nov 25 (Sat) 15:50-17:20 l 301 Grand Ballroom

CHAIRPERSONS

Yong Jeong (KAIST, Republic of Korea)

Yun Kyung Kim (KIST, Republic of Korea)

15:50 – 16:20 **Molecular Neuropathology of Chronic Traumatic Encephalopathy (CTE) Reveals Alzheimer's Disease-like Signatures**
Hoon Ryu (KIST, Republic of Korea)

16:20 – 16:50 **Molecular Mechanism of α-Synuclein in Non-AD Dementia**
Seung-Jae Lee (Seoul National University, Republic of Korea)

16:50 – 17:20 **Identifying the Early Events in ALS Pathogenesis**
Jeehye Park (University of Toronto, Canada)

SESSION 6 15:50 – 16:20 | 301 Grand Ballroom

Hoon Ryu

KIST, Republic of Korea

Educational Background & Experience

2019- Present	University of Science and Technology	Professor
2019-2020	Center for Neuroscience, Brain Science Institute, KIST	Head
2009-2013	Department of Biomedical Science, Seoul National University Graduate School	WCU Associate Professor
2007-2019	Department of Neurology, Boston University School of Medicine, MA, USA	Associate Professor
2004 - 2006	Department of Neurology, Boston University School of Medicine, MA, USA	Assistant Professor
2000 - 2003	Harvard Medical School and The Beth Israel Deaconess Medical Center, MA, USA	Instructor
1997-1999	Dana-Farber Cancer Institute and Harvard Medical School, MA, USA	Post-Doc & Research Associate
1983-1992	Jeonbuk National University, Graduate School	BS, MS, PhD

Molecular Neuropathology of Chronic Traumatic Encephalopathy (CTE) Reveals Alzheimer's Disease-like Signatures

Chronic traumatic encephalopathy (CTE) is a progressive neurodegenerative disorder associated with repetitive head injury with distinctive neuropathological features that differentiate it from other neurodegenerative diseases. Intraneuronal tau aggregates, albeit in different patterns, are diagnostic neuropathological features of CTE, but the exact mechanism of tauopathy is not known in CTE. We performed multiomic analyses of post-mortem brain tissues from CTE patients and compared the results to normal subjects to determine the molecular signature changes associated with CTE. We found that gene signatures related to MAP Kinase and calcium signaling pathways were significantly down regulated in CTE. The altered expression of protein phosphatases (PP) suggests that the tauopathy found in CTE shares common pathological mechanisms similar to Alzheimer's disease (AD). Using cell lines and animal models, we further verified that reduced PPP3CA/PP2B phosphatase activity is directly linked to and inversely correlated with an increase in phosphorylated tau. This finding provides an important insight into PP-dependent neurodegeneration that may be a novel biomarker and therapeutic target to modulate the tauopathy associated with CTE.

SESSION 6 16:20 – 16:50 | 301 Grand Ballroom

Seung-Jae Lee

Seoul National University, Republic of Korea

Educational Background & Experience

2015-Present	Seoul National University	Professor
2006-2015	Konkuk University	Professor
2000-2006	The Parkinson's Institute	Assistant Professor
1996-2000	Harvard Medical School	Instructor Postdoc
1995-1996	National Institutes of Health	Postdoc
1990-1995	POSTECH	PhD, MS
1985-1989	Seoul National University	BS

Molecular Mechanism of α-Synuclein in Non-AD Dementia

Neuropathological features of Alzheimer's disease (AD) include amyloid plaques, neurofibrillary tangles, and Lewy bodies, with the former preceding the latter two. However, how these compound proteinopathies are interconnected is not fully understood. Herein, we demonstrated that intracerebral transplantation of Aβ-activated microglia was sufficient to generate all the features of neurodegenerative diseases, including cognitive and motor deficits, compound proteinopathies such as tauopathy and synucleinopathy, gliosis, and neuroinflammation. The neuropathological features, including proteniopathies, gliosis, and neuroinflammation, were not limited to the injection site but rather spread progressively to diverse brain regions, reproducing another important feature of neurodegenerative diseases. These results suggest that our current protocol can be used to model neurodegenerative diseases, particularly the post-Aβ phase of AD. The relationships among these different proteinopathies have been investigated in the context of cross-seeding, and some positive results have been reported. We now propose an alternative mechanism in which Aβ oligomers activate microglia, creating an inflammatory microenvironment, which then promotes the aggregation of downstream aggregation-prone proteins, such as Tau and α-synuclein. The cross-seeding mechanism requires physical interactions between different aggregate proteins, whereas our microglia-driven mechanism relies on changes in the local environment that favors protein aggregation.

SESSION 6 16:50 – 17:20 | 301 Grand Ballroom

Jeehye Park

University of Toronto, Canada

Educational Background & Experience

2022-present	Genetics and Genome Biology Program, The Hospital for Sick Children, Canada	Senior Scientist
2016-present	Department of Molecular Genetics, University of Toronto, Canada	Assistant Professor
2015-2022	Genetics and Genome Biology Program, The Hospital for Sick Children, Canada	Scientist
2008-2015	Baylor College of Medicine, HHMI, USA	Postdoctoral Associate
2004-2008	Korea Advanced Institute of Science and Technology (KAIST), South Korea	PhD
2003-2004	Korea Advanced Institute of Science and Technology (KAIST), South Korea	MSc
1999-2003	Korea Advanced Institute of Science and Technology (KAIST), South Korea	BS

Identifying the Early Events in ALS Pathogenesis

Amyotrophic lateral sclerosis (ALS) is a devastating neurodegenerative disease that leads to progressive decline in motor impairment, muscle atrophy and paralysis. ALS studies provided significant insights into the disease process, which may involve various molecular pathways and cellular dysfunction that contribute to neurodegeneration. However, we still lack knowledge of how ALS starts to occur and develop, particularly the mechanism underlying the early phase of the disease process. Understanding the early disease stage rather than the late disease stage would enhance our chance of developing effective treatments that could stop or reverse the disease course. To identify the disease-initiating events leading to degeneration, we use our established ALS mouse model, MATR3 S85C knock-in (KI) mice. A missense mutation S85C is the most frequently identified ALS-linked mutation in MATR3, which encodes an RNA binding protein involved in RNA splicing. This newly established ALS model closely mimics the human disease genotype and phenotype, offering enhanced disease relevance compared to existing models in the ALS field and providing an unprecedented opportunity to study the early-stage development and progression of ALS. Using this mouse model, we pursue to 1) determine the early disease events in the disease process and 2) determine how the ALS-linked mutation alters MATR3 function and properties to cause neurodegeneration. Our findings will uncover the early disease process, which may change the view of how ALS develop and progress. Defining the key early events will facilitate the development of early prevention and intervention strategies for ALS.

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Poster Session

Poster Presenters

Basic Science and Pathogenesis

PE_001 Association between Western Diet-induced Visceral Adipose Tissue Inflammation and Alzheimer's Disease Pathology in a Mouse Model
Hae Won KIM (Keimyung University Dongsan Hospital)

PE_002 Immunotherapy Targeting Plasma ASM is Protective in a Mouse Model of Alzheimer's Disease
Byung Jo Choi (Kyungpook National University, Division of Biomedical Science)

PE_003 Discovery of a Novel Dual-action Small Molecule that Improves Multiple Alzheimer's Disease Pathologies
HEE JI YOON (Kyungpook National University, Division of Biomedical Science)

PE_007 Clinical Application of Sparse Canonical Correlation Analysis to Detect Genetic Associations with Cortical Thickness in Alzheimer's Disease
Bo-Hyun KIM (Samsung Medical Center)

PE_008 Discriminative Value of CSF Space Volume for Brain Atrophy for Neurodegenerative Diseases
Yu Hyun PARK (Samsung Medical Center)

PE_011 In Vivo and in Vitro Study of 17β Estradiol against Amyloid Beta Neurotoxicity in Synaptosomesof Agingfemale Rats : A Therapeutic Potential Drug for Alzheimer's Disease
Pardeep KUMAR (Jawaharlal Nehru University)

PE_012 Effects of the Ethanolic Extract of White Tea (Camellia sinensis) on Metabolic Functions in Alzheimer's Disease Rat Model
Rahul KUMAR (J K College)

PE_013 Deciphering Current Advances in Neuroinflammation in Alzheimer's Disease Through a Bibliometric Approach
Rian Ka PRAJA (Faculty of Medicine, Universitas Palangka Raya)

PE_014 Patient with PSEN1 Glu318Gly and Other Possible Disease Risk Mutations, Diagnosed with Early Onset Alzheimer's Disease
Seong Soo A An (Gachon University)

PE_015 Diminished Microglial Uptake Leads to Increased Amyloid Beta Depositions
Bo-Ram MUN (Chonnam National University)

PE_016 Generation of Human Induced Pluripotent Stem Cell (hiPSCs) based on Patients with Dementia: A Foundation for In Vitro Research
Su-Hee Jeon (Yonsei University College of Medicine)

PE_017 Positive Effects of Phosphatidylserine Adminstraition in 5xFAD Mice
Yeongjin Kim (Chonnam National University)

PE_018 Effect of Mitochondrial Deficiency in AD Model
Jin-Ha KIM (Chonnam National University)

PE_019 Synapse Density and Glial Activity was Altered in the Cortex of Ndufs4 HT Mice
Jiheon LEE (Chonnam National University)

PE_020 Methylation Profiling of Neurodegenerative Diseases
Kwanghoon LEE (Seoul National University College of Medicine)

PE_021 Glial Regulation in Alzheimer's Disease Model
Bo-Ram Mun (Chonnam National University)

PE_022 Effects of Mitochondrial Defect on Early-stage Mice Behavior
Su Been PARK (Chonnam National University)

PE_023 Visualization of 3R or 4R Tau Aggregation in Live Cells Using BiFC Platform
Dong Min Kang (Korea Institute of Science and Technology)

PE_024 Clinicopathological Mismatching in a Patient Presenting with Clinical Symptoms of Parkinson's Disease
Sang Jin Kim (Busan Paik Hospital, Inje University College of Medicine)

PE_025 Progranulin Haploinsufficiency Mediates TDP43 Cytoplasmic Aggregation with Lysosomal Dysfunction in the Human Model of Microglia
Min-Young Noh (College of Medicine, Hanyang University)

PE_026 Generation of iPSCs Derived from High Risk and Low Risk Alzheimer's Disease Patients Based on Polygenic Risk Score
Seung-Yeon Lee (Samsung Medical Center)

PE_027 Unraveling the Molecular Mechanism of Flavonoid Compounds in Bajakah as Potential Dual Inhibitory Effects to Prevent Amyloid-β Plaque and Tau Protein Aggregation
Muhammad Hasanul HAQ (Faculty of Mathematics and Natural Scienses, Palangka Raya University)

Biomarkers

PE_028 MRI-based Radiomics-informed Brain Age Matrices for Classifying Mild Cognitive Impairment Converters
Hanna LU (The Chinese University of Hong Kong)

PE_029 Predictive Modeling of Personalized Clinical Outcome Trajectories in Mild Cognitive Impairment
Si Eun Kim (Inje University College of Medicine, Haeundae Paik Hospital)

PE_030 Five-year Longitudinal Changes of Core Image Biomarkers, Amyloid and Tau, in Alzheimer's Disease Spectrum
Han-Kyeol KIM (Gangnam Severance Hospital, Yonsei University College of Medicine)

PE_031 Characteristics of Discordance between Amyloid Positron Emission Tomography and Plasma Amyloid-β 42/40 Positivity
Jung-Min PYUN (Soonchunhyang University)

PE_032 Aberrant GAP43 Gene Expression is Alzheimer's Disease Pathology-Specific
Jung-Min PYUN (Soonchunhyang University)

PE_034 Caudate Dopamine Loss, Occipital Hypoperfusion, and Dementia Conversion in Parkinson's Disease: A Dual-phase 18F-FP-CIT PET Study
Seok Jong CHUNG (Yonsei University College of Medicine)

PE_035 Predicting Superagers by Machine Learning Classification based on Gut Microbiome Features
Ha Eun Kim (Ewha Womans University)

PE_036 Independent Effect of Aβ Burden on Cognitive Impairment in Patients with Small Subcortical Infarction
Sung Hoon KANG (Korea University Guro Hospital)

PE_037 Ethnic Differences in the Effects of APOE ε4 and Vascular Risk Factors on Accelerated Brain Aging
Sung Hoon KANG (Korea University Guro Hospital)

PE_038 Sex-specific Relationship between Non-alcoholic Fatty Liver Disease and Amyloid-β in Cognitively Unimpaired Individuals
Sung Hoon KANG (Korea University Guro Hospital)

PE_039 Altered Functional Connectivity Density against Tau Accumulation in Alzheimer's Disease
Han-Kyeol KIM (Gangnam Severance Hospital, Yonsei University College of Medicine)

PE_040 Predicting Cognitive Stage Transition Using p-tau181, Centiloid, and Other Measures
Hyuk Sung KWON (Hanyang University Guri Hospital)

PE_041 Extra-neurite and Intra-neurite Conductivity Maps in Patients with MCI and AD
Geon-Ho JAHNG (Kyung Hee University Hospital at Gangdong)

PE_042 Gray-White Matter Boundary Tissue Volume and Its Z-Score Map in Patients with MCI and AD
Geon-Ho JAHNG (Kyung Hee University Hospital at Gangdong)

PE_044 Investigating Relative PSD Difference and Coherence Analysis in rEGG of Alzheimer's Disease
Chanda SIMFUKWE (Chung-Ang University)

PE_045 Distinct Effects of Cholesterol Profile Components on Amyloid and Vascular Burdens
Sung Hoon Kang (Korea University Guro Hospital)

PE_046 Elevated CSF pTau as a Predictor of Rapid Cognitive Decline in Preclinical Alzheimer's Disease
Soo Hyun CHO (Chonnam National University Hospital, Chonnam National University Medical School)

PE_047 Alteration of Limbic Metabolism Related to Alzheimer's Disease and Dementia with Lewy Bodies
Sung Woo KANG (Yonsei University College of Medicine)

PE_048 Association between T1w/T2w Ratio in White Matter and Cognitive Function in Alzheimer's Disease
Saenal LEE (Dongguk University Ilsan Hospital)

PE_049 Plasma Proteomic Profiling Predicts Proteins and Pathways Influencing Beta-Amyloid Oligomerization in the Blood
Dohyeon Kwon (Peoplebio Inc.)

PE_050 Distinct Prognostic Values of Non-Alzheimer's Pathologic Changes according to Cognitive Syndromal Stages: In individuals with Alzheimer's and Concomitant Cerebrovascular Burdens
Min Young CHUN (Samsung Medical Center, Sungkyunkwan University School of Medicine)

PE_051 A Case of Huntington's Disease Diagnosed by 18F-FDG-PET
Jae Young JOO (Uijeongbu Eulji Medical Center, Eulji University)

PE_052 Real World One Year Estimation of the Candidates for Lecanemab in a South Korea Memory Clinic
Kyunghwa SUN (Ajou University School of Medicine)

PE_053 Clinical and Pathological Validation of CT-Based Regional Harmonization Methods of Amyloid PET
Soo-Jong KIM (Samsung Medical Center, Sungkyunkwan University School of Medicine)

PE_054 Reversal of Age-dependent Amyloid Real-world Prevalence across Disease Severity Spectrum in a South Korean Memory Clinic
Kyunghwa SUN (Ajou University School of Medicine)

PE_055 Elevated Plasma Axon Guidance Molecule is Early Stage of Alzheimer's Disease-Specific and Associated with Amyloid and Tau Pathology
Ye Ji Lee (Hallym University, College of Medicine)

PE_056 Distinct Cerebral Cortical Microstructural Changes in Idiopathic Normal-Pressure Hydrocephalus
Kyunghun KANG (School of Medicine, Kyungpook National University)

PE_057 Association of Cerebrospinal Fluid (CSF) Synaptosomal-Associated Protein 25 (SNAP-25) and Cognitive Functions in Alzheimer Disease
Roland HELMIZAR (Baiturrahmah University)

PE_058 Genetic Analysis of Method, Kit and Device for Risk Assessment of Alzheimer's Dementia
Ramlah RAMLAH (Universitas Sulawesi Barat)

PE_059 Bibliometric Analysis on Brain Aging Biomarkers
Rian Ka PRAJA (Faculty of Medicine, Universitas Palangka Raya)

PE_060 Clinical Utility of Plasma Alzheimer's Biomarkers across Asian Neurodegenerative Dementias: Cross-sectional Study in Large Multi-center Cohort
Da Eun SHIN (Samsung Medical Center)

PE_061 Brain Metabolic Resilience in Alzheimer's Disease: A Predictor of Cognitive Decline and Conversion to Dementia
Hyun Woo Lee (Samsung Medical Center)

PE_062 fNIRS Signal as a Potential Biomarker for White Matter Hyperintensity Progression in Patients with Subcortical Vascular Cognitive Impairment
Qi Wang (Jeonbuk National University Medical School & Hospital)

PE_063 Assessing Hippocampal Atrophy as a Biomarker for Alzheimer's Disease in Indonesian Seniors
Sahnaz Vivinda PUTRI (International University Semen Indonesia)

PE_064 Early Detection of Alzheimer's Disease Progression Using Multi-Modal Machine Learning
Rifaldy FAJAR (Karlstad University)

PE_065 Elevated Aβ Oligomerization of Blood Plasma is Associated with Albuminome Profile in Alzheimer's Disease
Hongju Kim (Peoplebio Inc.)

PE_066 Investigating Hub Genes and Key Pathways Implicated in Alzheimer's Disease Using Bioinformatics Analysis
Payam HOSSEINZADEH KASANI (Kangwon National University Hospital)

PE_067 VR-EP-EEG-MRI Digital Biomarkers: Multi-modal Machine Learning Model for Detecting Mildcognitive Impairment
Hojin CHOI (Hanyang University College of Medicine, Guri Hospital)

PE_068 Exploring Hub Genes and Critical Pathways Involved in Vascular Dementia Development
Payam HOSSEINZADEH KASANI (Kangwon National University Hospital)

PE_069 Development of A Neuron-Selective Probe Incorporating into Live Neuronal Membranes
Kyu Hyeon Kim (Korea Institute of Science and Technology)

PE_070 Gingitracker-1: A Fluorescent Probe Labeling the Active Site of Gingipains of P. gingivalis
Hira Aziz (KIST)

PE_071 The effect of Neuroimaging Biomarkers on Gait Patterns in the Patients with Alzheimer's Disease
Min Seok BAEK (Wonju Severance Christian Hospital, Yonsei University Wonju College of Medicine)

PE_072 Machine Learning Model for Mild Cognitive Impairment based on Gait and MRI Images
Yeo Jin KIM (Kangdong Sacred Heart Hospital)

PE_073 A Deep Learning Approach with Analysis of Acoustics and Speech for Developing MCI Prediction Model
Jin Yong Jeon (Hanyang University)

PE_074 APOE4 Genetic Influence on Blood Biomarkers and Amyloid Pathology in Subjective Cognitive Decline
Dong Won Yang (College of Medicine, The Catholic University of Korea, Seoul St. Mary's Hospital)

PE_075 Prevalence of β-Amyloid Positivity in Dementia Syndromes in Korea: Impact of Age and APOE Genotypes
Min Young CHUN (Samsung Medical Center, Sungkyunkwan University School of Medicine)

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Na-Yeon JUNG (Pusan National University Yangsan Hospital)

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Sung-Ho WOO (Dongguk University)

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Hasom Moon (Samsung Medical Center, Sungkyunkwan University School of Medicine)

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San JUNG (Hallym University Medical Center, Kangnam Sarcred Heart Hospital)

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Seunghee NA (Incheon St. Mary's Hospital, the Catholic University of Korea)

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PE_105 Severe Bitemporal Lobe Atrophy Derived from Limbic-predominant age-related TDP-43 encephalopathy neuropathological change (LATE-NC) in progressive supranuclear palsy (PSP): An Autopsy Confirmed Case Report
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Dinesh Kumar PATEL (Sam Higginbottom University of Agriculture, Technology and Sciences)

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Kanika PATEL (Faculty of Health Sciences, SHUATS, Prayagraj)

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Vikas SHARMA (IDC Research center)

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Ranbir SINGH (Shri Maha maya vaishnav devi mandir research institute)

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Da-In Park (Hannam University)

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Sahnaz Vivinda PUTRI (International University Semen Indonesia)

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Vivi USMAYANTI (Universitas Sriwijaya)

PE_120 Biological Potential and Therapeutic Application of Karanjin on Brain Related Disorders in Medicine through Its Molecular Mechanism
Dinesh Kumar PATEL (Sam Higginbottom University of Agriculture, Technology and Sciences)

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Devi Yulia RAHMI (Universitas Andalas)

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Nataliia Lukianenko (Korea Institute of Science and Technology)

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Fitri KURNIA (Universitas Muhammadiyah Sumatera Barat)

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Buongo CHUN (Myongji University)

PE_127 Perspectives about Life-sustaining Treatment and Physician-assisted Suicide among Dementia Caregivers in Korea
YUMI LEE (Kyung Hee University)

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Taeho SEO (CHA Bundang Medical Center, CHA University School of Medicine)

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Sun Min LEE (Ajou University School of Medicine)

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Ha Eun KIM (Ewha Womans University)

PE_132 Eye-Tracker Assessment of the Impact of Donepezil on Visuospatial Abilities in Mild Cognitive Impairment: Preliminary Findings
Qi Wang (Jeonbuk National University Medical School & Hospital)

PE_133 Facial Emotion Recognition Deficits in Individuals with Mild Behavioral Impairment
Bora YOON (Konyang University College of Medicine, Konyang University Hospital)

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Giho JEON (Pusan National University)

PE_136 The Development of Conversion Scoring System in Neuropsychological Test (Part 1): Cognitive Impairment Screening Test as a Screening Tool for Dementia: The Correlation Study of Subtest Scores with Mini Mental State Examination
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PE_137 Association between of Brain Regional Atrophy and Neuropsychological Test Performance in Patients with Definite Alzheimer's Disease
Do-yun HEO (Hanyang University Hospital)

PE_138 The Development of Conversion Scoring System in Neuropsychological Test (Part 2): Correlation Study between Subtest Scores of Seoul Neuropsychological Screening Battery and Consortium to Establish a Registry for Alzheimer's Disease in Korea
Min Seong KIM (Hanyang University Hospital)

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Hui Jin RYU (Konkuk University Medical Center)

PE_140 Two Different Patterns of Cognitive Change in SCD Patients: Neuropsychological Perspectives
Seunghee NA (Incheon St. Mary's Hospital, the Catholic University of Korea)

PE_141 Remote Neurocognitive Assessment in Clinical Practice: A Pilot Study Using a Mobile Application
Chonghwee LEE (The Catholic University of Korea, Seoul ST. Mary's Hospital)

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Sangheon Kim (Jeonbuk National University Medical School)

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Da-Ye Yoon (Dong-A University College of Medicine)

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Jan TENIJENHUIS (Chosun University)

PE_145 The Clinical Utility of Cognitive Impairment Screening Test (CIST) in Memory Disorder Clinic
Hye Seon HAN (Samsung Medical Center, Sungkyunkwan University School of Medicine)
So Yeon Lim (Samsung Medical Center, Sungkyunkwan University School of Medicine)

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Hye Soo Kim (Samsung Medical Center, Sungkyunkwan University School of Medicine)
Ina Kim (Samsung Medical Center, Sungkyunkwan University School of Medicine)

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Byung Hwa LEE (Samsung Medical Center, Sungkyunkwan University School of Medicine)

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Seonyoung KIM (Ewha Womans University)

PE_150 Cognitive Subgroups of Older Adults Living in Rural Korea and Their Characteristics Observed in Structural and Functional Brain Imaging: Results from the Korean Genome and Epidemiology Study (KoGES)-Cardiovascular Disease Association Study (CAVAS)
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PE_152 Microcurrent as a Novel Therapeutic Approach for Alzheimer's Disease Model
Dong Rak KWON (the Catholic, University of Daegu, School of Medicine)

PE_153 Effect of Tablet-based Cognitive Intervention on Cognition in Patients with Mild Cognitive Impairment: A Pilot Study
Sung Hoon KANG (Korea University Guro Hospital)

PE_154 The Effectiveness of VR-based Cognitive Training Program: A Pilot Study
Eek-Sung Lee (Soonchunhyang University Bucheon Hospital)

PE_156 The Effect of Home-based Cognitive Training Using Workbook and Tablet PC in Presenile Dementia Patients
Jay KWON (Changwon Fatima Hospital)

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So-Hee PARK (Bobath Memorial Hospital)

PE_160 Optimization and In-silico Studies of Covalently-acting Tau Aggregation Inhibitors for the Treatment of Alzheimer's Disease
Lizaveta Gotina (Korea Institute of Science and Technology)

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Sun Min Lee (Ajou University School of Medicine)

PE_163 Personalized Hippocampal Network-targeted Stimulation for Alzheimer's Disease: A Randomized Controlled Trial
Young Hee JUNG (Myoungji Hospital)

PE_164 Evaluation of Efficacy and Safety Using Low Dose Radiation Therapy with Alzheimer's Disease: Interim Results of Multicenter Phase II Clinical Trial
Weon Kuu CHUNG (Kyung Hee University Hospital at Gangdong)

PE_165 Exploring the Benefits of Tai Chi: Cognitive and Physical Outcomes in Adults Aged 65 and Older
Jiale Yu (MYONGJI UNIVERSITY)

PE_166 High-intensity Interval Training (HIIT) as an Intervention for Sleep Quality Enhancement in Middle-aged Women
Kuan Dong (Graduate School of Myongji University)

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Tenghao Yu (Myongji University)

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Ying Sun (Myongji University)

PE_169 The Effects of High-intensity Interval Training on Cognitive functioning in Middle-aged Women
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Reny ROSALINA (Faculty of Mathematics and Natural Sciences, Palangka Raya University)

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Jaeho Kim (Hallym University Dongtan Sacred Heart Hospital)

PE_175 Enhanced Dynamic Glymphatic Activity Using Low-intensity Ultrasound in Alzheimer's Disease
Jaeho KIM (Hallym University Dongtan Sacred Heart Hospital)

PE_177 South Korean Study to Prevent Cognitive Impairment and Protect Brain Health through Multidomain Interventions via Face-to-face and Video Communication Platforms in Mild Cognitive Impairment (SUPERBRAIN-MEET): A Randomized Controlled Trial
Seong Hye CHOI (Inha University Hospital College of Medicine)

PE_178 Enhancement of cognitive restoration by glia-like human mesenchymal stem cells in an animal model of vascular dementia
Ye-Jin RYU (Hanyang University Graduate School of Biomedical Science & Engineering)

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Hyo Jin SON (Department of Neurology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul)

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Muhammad IRZAQ (Padang State University)

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Young Chul YOUN (Chung-Ang University College of Medicine)

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Seonjae Been (Inje University)

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Seonjae Been (Inje University)

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Si Eun Kim (Inje University College of Medicine, Haeundae Paik Hospital)

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Javad ALIZARGAR (NTUNHS)

PE_189 The Correlation between Physical Fitness and Cognition Function in Korean Elderly People
Hong- Sun Song (Korean Institute of Sport Science)

PE_190 A Systematic Review of Sedentary Behavior and Its Impact on Cognitive Function, Dementia Onset, and Subjective Cognitive Complaints in Older Adults: Passive vs. Active Sedentary Behavior
Mokyung Jung (Graduate School of Education, The University of Tokyo)

PE_191 Association of Physical Fitness and Cognitive Function in Community-based Older Adults
Da-ae KIM (Korean Institute of Sport Science)

PE_192 Overestimated Prediction of Alzheimer's Disease Using Polygenic Risk Score Derived from Summary Statistics
Jonghun KIM (Ilsan Hospital)

PE_193 The Impact of Metabolic Health on the Relationship of Obesity with and Alzheimer's and Vascular Markers
Eun Hye LEE (Samsung Medical Center)

PE_194 Age- and sex-specific Mediating Effects of Depression in the Relationship between Frailty and Cognitive Function in Korean Middle Aged and Older Adults: Results from the Korean Genome and Epidemiology Study (KoGES)-Cardiovascular Disease Association Study (CAVAS)
Haeyoon Kim (Chonnam National University Hospital)

PE_195 Physical Frailty and Cognitive Functions in Older Adults Living in Rural Korea: Results from the Korean Genome and Epidemiology Study (KoGES)-Cardiovascular Disease Association Study (CAVAS)
Minji SONG (Hallym University)

PE_196 Estimate of Gait Speed by Physical Fitness Test in older adults
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Rifaldy FAJAR (Karlstad University)

PE_198 The Association between Glucose Variability and Parkinson's Disease: Using the PPMI Datasets
Yeoju Kim (Yonsei University College of Medicine)

PE_199 Partivulate Matter Exposure Accelerates Tau Pathophysiology, Inflammation and Cognitive Deficits in Tau-BiFC Mice
Nicolette BOESEN (Korea Institute of Science and Technology)

PE_200 Clinicopathological Correlation of Neurodegenerative Diseases in National Brain Biobank of Korea (NBBK)
Young Hee Jung (Myoungji Hospital)

PE_201 Indonesian's Health Service Apps for Caregivers of Dementia Patients: Future Challenges
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PE_202 Quality of Life Memory-Related Disease Patients in Indonesia Using Indonesia Family Life Survey
Derizal DERIZAL (IP Trisakti)

PE_203 A Study on the Relationship Between Physical Activity Levels in the Elderly and the Experience of Cognitive Impairment
Daniela Andrea Gomez ortiz (Gachon University)

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PE_205 Frequency of Limbic-predominant age-related TDP-43 encephalopathy neuropathological change (LATE-NC) in a Dementia Clinic-based Cohort: A Preliminary Study
Sohyun YIM (Pusan National University Hospital)

PE_206 Early Detection of Dementia Disease: How Community-based Health Centers (puskesmas) Take the Important Role among 17k Islands in Indonesia?
Rosinta Hotmaida Pebrianti PURBA (Learning-up Institute)

PE_207 Effect of Dietary Habits on Alzheimer's Disease Progression
Seong Hye CHOI (Inha University College of Medicine)

PE_208 Prediction Model for Mild Cognitive Impairment in Patients with Type 2 Diabetes Using an Autonomic Function Test
Heeyoung KANG (Gyeongsang National University Hospital)

PE_209 Health Literacy Status of Caregivers of People with Dementia in South Korea
Gwanwook Bang (Kyunghee University, College of medicine)

PE_210 Baseline Demographic and Clinical Characteristics of Longitudinal Study of Early Onset Dementia And Family Members (LEAF)
Na-Yeon JUNG (Pusan National University Yangsan Hospital)

PE_211 Dementia Prevention: The Challenges and the Future from Literature Review
Zulfa SAUMIA (Universitas Jambi)

PE_212 Updated Treatment for Tremor: Cutting-Edge Brain Surgery with No Cutting and Pharmacotherapy
Rani MARSYANDA (Sulthan Thata Islamic State University)

PE_213 Clinical Research Platform for Multisource Brain disease (CLIMB) Registry: An National-wide Platform for Recruitment, Assessment, and Longitudinal Monitoring of Participants for Neuroscience Studies
Sujung Oh (SAIHST, Sungkyunkwan University)

PE_214 Relationsip between Amyloid Burden and Sleep Characteristics in the Elderly with Subjective Cognitive Decline
Kyung Joon Jo (College of Medicine, Gachon University Gil Medical Center)

PE_215 Physical Fitness, Depression, and Their Influence on Cognitive Frailty Among Community-Dwelling Elderly
Ngeemasara Thapa (Dong-A University)

PE_216 Sleep Characteristics and Incident Dementia and All-cause Mortality: The Korean Genome and Epidemiology Study of Middle-aged to Older Participants
Soriul KIM (Korea University College of Medicine)

PE_218 Genetic Screening of ANXA11 in Korean Patients with Frontotemporal Dementia Syndrome
Sun Min LEE (Ajou University School of Medicine)

PE_219 What Physical Functions are Associated with Cognitive Decline in Community-dwelling Middle-aged and Older Adults?

KAI WANG (Dong-A University)

PE_220 Association between Metabolic Syndrome and Cognitive Decline over 14 Years Modified by Sex and Inflammation

Chi-Hun KIM (Hallym University Sacred Heart Hospital)

PE_221 Association of Cognitive Function and Depressive symptoms of the Elderly Residents in A Rural Community

Oh Dae KWON (Daegu Catholic University Medical Center; Daegu Catholic University School of Medicine)

PE_001 Basic Science and Pathogenesis

Association between Western Diet-induced Visceral Adipose Tissue Inflammation and Alzheimer's Disease Pathology in a Mouse Model

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Objective

The aim of this study was to evaluate the relationship between Western Diet (WD)-induced inflammation in visceral adipose tissue (VAT) and Alzheimer's Disease (AD) pathology. Additionally, we aimed to identify the VAT-derived pro-inflammatory cytokines that contribute to neurotoxic effects in mouse brain tissue.

Methods

Male C57BL/6 mice were assigned to either a control chow diet or a Western diet for 20 weeks. Inflammation in VAT was confirmed through western blot analysis, which measured levels of NLRP3, pNFkB, and IL-1 beta. We also quantified levels of AD-associated proteins such as amyloid-beta (Aβ) oligomers, beta-site amyloid precursor protein cleaving enzyme 1 (BACE1), and amyloid precursor protein (APP) in brain tissue using Western blot analysis. Cognitive function was assessed using Y-maze and Morris water maze tests. Pro-inflammatory cytokines that were concurrently upregulated in both VAT RNA-sequencing and plasma antibody array analyses were classified as VAT-derived and evaluated for their neurotoxic effect on hippocampal neurons in vitro.

Results

Mice fed a WD exhibited elevated levels of NLRP3, pNFkB, and IL-1 beta in VAT, confirming significant inflammation. These mice also showed increased levels of Aβ oligomers, BACE1, and APP in brain tissue, along with cognitive impairments. Both VAT RNA-sequencing and plasma antibody array analyses consistently revealed upregulation of specific VAT-derived pro-inflammatory cytokines, including CCL5, CCL8, CCL9, CXCL13, and interleukin-18, which were also elevated in brain tissue. Subsequent in vitro experiments using a neuron-microglia co-culture system confirmed that these cytokines induce neuronal cell death in mouse hippocampal neurons.

Conclusion

WD-induced VAT inflammation is related with AD pathology. The VAT-derived pro-inflammatory cytokines, elevated in response to WD diet, exhibit neurotoxic effects on hippocampal neurons. These findings underscore the potential of targeting VAT inflammation in AD management and prevention.

PE_002 Basic Science and Pathogenesis

Immunotherapy Targeting Plasma ASM is Protective in a Mouse Model of Alzheimer's Disease

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Objective

Acid sphingomyelinase (ASM) has been implicated in neurodegenerative disease pathology, including Alzheimer's disease (AD). However, the specific role of plasma ASM in promoting these pathologies is poorly understood.

Methods

We explore plasma ASM as a circulating factor that accelerates neuropathological features in AD by exposing young APP/PS1 mice to the blood of mice overexpressing ASM, through parabiotic surgery.

Results

Elevated plasma ASM was found to enhance several neuropathological features in the young APP/PS1 mice by mediating the differentiation of blood-derived, pathogenic Th17 cells. Antibody-based immunotherapy targeting plasma ASM showed efficient inhibition of ASM activity in the blood of APP/PS1 mice and, interestingly, led to prophylactic effects on neuropathological features by suppressing pathogenic Th17 cells.

Conclusion

Our data reveals new insights into the potential pathogenic mechanisms underlying AD and highlights ASM-targeting immunotherapy as a potential strategy for further investigation.

Discovery of a Novel Dual-action Small Molecule that Improves Multiple Alzheimer's Disease Pathologies

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Objective

The importance of acid sphingomyelinase (ASM) activation has been recognized as a contributor to multiple Alzheimer's disease (AD) pathologies, leading to the concept of using ASM inhibitors for AD treatment.

Methods

Chemical compounds (1,273) were tested in AD fibroblasts with abundance ASM activity. The compounds backbone with 30% inhibition was identified and optimization was performed based on lipophilicity. Further qualification was performed through biochemical and cellular assays, drug ability, and in vivo efficacy.

Results

We found KARI 201 with selectivity ASM inhibition effects, excellent pharmacokinetic properties, and especially brain distribution. Unexpectedly, another role of KARI 201 was revealed as a ghrelin receptor agonist, which has novel therapeutic potential for AD. This dual role of KARI 201 in neurons efficiently rescued multiple pathologies in AD mice, leading to memory function improvement.

Conclusion

Our data highlights the potential clinical application of KARI 201 as innovative and multi-faceted drug for AD treatment.

PE_007 Basic Science and Pathogenesis

Clinical Application of Sparse Canonical Correlation Analysis to Detect Genetic Associations with Cortical Thickness in Alzheimer's Disease

Bo-Hyun Kim[1*], Sang Won Seo[1], Yu Hyun Park[1], Hee Jin Kim[1], Hyemin Jang[2,1], Jihwan Yun[1], Mansu Kim[3], Jun Pyo Kim[1]

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Objective

Many genetic variants have been successfully identified for Alzheimer's disease (AD); however, the identified genetic variants explain a small portion of the heritability of AD. One way to increase the power of association studies is to use an imaging genomics approach that assesses the impact of genetic variation on neuroimaging measures. In this study, we performed an imaging genetic study using the SCCA approach to identify novel genetic factors associated with AD in the Korean population.

Methods

The 1125 participants were recruited from the Korea-Registries to Overcome and Accelerate Dementia research project (K-ROAD). T1-weighed images and genotype data of 1125 participants were used for this study. First, we estimated lobal cortical thickness using CIVET2.1 pipeline and selected 344 SNPs with p-value < 10-4 from IGAP summary stats. Then, we performed SCCA with 344 SNPs and cortical thickness in each group Aβ positive group and negative group and compared the weights of selected SNPs between the two groups. Finally, we performed the gene-set enriched analysis with the top 10 SNPs in each group using Enrichr.

Results

We selected the top 10 SNPs in each group which has the highest weights. For Aβ negative, we identified rs6743470 located near BIN1 gene, rs141622900 located near APOC1 gene associated with imaging features. For Aβ positive, rs7550917 and rs9270850 located near HLA-DQA1 gene have identified as genetic variants associated with imaging features. In the Aβ negative, the enriched gene sets included those associated with regulation of efflux, synaptic transmission and whereas gene sets related to MHC class protein bindings are enriched in Aβ positive.

Conclusion

In this study, we performed SCCA to test the effect of SNPs on cortical thickness in the Aβ positive and negative groups. Although further investigation in the larger independent cohort is needed, we identified important contributors to cortical thickness also related to AD.

Discriminative Value of CSF Space Volume for Brain Atrophy for Neurodegenerative Diseases

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Objective

Cortical thickness using MRI is mainly used as a surrogate marker in relation to dementia diagnosis. However, due to the highly folded nature of the cortex, cortical thickness can be properly measured only when both the GM/WM and surface positions and orientations are known. To solve these difficulties, dementia diagnosis should be applied by considering other MRI characteristics of dementia. This study is intended to provide a method for distinguishing between normal control and Alzheimer's disease dementia using CSF space, including extracerebral CSF and ventricular spaces.

Methods

This study included 616 participants with ADD who tested positive for beta-amyloid on amyloid PET and 605 NCs without beta-amyloid on amyloid PET. In addition, a head-to-head MRI obtained from SMC and Chaum was used to confirm whether the region corresponding to the CSF space correlated regardless of vendor. eCSF volume, ventricular volume, and cortical thickness were extracted using the CIVET anatomical pipeline. We obtained the cortical thickness of each lobe and subcortical structural volumes. To individually distinguish MRI characteristics of NC and ADD, various groups of dementia-related indicators were applied to a GLM. We quantified the performance of classifiers using ROC curves to evaluate machine learning algorithms.

Results

To distinguish the two groups, we developed classification models. ROI related to dementia-related indicators were assessed based on the following: 1)global eCSF and ventricular regions, 2)all subregions of eCSF and ventricular regions were significant. Classifiers using CSF space sub-regions as ROIs performed slightly better. Furthermore, it was confirmed that the performance of the classifier is improved when additional information such as patient information is used.

Conclusion

This study found that brain atrophy can be measured through the volume of CSF space that is better differentiated than cortical thickness. These findings can be used in the diagnosis of dementia to diagnose dementia early and to predict the progression.

PE_011 Basic Science and Pathogenesis

In Vivo and in Vitro Study of 17β Estradiol against Amyloid Beta Neurotoxicity in Synaptosomesof Agingfemale Rats : A Therapeutic Potential Drug for Alzheimer's Disease

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Objective

The aim of the present study was to determine the effects of neuropeptide, neurokinin B (NKB) andamyloid beta fragment Aβ (25-35) on 17β estradiol (E2) treated aging female rat brain of 3 months (young), 12months (adult) and 24 months (old) age groups.

Methods

The aged rats (12 and 24 months old) were given subcutaneous injection of E2 (0.1 µg/gbody weight) for30 days. Synaptosomes were incubated with NKB, Aβ (25–35) and NKB+ Aβ (25–35)in a microfuge tubes at 37˚C for60 min in a shaking water bath with 0.1, 1 and 5 µM concentration of each of the peptides in all age groups of controland E2 treated rats. The learning and memory functionwere assessed by Morris water maze test. The mRNA andprotein levels of PPARγ were evaluated by real time (RT)-PCR and Western blot analysis.

Results

The results obtained in the present work revealed that increased activities of antioxidant enzymes(glutathione reductase, superoxide dismutase and decrease in calcium levels, acetylcholinesterase (AChE) activity,neurolipofusicin accumulation and malondialdehyde (MDA) in presence of NKB and combined NKB and Aβ in vivo E2treated aging rat brain. An in vitro incubation of E2 treated synaptosomes with Aβ showed toxic effects on all theparameters, while NKB showed stimulating effects and the combined NKB and Aβ showed a partial effects ascompared to Aβ (25-35) and NKB alone. Similar results were obtained with the increased antioxidant enzymes levels,improved learning and memory performances, reduced AChE activity and MDA levels, significantly increased PPARγexpression, and alleviated TNF-α, IL-1β, and IL-6 compared with the E2 treated aging rat hippocampus.

Conclusion

Present study elucidates an antioxidant,anti-aging and neuroprotective role of tachykinin peptide NKBagainst the beta amyloid induced toxicity in E2 treated female rats.

Effects of the Ethanolic Extract of White Tea (Camellia sinensis) on Metabolic Functions in Alzheimer's Disease Rat Model.

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Objective

Present study was designed to investigate effects of ethanolic extract of White tea (WT) on ions homeostasis, antioxidant enzymes, memory functions, motor learning ability, cytokine production and neuronal loss in the monosodium glutamate-induced non-transgenic rat model of Alzheimer's disease (NTAD).

Methods

The experimental design included oral administration of ethanolic extracts of WT (100, 200 mg/kg body weight) for 20 weeks to 3-month and 12-month-old NTAD rats. Estimation of calcium, sodium and potassium ions in brain tissue and gamma aminobutyric acid level in serum was carried out. Memory function was evaluated using Morris Water Maze and passive avoidance tests, and brain levels of malondialdehyde (MDA), oxidative stress, insulin levels, SOD and AChE activity and brain-derived neurotrophic factor (BDNF) were determined with biochemical experiments. Enzyme-linked immunosorbent assay was used to determine levels of interleukin-1β, tumor necrosis factor α, and interleukin-6 in the hippocampus and cerebral cortex.

Results

The results demonstrated that WT treatment improved the insulin sensitivity with antioxidant enzymes, and improved the learning ability in NTAD rats. Histological immunostaining evaluation has shown restoration of intracellular hyperphosphorylated tau of hippocampus upon treatment with WT. Treatment with WT extract (200 mg/kg) prevented the memory impairment in both behavioral tests along with normalize cytokine production and acetylcholinesterase activity, and increased brain levels of BDNF in NTAD rats. Significant decrease in Ca+2 and Na+, MDA levels and increase in the level of K +, superoxide dismutase and catalase was observed in WT treated group.

Conclusion

Data of this study suggest that extract of WT is effective to reduce most of the AD associated abnormalities in rats and it seems that WT favorable effect is due to its effectiveness in lessening of oxidative stress in rat.

Deciphering Current Advances in Neuroinflammation in Alzheimer's Disease Through a Bibliometric Approach

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Objective

Alzheimer's disease (AD), a complicated neurological condition, continues to challenge biomedical researchers and clinicians across the world. Neuroinflammation, defined as a cascade of immunological reactions in the central nervous system, has emerged as an important focus in Alzheimer's research. The goal of this study was to provide an extensive bibliometric analysis for the decade from 2013 to 2023, giving an in-depth assessment of the growing landscape of neuroinflammation in the context of AD, as documented in the Scopus database.

Methods

An extensive search of the Scopus database using relevant keywords linked to neuroinflammation and Alzheimer's disease was conducted. The database search focused solely on research papers published between 2013 and 2023. Co-authorship and co-occurrence analyses were performed using VOSviewer software, version 1.6.19.

Results

Between 2013 and 2023, a total of 4,625 scientific papers on neuroinflammation in AD were found in the Scopus database. The scientific community has noticed an increase in publications focused on neuroinflammation in AD during the last decade, confirming its recognition as an essential player in the progression of the disease. According to the geographical distribution of research output, the United States, China, the United Kingdom, South Korea, and Italy were the most prolific contributors to neuroinflammation research in AD. Keyword co-occurrence analysis revealed the most frequently studied subjects such as "microglia", "neurodegeneration", "oxidative stress", "cognitive impairment", and "neuroprotection". These themes highlighted the diverse aspects of neuroinflammation, and the various methodologies used to uncover its intricacies in AD.

Conclusion

In conclusion, this bibliometric analysis is a useful tool for researchers and clinicians interested in furthering the comprehension of AD and its associated neuroinflammatory processes. It provides an overview of the neuroinflammation landscape, emphasizing tremendous progress and prospects in the effort to reduce the burden of AD on individuals and societies worldwide.

Patient with PSEN1 Glu318Gly and Other Possible Disease Risk Mutations, Diagnosed with Early Onset Alzheimer's Disease

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Objective

In this study, we introduced a French EOAD patient in Korea, who carried the PSEN1 Glu318Gly mutations with four possible risk variants, including Sortilin Related Receptor 1 Glu270Lys, ABCA7 Val1946Met, TOMM40 Arg239Trp and GRN Ala505Gly. The patient started to present memory decline and behavioral dysfunctions in his early 60s. His brain imaging presented amyloid deposits by positron emission tomography (PET-CT). The Multimer Detection System (MDS) screening test for plasma for amyloid oligomers also was positive, which supported the AD diagnosis.

Methods

Whole-exome analysis was performed on the patient. In silico, and structure predictions were performed on the possible dementia-related genes. Pathway analysis was also performed on them.

Results

Five probable interesting variants were found in PSEN1, SORL1, ABCA7, TOMM40, and GRN. These genes may share several common pathways (amyloid processing, and inflammation).

Conclusion

It was verified that PSEN1 Glu318Gly itself may not impact amyloid production. However, additional variants were found in other AD and non-AD risk genes were found. SORL1 Glu270Lys was suggested as a risk mutation for AD and could increase the amyloid peptide production and impair the endosome functions. ABCA7 Val1946Met was a novel variant, which was predicted to be damaging. The GRN Ala505Gly was a variant with uncertain significance, however, it may reduce the granulin levels in the plasma of dementia patients. Pathway analysis revealed that PSEN1 Glu318Gly may work as a risk factor along with the SORL1 and ABCA7 variants since pathway analysis revealed that they may interact through amyloid-related and lipid metabolism pathways. TOMM40 and PSEN1 could have common mechanisms through mitochondrial dysfunctions. It may be possible that PSEN1 Glu318Gly and GRN Ala505Gly would impact disease by impairing the immune-related pathways. Taken together, the five risk factors may contribute to disease-related pathways, including amyloid and lipid metabolism, or impair immune mechanisms.

PE_015 Basic Science and Pathogenesis

Diminished Microglial Uptake Leads to Increased Amyloid Beta Depositions

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Objective

Imbalance between amyloid beta generation and degradation was one of the causes of Alzheimer's disease (AD). The primary role in the endocytosis of amyloid beta is played by microglia, with astrocytes and neurons following suit. Inhibition of amyloid beta endocytosis in microglia results in the accumulation of amyloid beta in the tissues.

Methods

In this study, we conducted a series of experiments to investigate the effect of amyloid beta on microglial endocytosis activity.

Results

We confirmed that amyloid beta inhibits microglial endocytosis. Amyloid beta reduced membrane ruffling events comparing to the control in tomographic analysis. The level of early endocytosis marker, Rab5, was similar between control and 5xFAD dementia model mice. Inhibition of microglial endocytosis induced by amyloid beta in primary cortical neurons results in intracellular accumulation of amyloid beta.

Conclusion

Taken together, these findings indicate that amyloid beta may play a role in hastening the progression of AD through the inhibition of microglial endocytosis function.

This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number: HU23C0199, WSC).

Generation of Human Induced Pluripotent Stem Cell (hiPSCs) based on Patients with Dementia: A Foundation for In Vitro Research

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Objective

We generated human induced pluripotent stem cells (hiPSCs) from patients with Alzheimer's disease (AD), patients with Lewy body disease (LBD), and those with mixed dementia to establish a foundation for in vitro research for these dementing disorders.

Methods

Peripheral blood mononuclear cells obtained from patients with dementia (AD=3, LBD=1, and Mixed Dementia=7) were cultured to generate and multiply erythroid progenitor cells, which were subsequently reprogrammed into hiPSCs. The stability of hiPSC lines was rigorously assessed through chromosomal analysis, Quantitative Real- Time Polymerase Chain Reaction (qRT-PCR) and flow cytometry.

Results

The pluripotency of hiPSCs was assessed using colonies from passages 8–10. qRT-PCR confirmed the expression of transfected reprogramming factor genes. Flow cytometry analysis demonstrated the expression of TRA-1-60 and SSEA4, pluripotency markers, in a single cell level. Immunocytochemistry procedure indicated that iPSC clones retained typical characteristics of pluripotent stem cells, including the expression of embryonic stem cell markers such as OCT4, SOX2, NANOG, TRA-1-60, and SSEA4.

Conclusion

We successfully generated iPSC lines with confirmed pluripotency from patients with AD, LBD, and mixed dementia.

PE_017 Basic Science and Pathogenesis

Positive Effects of Phosphatidylserine Adminstraition in 5xFAD Mice

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Objective

Phosphatidylserine (PS) is crucial for the maintenance of nerve cell membranes and overall nervous system health. In human, brain aging can affect brain function and neurotransmission. Ensuring an adequate supply of phosphatidylserine and other essential nutrients is important for supporting brain health and cognitive function during aging. Recent studies have shown that exogenous PS can be effectively absorbed by human body and has the ability to cross the blood-brain barrier, making it a promising candidate material having potential brain health benefits. This research suggests that PS supplementation may help counteract some of the biochemical and structural changes that occur in nerve cells during the aging process.

Methods

In the context of Alzheimer's disease (AD), which is a significant health challenge, particularly due to the aging global population, we conducted a study involving the oral administration of freeze-dried food containing phosphatidylserine to 5xFAD mice. These mice received phosphatidylserine for a duration of 3 months. As determined by the Cross Maze, Novel Object Recognition, and Morris Water Maze (MWM) tests.

Results

These mice received phosphatidylserine for a duration of 3 months. The results of our study demonstrated that phosphatidylserine administration led to improvements in recognition memory and spatial memory in these 5xFAD mice, as determined by the Cross Maze, Novel Object Recognition, and Morris Water Maze (MWM) tests

Conclusion

These findings suggest that phosphatidylserine may be an effective supplement for treating memory-related problems such as AD.

This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number: HU23C0199, WSC).

Effect of Mitochondrial Deficiency in AD Model

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Objective

Alzheimer's disease (AD) is a prevalent neurodegenerative disorder marked by memory loss and cognitive function decline. Key pathological features of AD include amyloid beta (Aβ) plaques and neurofibrillary tangles (NFT) formation. Furthermore, mitochondrial dysfunction is believed to cause ATP energy deficit and oxidative stress, possibly influencing the Alzheimer's disease onset and progression.

Methods

In this study, we examined how mitochondrial dysfunction, which was induced by the reduction of Ndufs4 expression, affects brain function in 3xTG AD model mice. While a complete knockout of Ndufs4 resulted in fatal deficiency, a heterozygous mice can survive and be used to study the impact of mild mitochondrial deficiency in 3xTG mice.

Results

The 3xTG/Ndufs4 mice exhibited more severe decline in memory and cognitive function, coupled with an increase in depression levels compared to their 3xTG counterparts.

Conclusion

These results imply that even a mild mitochondrial deficiency might accelerate AD progression. Nevertheless, additional research is required to comprehend the complex interplay between mitochondria and AD pathology.

This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number: HU23C0199, WSC).

Synapse Density and Glial Activity was Altered in the Cortex of Ndufs4 HT Mice

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Objective

Alzheimer's disease is a neurodegenerative disorder characterized by progressive cognitive decline and memory loss. In Alzheimer's disease (AD), neuronal ATP levels decrease, accompanied by overproduction of reactive oxygen species (ROS) and mitochondrial dysfunction. Specifically, mitochondrial dysfunction is a significant hallmark in the early-stage AD, but the relation between mitochondrial dysfunction and AD pathogenesis remains uncertain.

Methods

The Ndufs4 is a subunit of mitochondrial complex 1 involved in mitochondrial electron transport chain and plays an important role in ATP production in mitochondria. Mutations or defects in Ndufs4 can cause Leigh syndrome, which presents with severe neurological disorders predominantly in infants and young children, leading to early death. In this study, we utilized the Ndufs4 heterozygous (HT) mice, which has a mild deficiency in mitochondrial function, to investigate whether AD-related pathologies appear during aging.

Results

As a result, we observed a reduction in the expression of synaptic protein and an increase in glial activity in the cortex of Ndufs4 HT mouse.

Conclusion

This suggests that the mild deficiency of mitochondria induces synaptic defects, which are associated with memory decline in AD. Additionally, the modified glial activity indicates a neuroinflammatory response observed in AD.

This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number: HU23C0199, WSC).

Methylation Profiling of Neurodegenerative Diseases

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Objective

To accurately diagnose neurodegenerative diseases, we conducted a pilot study involving methylation profiling of post-mortem cases diagnosed with Alzheimer's disease (AD), Lewy body disease (LBD), and Primary Age-Related Tauopathy (PART) using the MethylationEPIC v1.0 platform.

Methods

All cases were obtained autopsy at the Seoul National University Hospital Brain Bank, and neuropathological examinations of the brain followed established guidelines for neurodegenerative diseases, employing immunohistochemical biomarkers. We selected 6 cases of AD, 4 cases of LBD, and 3 cases of PART, ensuring the absence of other comorbidities, and extracted DNA from the prefrontal cortex. This extracted DNA was then analyzed using MethylationEPIC v1.0. All data analyses were conducted using R version 4.2.0 with the R packages 'ChAMP,' 'methylationArrayAnalysis,' and 'Rtsne.'

Results

In the case of AD, the mean Thal phase was 3, and the Tau Braak stage averaged 3.8, while LBD cases had a mean Lewy Body Braak stage of 5.8. PART cases exhibited a mean Thal phase of 0 and Tau Braak stage of 1. Differentially methylated probe (DMP) analysis for AD and PART revealed disparities in 22,675 probes, with 4,298 showing hypermethylation and 18,377 showing hypomethylation in AD. Among these, 62 DMPs were consistent with AD-associated probes previously identified through EWAS analysis. In contrast, there was no significant DMP between PART and LBD, necessitating further analysis using a different approach. We selected the 1,000 most variable probes based on a standard deviation of beta values (SD > 0.2) and visualized the clustering of the three groups using a t-SNE plot. The results indicated some degree of segregation.

Conclusion

Methylation profiling has proven to be a powerful tool in the differential diagnosis of CNS tumors. Further studies are required to verify the diagnostic power of methylation patterns in heterogeneous neurodegenerative disease tissue, uncovering notable clustering and epigenetic differences.

PE_021 Basic Science and Pathogenesis

Glial Regulation in Alzheimer's Disease Model.

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Objective

Alzheimer's disease (AD) is a common neurodegenerative disease which has been corelated with aging and the main cause of dementia. The symptom of AD includes a gradual loss of memory and cognitive function. In the brain tissue of AD, senile plaques and neurofibrillary tangles (NFTs) are characteristically generated in hippocampus and cortex of AD brain, of which amyloid beta (Aβ) and tau proteins are main components correspondingly. Though the exact pathology of AD is not fully understood, deficiency of Aβ clearance and corresponding accumulation of Aβ have been suggested as major cause for the disease. Generally, Aβ clearance is mainly mediated by glial cells which is also a target of Aβ toxicity.

Methods

In this study, we studied the activity of glial cells, microglia and astrocyte in the brain of AD model mouse, 5XFAD. We also examined the expression of various factors that has been implicated in the regulation of Aβ clearance.

Results

As a result, we observed Aβ accumulation in the brains of AD model mice. Astrocyte and microglia are activated in the brain of AD mice. Phosphorylation of AKT and GSK3beta was increased in 5xFAD brain. The expression of ATG5/12, LC3B, and LAMP2 was modified too.

Conclusion

Glial cells are activated in AD model mouse brain where Aβ is accumulated. Further research on glial cell regulation in AD models could define the mechanism of Aβ clearance and AD pathology.

This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number: HU23C0199, WSC).

Effects of Mitochondrial Defect on Early-stage Mice Behavior

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Objective

Mitochondrial dysfunction reduces cellular ATP production and increases ROS production. The hypothesis that mitochondrial dysfunction correlates with neurodegenerative disorders, including Alzheimer's disease (AD) and Parkinson's disease (PD), is widely acknowledged. AD is an important form of neurodegeneration with a pathophysiological feature characterized by the formation of amyloid beta (Aβ) plaques, neurofibrillary tangles (NFTs) and the decline in memory, orientation, and judgment.

Methods

In this study, we used Ndufs4 heterozygous (HT) mice (6 month) with decreased mitochondrial complex I activity to demonstrate that memory behavior dysfunction in AD is associated with defects in mitochondrial activity.

Results

As a result, the basic motor tests revealed no significant difference between wild-type (WT) and Ndufs4 HT mice. Likewise, similar level of memory has been observed in both genotypes using several memory behavioral tests.

Conclusion

These results suggest that mitochondrial dysfunction is not significantly associated with memory impairment in early stage of life. Further studies using aged mice are needed to fully understand the effect of mitochondrial defect on aging-related brain dysfunction.

This research was supported by a grant of the Korea Dementia Research Project through the Korea Dementia Research Center(KDRC), funded by the Ministry of Health & Welfare and Ministry of Science and ICT, Republic of Korea (grant number: HU23C0199, WSC).

PE_023 Basic Science and Pathogenesis

Visualization of 3R or 4R Tau Aggregation in Live Cells Using BiFC Platform

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Objective

Tau is a microtubule-associated protein which plays an important role in the stabilization of microtubules. Tau exists of six isoforms, which are categorized as 3R or 4R tau based on whether they contain three or four repeat domain. In normal brain, 3R and 4R tau are found in a 1:1 ratio. However, the ratio of 3R and 4R tau can be alternated under pathological conditions, but this process is not yet fully understood in terms of 3R and 4R tau pathology. A number of therapeutic strategies are investigated for tauopathies, however these strategies have not yet developed effective drugs for targeting tauopathies. Therefore, a 3R or 4R tau cell model is necessary for understanding the pathology of 3R and 4R tau and developing selective therapeutic drugs.

Methods

To generate 3R HEK293 Tau-BiFC cell line, HEK293 cells were co-transfected with pCMV6-TauK19-VN173 and pCMV6-TauK19-VC155. HEK293 cells were co-transfected with pCMV6-TauK18-VN173 and pCMV6-TauK19-VC155 for the generation of 3R/4R HEK293 Tau-BiFC cell line. For further enrichment of BiFC positive cell population, the transfected cells were sorted by FACS Aria.

Results

The BiFC intensity was significantly increased by various activators for inducing tau aggregation in 3R, 4R, and 3R/4R tau-BiFC cell lines. Interestingly, the BiFC intensity of 3R HEK293 Tau-BiFC cell line has more sensitivity to pan-HDAC inhibitors, compared with 4R HEK293 Tau-BiFC cell line. These cell lines can be used for therapeutic drug screening.

Conclusion

Our Tau-BiFC cell lines can be benefits in study of 3R and 4R pathology and drug development.

Clinicopathological Mismatching in a Patient Presenting with Clinical Symptoms of Parkinson's Disease

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Objective

Herein, we report the clinicopathological mismatching of an autopsy-confirmed PSP in a patient clinically diagnosed with idiopathic Parkinson's disease.

Methods

A patient performed B-MRI and FP-CIT PET. The patient and his wife gave antemortem consent for a postmortem examination. After a macroscopic examination of his fixed brain, H&E stain and immunohistochemistry were performed in the middle frontal, superior temporal, inferior parietal and occipital cortices, thalamus, subthalamus, amygdala, nucleus basalis of Maynert, hippocampus, caudate nucleus, globus pallidus, putamen, midbrain tectum, basis pontis, and cerebellum

Results

In the neurological examination, dysarthria, dysphagia, extraocular movement abnormalities were not observed. He showed rest type tremor on left hand and leg. Bradykinesia and rigidity were observed on both hands and leg, but more severe on the left. His posture mild stooped and he leaned on the left side. The first brain magnetic resonance imaging (MRI) revealed mild small vessel ischemic change in the corona radiata. Three years later, MRI was re-examined because of acute cerebral infarction that revealed left basal ganglia and CR. FP-CIT PET revealed asymmetrically bilateral decreased FP-CIT uptake in both the putamen and caudate nucleus (CN).

The whole brain weighed 1,270 gram. In the gross findings, substantia nigra (SN) and locus coeruleus (LC) were moderately pallor. AT8 (phosphorylated tau) immunohistochemistry IHC showed tufted astrocytes in the middle frontal gyrus (mild), hippocampus (moderate), trans-entorhinal cortex as well as coiled bodies in the middle frontal gyrus. But, they were not found in the brainstem. α-synuclein and TDP-43 IHC were also performed to exclude other neurodegenerative diseases. Alpha-synuclein IHC highlighted the absence of Lewy bodies in the amygdala, cingulate, or midbrain. TDP-43 IHC did not

Conclusion

This patient was clinically diagnosed with typical idiopathic Parkinson's disease. However, neuropathological findings did not show the Lewy body pathologies. Instead, PSP pathology based on the tufted astrocytes was observed.

Progranulin Haploinsufficiency Mediates TDP43 Cytoplasmic Aggregation with Lysosomal Dysfunction in the Human Model of Microglia

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Objective

Progranulin (PGRN) haploinsufficiency due to granulin (GRN) variants causes frontotemporal dementia (FTD) with TAR DNA-binding protein 43 (TDP-43) accumulation. Previous models of PGRN haploinsufficiency have demonstrated neuronal TDP43 pathology with microglial dysfunction. However, the precise pathomechanisms of microglia, including whether microglial TDP43 pathology is present and how it is triggered, are not clearly delineated.

Methods

Induced microglia-like cells (iMGs) were developed from FTD-GRN patients' monocytes carrying pathogenic or likely pathogenic variants (p.M1? and p.W147*) to design a human microglial model with PGRN haploinsufficiency. GRN mRNA levels and microglial markers, pro-inflammatory cytokines, and lysosomal-related gene expression of patient-derived iMGs were analyzed by qRT-PCR to evaluate phagocytic function. Patient-derived iMGs were used in immunocytochemical analysis to detect microglia TDP-43 pathology and lipid droplets and complement levels were assessed by ELISA.

Results

Monocyte-derived iMGs from each patient revealed reduced GRN mRNA and PGRN levels. Furthermore, each type of PGRN-deficient iMGs failed to maintain its homeostatic molecular signatures. The human model of microglia showed prominent cytoplasmic TDP-43 pathology and lipid droplets with profound lysosomal dysfunction and impaired phagocytosis. Additionally, these pathomechanisms were mediated by C1q complement activation and upregulated pro-inflammatory cytokines.

Conclusion

This study demonstrated that loss-of-function variants of GRN in the human cell model caused microglial dysfunction with abnormal cytoplasmic TDP-43 aggregation as well as impaired lysosomal function. These pathological and functional characteristics shown in this microglia model are an important clue for developing a precisional therapeutic strategy for FTD patients with PGRN haploinsufficiency.

Generation of iPSCs Derived from High Risk and Low Risk Alzheimer's Disease Patients Based on Polygenic Risk Score

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Objective

Alzheimer's Disease (AD) is associated with multiple genetic, environmental, and lifestyle factors. The strongest genetic risk factor for sporadic AD is APOE e4 but genome-wide association studies (GWAS) have identified other single nucleotide polymorphisms (SNPs) associated with AD. Polygenic Risk Score (PRS) is an effective strategy to combine the relatively smaller effects of AD associated SNPs to assess genetic risk beyond APOE e4. In a previous study, we developed and validated PRS for AD consisting of 39 SNPs, independent of APOE e4 status (S.H.Jung,2022,JAMA Network Open).
In this study, we generated induced pluripotent stem cell (iPSC) from sporadic AD patients based on PRS with high PRS (n=3) and low PRS (n=4) to better understand genetic impacts of sporadic AD, beyond APOE.

Methods

According to the PRS in the cohort of 1634 Korean AD patients, the patients were tiered into quartile. We selected 3 AD patients in the highest PRS group (high risk for AD) and 4 AD patients in the lowest PRS group (low risk for AD) and 1 normal candidate for control. The selected AD patients were all female, amyloid positive on PET scans, and had mean (standard deviation) age of 63 (8.79). We selected patients with APOE ε3/ε4 because the effect of PRS was greater among APOE e4 carriers (S.H.Jung,2022,JAMA Network Open).

Results

We isolated 8 candidates' peripheral blood mononuclear cells (PBMCs) which were transduced with reprogramming factors using Sendai virus. To characterize the iPSC lines, we confirmed that each iPSC line had normal karyotype and the same APOE genotype as donor, and expressed PSC markers, and 3 germ layers differentiation ability.

Conclusion

In this study, we established iPSC models from high risk and low risk AD patients based on PRS. Our PRS-iPSC model is important in that it may represent genetic nature of sporadic AD beyond APOE.

PE_027 Basic Science and Pathogenesis

Unraveling the Molecular Mechanism of Flavonoid Compounds in Bajakah as Potential Dual Inhibitory Effects to Prevent Amyloid-β Plaque and Tau Protein Aggregation

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Objective

Alzheimer's disease (AD) is characterized by progressive neuron degeneration due to the accumulation of misfolded amyloid-β (Aβ) and tau proteins. Therefore, anti-amyloid treatments become promising therapies for AD. Recently, several dual inhibitors of Aβ and tau aggregation, including piperidine and curcumin derivatives have been reported. This study employs a computational model to investigate the mechanism of flavonoid compounds derived from Bajakah Spatholobus suberectus, a medicinal plant native to Central Kalimantan, Indonesia, to inhibit the aggregation of Aβ and tau protein.

Methods

This study examined the molecular binding of 15 flavonoid compounds to α-helical monomer Aβ(1-42) and tau protein employing Autodock Vina 4. Additionally, absorption, distribution, metabolism, excretion, toxicity (ADMET), and drug-likeness properties were predicted using SwissADME.

Results

The findings indicate that among the 15 flavonoid compounds examined, six exhibited a greater affinity for binding with α-helical monomer Aβ and tau protein in comparison to the piperidine derivative (which possessed a binding energy of -5.5 kcal/mol). The active compounds were arranged in a hydrogen bonding and hydrophobic interaction along the α-helix Aβ(1-42). Whereas, in the tau protein the binding location was varied. Formononetin, an isoflavonoid, is the best dual inhibitor in terms of the highest binding affinity to Aβ and its ability to bind to a central part of misfolded tau protein, which may prevent the elongation of filaments. According to ADMET analysis, Formononetin has sufficient absorbency, solubility, and meets the criteria for permeating the Blood-Brain Barrier. The zero violation in Lipinski's rule signifies the potential as drug candidates.

Conclusion

In conclusion, the flavonoid compounds in Bajakah have the potency to be dual inhibitors against Aβ plaque and tau protein aggregation for AD therapy. Formononetin is the best dual inhibitor with drug-likeness properties. These findings also give the knowledge of the health benefits of Bajakah for AD patients.

PE_028 Biomarkers

MRI-based Radiomics-informed Brain Age Matrices for Classifying Mild Cognitive Impairment Converters

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Objective

Brain age matrices, as a set of promising biomarkers of ageing, plays an important role in the diagnosis and prognosis of age-related neurodegenerative diseases. Based on imaging data, greater brain age and brain-predicted age difference (brain-PAD) were found to be related to worse cognition in preclinical dementia. This study aimed to investigate the radiomics-informed brain age matrices in mild cognitive impairments (MCI) converters and their values in classifying MCI conversion.

Methods

Baseline, 1-year and 3-year follow-up cognitive assessments and structural magnetic resonance imaging scans from normal ageing (NA) adults (n = 32), and MCI converters (n = 22) were drawn from Open Access Series of Imaging Studies (OASIS-2). The quantitative measures of radiomic features included total intracranial volume (TIV), gray matter volume (GMV) and cortical thickness. Brain age matrices were calculated based on the individual's radiomic features.

Results

With comparable chronological age, MCI converters showed significant increased TIV-informed and left GMV-informed brain age than NA adults at all time points. Higher brain-PAD scores were associated with worse global cognition. TIV-informed and left GMV-informed brain age demonstrated acceptable classification performance, which can successfully differentiate the MCI converters from normal ageing adults at baseline.

Conclusion

This is the first demonstration that radiomics-informed brain age matrices exhibit lateralized patterns. Greater left GMV-informed brain age in MCI converters highlight the imaging signatures that may aid in classifying MCI converters at early stage. Our findings added value compared to existing imaging indicators and might help to develop personalized biomarkers for neurodegenerative disease.

PE_029 Biomarkers

Predictive Modeling of Personalized Clinical Outcome Trajectories in Mild Cognitive Impairment

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Objective

It is a formidable challenge at baseline to accurately predict when patients with mild cognitive impairment (MCI) will ultimately progress. Therefore, we aimed to develop a predictive model based on a deep recurrent network with an attention mechanism that can accurately predict future cognitive decline and magnetic resonance imaging (MRI) biomarker changes over time for MCI patients at the individual level.

Methods

We recruited 657 amnestic MCI patients from Samsung Medical Center who underwent cognitive tests, brain MRI scanning, and amyloid-β (Aβ) positron emission tomography (PET) scanning. We devised a simple but efficient deep learning framework that combined a recurrent neural network with an attention mechanism and trained a predictive model by inputting age, gender, education, apolipoprotein E (APOE) genotype, neuropsychological test scores, and brain MRI and amyloid PET features. Cognitive outcomes and MRI features of an MCI subject were predicted using this network.

Results

Along with obtaining a good prediction performance (AUC=0.814±0.035) in 5-fold cross-validation, our proposed predictive model also showed a reliable prediction in cognitive decline and MRI biomarkers over time. Notably, faster cognitive decline and brain atrophy in larger regions were forecasted in Aβ (+) than Aβ (-) MCI patients.

Conclusion

Our proposed method provides an effective and accurate means for prognosis with individuals likely to progress within a specific temporal period. This model could assist clinicians in identifying subjects at a higher risk of rapid cognitive decline by predicting future cognitive decline and MRI marker changes over time for mild cognitive impairment patients at the individual level. Future studies should further validate and refine our predictive model, leading to improved clinical decision-making.

PE_030 Biomarkers

Five-year Longitudinal Changes of Core Image Biomarkers, Amyloid and Tau, in Alzheimer's Disease Spectrum

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Objective

We aimed to follow up the changes in core biomarkers of the AD spectrum, amyloid and tau PET, to observe their progression over five years.

Methods

In 275 participants [96 cognitively unimpaired (CU), 108 mild cognitive impairment (MCI), and 71 AD] who completed 18F-florbetaben and 18F-flortaucipir PET studies for visit 1 (V1), 189 participants (74 CU, 77 MCI, and 38 AD) completed visit 2 (V2) PET studies at two years, and subsequently 83 participants (34 CU, 39 MCI, and 10 AD) completed visit 3 (V3) PET studies at about four years (mean 4.8 years) after the V1 study. A and T biomarker profiles were determined by using the cut-off standardized uptake value ratios of composite regions most vulnerable to each pathology.

Results

5.4% (6/111) of participants converted from A- to A+ at V2 and 17.9% (7/39) at V3. Likewise, 2.9% (4/138) of participants converted from T- to T+ at V2 and 17.7% (11/62) at V3. In comparison with lower conversion rate from T- to T+ in the A-T- participants [0.9% (1 A-T+ / 106 A-T-) at V2 and 5.1% (2 A+T+ / 39 A-T-) at V3], A+T- participants exhibited higher conversion rate from T- to T+ [9.4% (3 A+T+ / 32 A+T-) at V2 and 39.1% (9 A+T+ / 23 A+T-) at V3].

Conclusion

Positive conversion of A and T image biomarkers occurs steadily throughout the long-term period. Compared to A- individuals, positive conversion of T biomarker occurs four times more frequently in A+ individuals.

PE_031 Biomarkers

Characteristics of Discordance between Amyloid Positron Emission Tomography and Plasma Amyloid-β 42/40 Positivity

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Objective

Although plasma biomarkers for amyloid-β showed high predictability of amyloid positron emission tomography (PET) positivity, the characteristics of discordance between PET and plasma amyloid positivity is poorly understood.

Methods

We compared tau burden measured by PET, brain volume assessed by magnetic resonance imaging, cross-sectional cognitive function, longitudinal cognitive decline and polygenic risk score (PRS) between PET/plasma groups (PET-/plasma-, PET-/plasma+, PET+/plasma-, PET+/plasma+) using Alzheimer's Disease Neuroimaging Initiative database. Additionally, we investigated inter-assays variability between immunoprecipitation followed by mass spectrometry method and Elecsys immunoassay.

Results

The PET-/plasma+ showed intermediate changes between PET-/plasma- and PET+/plasma+ in terms of tau burden, hippocampal and precuneus volume, cross-sectional and longitudinal cognition, and PRS. PET+/plasma- represented heterogeneous characteristics with variability depending on plasma assays.

Conclusion

Characteristics of PET-/plasma+ support plasma biomarkers as early biomarker of amyloidopathy prior to amyloid PET. Various plasma biomarker assays might be applied distinctively to detect different target subjects or disease stages.

PE_032 Biomarkers

Aberrant GAP43 Gene Expression is Alzheimer's Disease Pathology-Specific

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Objective

The relation of presynaptic dysfunction with Alzheimer's disease (AD) pathology has been increasingly elucidated. A recent study reported significantly higher CSF growth-associated protein-43 (GAP43) protein levels in positive amyloidopathy (A+)/positive tauopathy (T+) compared to negative amyloidopathy (A-)/negative tauopathy (T-) or A+/T- and an association of CSF GAP43 with CSF tau levels independent of amyloid positivity and clinical diagnosis. Upstream of GAP43 protein synthesis, we investigated the association of GAP43 gene expression levels with AD pathology.

Methods

We used brain bulk RNA-Seq and cell-type specific (CTS) gene expression data from the Religious Orders Study and Rush Memory and Aging Project (ROS/MAP; N=583). Association analyses of GAP43 gene expression levels with A/T groups (A-/T-, A+/T-, and A+/T+) in brain bulk tissue and CTS expression were performed, adjusting for age, sex, and APOE ε4 status. CTS expression levels were estimated from bulk RNA-Seq data using a Bayesian model bMIND. Amyloidopathy and tauopathy were dichotomized neuropathologically by the Consortium to Establish a Registry for Alzheimer's Disease scores and Braak staging, respectively.

Results

Compared to A-/T-, GAP43 expression levels were significantly lower in A+/T+ (odd ratio (OR)=0.69, p-value=4.69×10-4). Compared to A-/T-, GAP43 expression levels were marginally lower in A+/T- (OR=0.81, p-value=9.81×10-2). On cell-type levels, GAP43 expression levels were lower in astrocyte (OR=0.87, p-value=1.20×10-2), microglia (OR=0.89, p-value=1.35×10-2), and oligodendrocyte (OR=0.80, p-value =1.20×10-2) in A+/T+ compared to A-/T-.

Conclusion

In conclusion, we found lower expression levels of GAP43 in A+/T+ compared to A-/T- and no significant difference between A+/T- and A-/T- in brain bulk tissue. In CTS analyses, lower GAP43 expression levels in glial cells of A+/T+, but not in neurons, may indicate that the GAP43-related synaptic pathway in AD could involve glial cells rather than neurons. Future studies are needed to investigate the relationship between decreased cortical GAP43 gene expression and increased CSF GAP43 protein expression in AD.

PE_034 Biomarkers

Caudate Dopamine Loss, Occipital Hypoperfusion, and Dementia Conversion in Parkinson's Disease: A Dual-phase 18F-FP-CIT PET Study

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Objective

This study aimed to investigate the association between dopamine depletion in the caudate, occipital hypoperfusion, and longitudinal cognitive decline in patients with Parkinson's disease (PD).

Methods

We retrospectively reviewed the medical records of 398 patients with newly diagnosed PD who underwent dual-phase 18F-FP-CIT PET scans. Cox regression analyses were performed to assess the effect of dopamine transporter (DAT) availability in the caudate (on late-phase 18F-FP-CIT PET images) or uptake in the occipital region (on early-phase 18F-FP-CIT PET images) on the risk of dementia conversion in PD. Additionally, mediation analyses were conducted to evaluate the relationship between DAT availability of the caudate, occipital hypoperfusion, and dementia conversion in Cox regression models.

Results

Cox regression analyses demonstrated that greater DAT availability in the caudate (hazard ratio [HR] = 0.120, P <0.001) and preserved occipital perfusion (HR = 0.003, P <0.001) were associated with a lower risk for developing dementia, respectively. Cox regression model including the DAT availability of the caudate with additional adjustment for occipital uptake demonstrated that these two variables remained significant predictors of future dementia conversion in PD. Mediation analyses showed that the direct effect of caudate dopamine loss (HR = 0.155, P <0.001), the direct effect of occipital perfusion (HR = 0.021, P = 0.027), and the indirect effect of occipital perfusion through caudate dopamine depletion (HR = 0.203, P = 0.010) on the risk of dementia conversion were significant, while the indirect effect of caudate dopamine loss through occipital hypoperfusion was not significant (HR = 0.821, P = 0.080).

Conclusion

These findings suggest that both dopamine depletion in the caudate and hypoperfusion in the occipital region are associated with future cognitive decline in PD, while DAT availability in the caudate also mediates the association between occipital hypoperfusion and the risk of dementia conversion.

PE_035 Biomarkers

Predicting Superagers by Machine Learning Classification based on Gut Microbiome Features

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Objective

Superagers are elderly individuals with cognitive abilities comparable to middle-aged people. Recent research has been conducted to explore the link between dementia, mild cognitive impairment (MCI), and the microbiome, as there is a growing focus on the microbiome's role in health and diseases. This study aims to understand the relationship between gut microbiome composition and preserved cognitive function in superagers. It focuses on identifying key biomarkers differentiating typical agers from superagers and developing classifiers for superagers identification.

Methods

Among the 102 cognitively normal participants, 57 individuals were identified as superagers through cognitive test. The preprocessing of gut-microbiome data with fecal microbiome analysis was conducted by CJ Bioscience. Statistical analyses based on the relative abundance of bacterial taxa were performed, and machine learning classification models were experimented using features extracted from statistical analyses and Recursive Feature Elimination with Cross-Validation (RFECV).

Results

While there is no significant difference in nutrient intake and BMI between superagers and typical agers, superagers demonstrated higher abundances of PAC001115_g, Eisenbergiella, PAC001138_g, PAC001236_g, Eubacterium_g8, Subdoligranulum, Lactobacillaceae, Leuconostoc within the Firmicutes, and elevated Odoribacteraceae levels within the Bacteroidetes phylum, while displaying lower abundances of Sellimonas and Romboutsia. Additionally, Actinobacteria, Actinobacteria_c, PAC001236_g, Eubacterium_g8, and Rothia exhibited positive correlations with superagers, while Coprococus, Ruminococcus_g4, and Sellimonas showed negative correlations. However, the correlation coefficients were all below an absolute value of 0.3.

LightGBM initially achieved accuracy of 0.810, AUC of 0.769 and sensitivity of 0.833 using key features from statistical analyses. Incorporating additional features selected through RFECV (Pseudoflavonifractor with p=0.1, Alistipes with p=0.06, and PAC001137_g with p=0.57) improved the model's performance to accuracy of 0.857, AUC of 0.778 and sensitivity of 0.917.

Conclusion

These findings suggest that the composition of the gut microbiome may contribute to preserved cognitive performance, and specific bacteria within the microbiome could serve as important features for classifying superagers.

PE_036 Biomarkers

Independent Effect of Aβ Burden on Cognitive Impairment in Patients with Small Subcortical Infarction

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Objective

The effect of amyloid-β (Aβ) on cognitive impairment in patients with small subcortical infarction remains controversial, although a growing body of evidence shows a substantial overlap between Alzheimer's disease (AD) and subcortical ischemic vascular dementia, another form of cerebral small vessel disease (cSVD). Therefore, we investigated the relationships between Aβ positivity and the development of post-stroke cognitive impairment (PSCI) in patients with small subcortical infarction.

Methods

We prospectively recruited 37 patients aged ≥50 years, with first-ever small subcortical infarction, who underwent amyloid positron emission tomography, 3 months after stroke at Korea University Guro Hospital. We also enrolled CU participants matched for age and sex with stroke patients for comparison of Aβ positivity. Patients were followed up at 3 and 12 months after the stroke to assess cognitive decline. Logistic and linear mixed-effect regression analyses were performed to identify the effect of Aβ positivity on PSCI development and long-term cognitive trajectories.

Results

At 3 months after stroke, 12/37 (32.4%) patients developed PSCI and 11/37 (29.7%) patients had Aβ deposition. Aβ positivity (odds ratio [OR]=72.2, p=0.024) was predictive of PSCI development regardless of cSVD burden. Aβ positivity (β=0.846, p=0.014) was also associated with poor cognitive trajectory, assessed by the Clinical Dementia Rating-Sum of Box, for 1 year after stroke.

Conclusion

Our findings highlight that Aβ positivity is an important predictor for PSCI development and cognitive decline over 1 year. Furthermore, our results provide evidence that anti-AD medications may be a strategy for preventing cognitive decline in patients with small subcortical infarctions.

PE_037 Biomarkers

Ethnic Differences in the Effects of APOE ε4 and Vascular Risk Factors on Accelerated Brain Aging

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Objective

The frequency of the apolipoprotein E (APOE) ε4 allele and vascular risk factors differs among ethnic groups. We aimed to assess the combined effects of APOE ε4 and vascular risk factors on brain age in Korean and UK cognitively unimpaired (CU) populations. We also aimed to determine differences in the combined effects between the two populations.

Methods

We enrolled 2,314 CU individuals from Korea and 6,942 CU individuals from the UK, who were matched using propensity scores. Brain age was defined using the brain age index (BAI). The APOE genotype (ε4 carriers, ε2 carriers, and ε3/ε3 homozygotes) and vascular risk factors (age, hypertension, and diabetes) were considered predictors.

Results

APOE ε4 carriers in the Korean (p=0.012) and UK (p=0.006) groups had higher BAI values. The adverse effects of the APOE genotype on BAI values increased with age in the Korean group alone (ε2 carriers, p=0.009; ε4 carriers, p<0.001). The APOE genotype, age, and ethnicity showed a three-way interaction with BAI (p for age×ε2×ethnicity=0.022, p for age×ε4×ethnicity=0.003). The effects of APOE ε4 on BAI values were more pronounced in individuals with hypertension in the Korean group alone (p=0.038). The APOE genotype, age, and ethnicity showed a three-way interaction with BAI (p for hyperte nsion×ε4×ethnicity=0.007).

Conclusion

We highlight ethnic differences in the combined effects of the APOE ε4 genotype and vascular risk factors on accelerated brain age. These findings emphasize the need for ethnicity-specific strategies to mitigate APOE ε4-related brain aging in CU individuals.

PE_038 Biomarkers

Sex-specific Relationship between Non-alcoholic Fatty Liver Disease and Amyloid-β in Cognitively Unimpaired Individuals

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Objective

Non-alcoholic fatty liver disease (NAFLD) is known to be associated with a high risk of clinically diagnosed Alzheimer's disease (AD). Additionally, the prevalence of NAFLD and AD is higher in elderly females than in males. However, a sex-specific association between NAFLD and amyloid-beta (Aβ) deposition remains unclear. Therefore, we investigated the sex-specific relationship between NAFLD and Aβ deposition in a large-sized cohort of cognitively unimpaired (CU) individuals.

Methods

We enrolled 673 (410 [60.9%] females and 263 [39.1%] males) CU individuals aged ≥ 45 years who underwent Aβ positron emission tomography (PET). The presence of NAFLD, assessed using the hepatic steatosis index, and the severity of NAFLD, assessed using the Fibrosis-4 index, were considered predictors. Aβ deposition on PET was considered as an outcome.

Results

Females had a higher frequency of NAFLD than males (48% and 23.2%, $p<0.001$). Among females, the presence of NAFLD ($\beta=0.216$, $p<0.001$) was predictive of increased Aβ deposition, whereas among males, the presence of NAFLD ($\beta=0.191$, $p=0.064$) was not associated with Aβ deposition. Among females, the presence of NAFLD with low ($\beta=0.254$, $p=0.039$), intermediate ($\beta=0.201$, $p=0.006$), and high fibrosis ($\beta=0.257$, $p=0.027$) was predictive of increased Aβ deposition. Aβ deposition also increased as the severity of NAFLD increased in females (p for trend=0.001).

Conclusion

We highlight the marked influence of NAFLD and its severity on the risk of Aβ deposition in relation to sex. Furthermore, our findings suggest that sex-specific strategies regarding the management of NAFLD are necessary for the prevention of Aβ deposition.

PE_039 Biomarkers

Altered Functional Connectivity Density against tau accumulation in Alzheimer's Disease

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Objective

To investigate the change in functional connectivity density (FCD) obtained by resting state functional magnetic resonance imaging (rs-fMRI) and its association with cognitive decline and tau burden in Alzheimer's disease (AD).

Methods

We enrolled 143 participants [45 amyloid negative cognitively unimpaired (CU-), 39 amyloid positive mild cognitive impairment (MCI+), and 59 amyloid positive dementia (DEM+)] who completed ^{18}F-florbetaben and ^{18}F-flortaucipir positron emission tomography (PET) and rs-fMRI. Globally normalized (FCDnorm) and log-transformed (FCDlog) FCD images were created for three types of global, local, and distant connection degrees. The ^{18}F-flortaucipir uptake and FCD mapped on the cortical surface were compared between the three groups. We also investigated the relationship between the FCD, cognitive function and tau burden.

Results

Compared to CU-, DEM+ exhibited higher global and distant FCDnorm in the posterior cingulate, inferior parietal, and lateral frontal cortices, and the posterior cingulate cortex survived after correcting for multiple comparisons. There was a tendency of lower FCDnorm and FCDlog in DEM+ particularly in the lateral temporal cortex, which did not survive after correcting for multiple comparisons. Cognitive decline and global cortical and regional tau burden were associated with an increase in the distant FCDnorm in the posterior cingulate, precuneus, inferior parietal, and medial frontal cortices and with a decrease in the distant FCDnorm in the lateral temporal and occipital cortices. The distant FCDlog also decreased with an increase in global cortical and regional tau burden in the high tau regions.

Conclusion

Tau accumulation causes network change and cognitive decline in AD. Unlike the extra-hub regions, the FCD in the network hub regions may be relatively resistant to tau burden. To compensate the loss of connections, these hub regions may recruit more regions relatively and may serve as a source of tau spreading via network even in the dementia stage of AD.

PE_040 Biomarkers

Predicting Cognitive Stage Transition Using p-tau181, Centiloid, and Other Measures

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Objective

A combination of plasma phospho-tau (p-tau), amyloid beta (Aβ)-PET, brain magnetic resonance imaging, cognitive function tests, and other biomarkers might predict future cognitive decline. This study aimed to investigate the efficacy of combining these biomarkers in predicting future cognitive stage transitions within 3 years.

Methods

Among the participants in the Korean Brain Aging Study for the Early Diagnosis and Prediction of Alzheimer's Disease (KBASE-V) study, 49 mild cognitive impairment (MCI) and 113 cognitively unimpaired (CU) participants with Aβ-PET and brain imaging data were analyzed.

Results

Older age, increased plasma p-tau181, Aβ-PET positivity, and decreased semantic fluency were independently associated with cognitive stage transitions. Combining age, p-tau181, the Centiloid scale, semantic fluency, and hippocampal volume produced high predictive value in predicting future cognitive stage transition (AUC = 0.879).

Conclusion

Plasma p-tau181 and Centiloid scale alone or in combination with other biomarkers, might predict future cognitive stage transition in non-dementia patients.

PE_041 Biomarkers

Extra-neurite and Intra-neurite Conductivity Maps in Patients with MCI and AD

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Objective

To investigate extra-neurite conductivity (EC) and intra-neurite conductivity (IC) changes in Alzheimer's disease (AD) patients compared with cognitively normal (CN) elderly people and patients with amnestic mild cognitive impairment (MCI) and to evaluate the association between conductivity indices and cognitive decline.

Methods

In this prospective single-center study, brain MRI-based electrical property tomography (MREPT) and multi-shell multi-gradient direction diffusion tensor images (b=0, 800, and 2000 s/mm2) were acquired to calculate high-frequency conductivity (HFC) and decomposed it into extra- and intra-neurite conductivities, EC and IC, respectively. Conductivity values were compared between the three participant groups and evaluated the association with either age or the Mini-Mental State Examination (MMSE) scores.

Results

A total of 66 patients were included including 20 AD patients, 25 amnestic MCI patients, and 21 CN old people. Compared with CN, HFC was higher in the AD group in the hippocampus (p=0.003), insular (p=0.001), and middle temporal gyrus (MTG) areas (p=0.018). EC was higher in the AD group in the hippocampus (p=0.009) and insular (p=0.020). IC was not significantly different between groups in any regions-of-interest. Both HFC and EC were significantly negatively associated with the K-MMSE in the insular (rho r = -0.427/p = 0.0004 for HFC, rho r = -0.426/p = 0.0004 for EC) and MTG (rho r = -0.438/p = 0.0003 for HFC, rho r = -0.365/p = 0.003 for EC), but IC were significantly positively associated with the K-MMSE in the corpus callosum (rho r = 0.370/p = 0.002). HFC and EC show significant differentiation between AD from CN and from MCI.

Conclusion

Since EC values increased in the AD group and negatively correlated with MMSE scores, the EC value might be used as an imaging biomarker to aid in the monitoring of cognitive function.

PE_042 Biomarkers

Gray-White Matter Boundary Tissue Volume and Its Z-Score Map in Patients with MCI and AD

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Objective

Alzheimer's disease (AD) presents typically gray matter atrophy and white matter abnormalities in neuroimaging, suggesting that the gray-white matter boundary could be altered in individuals with AD. The purpose of this study was to explore differences in gray-white matter boundary Z-score (gwBZ) and its tissue volume (gwBTV) between patients with AD, amnestic mild cognitive impairment (MCI), and cognitively normal (CN) elderly participants.

Methods

Three-dimensional T1-weight images of a total of 227 participants were prospectively obtained from our institute from 2006 to 2022 to map gwBZ and gwBTV on images. Statistical analyses of gwBZ and gwBTV were performed to compare the three groups (AD, MCI, CN), to assess their correlations with age and the Korean version of the Mini-Mental State Examination (K-MMSE), and to evaluate their effects on AD classification in the hippocampus.

Results

This study included 62 CN participants (71.8 ± 4.8 years, 20 males, 42 females), 72 MCI participants (72.6 ± 5.1 years, 23 males, 49 females), and 93 AD participants (73.6 ± 7.7 years, 22 males, 71 females). The AD group had lower gwBZ and gwBTV than the CN and MCI groups. K-MMSE showed positive correlations with gwBZ and gwBTV whereas age showed negative correlations with gwBZ and gwBTV. The combination of gwBZ or gwBTV with K-MMSE had a high accuracy in classifying AD from CN in the hippocampus with an area under curve (AUC) value of 0.972 for both.

Conclusion

gwBZ and gwBTV were reduced in AD. They were correlated with cognitive function and age. Moreover, gwBZ or gwBTV combined with K-MMSE had a high accuracy in differentiating AD from CN in the hippocampus. These findings suggest that evaluating gwBZ and gwBTV in the AD brain could be a useful tool for monitoring AD progression and diagnosis.

PE_044 Biomarkers

Investigating Relative PSD Difference and Coherence Analysis in rEGG of Alzheimer's Disease

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Objective

Electroencephalography (EEG) is a valuable non-invasive technique for comprehensively assessing the electrical activity of the brain's cerebral cortex. In this study, EEG was employed to investigate potential neuropsychological biomarkers in detecting varying stages of Alzheimer's disease (AD) through quantitative EEG (qEEG) analysis of resting state EEG (rEEG) signals under eyes-open (EOR) and eyes-closed (ECR) conditions. Abnormalities in rEEG signals were compared between AD patients and healthy controls (HC) using 19-scalp electrode EEG signals.

Methods

The study analyzed rEEG data from 534 subjects aged 40-90, comprising 269 HC and 265 AD subjects in Korea. Quantitative EEG analysis for EOR and ECR states was conducted separately for HC and AD subjects to measure relative power spectrum density (PSD) and coherence, evaluating abnormalities. Data preprocessing and analysis were performed using EEGlab and Brainstorm toolboxes in MATLAB R2021a, with statistical analyses conducted via ANOVA.

Results

The analysis, employing the Welch method, revealed increased relative PSD in the delta frequency band across 19 EEG channels, particularly in the frontal, parietal, and temporal regions in the AD group compared to HC, demonstrating a significant difference. Delta power band at the source level was increased in AD but decreased in HC. Moreover, activities in alpha, beta, and gamma frequency bands were significantly reduced in the AD group, notably the beta frequency band in all brain areas. Coherence analysis demonstrated a remarkable increase in pair-wise coherence between different brain areas in the AD group during the ECR state, with subsequent reduction after subtracting the EOR state.

Conclusion

The study indicates that analyzing PSD and functional connectivity through coherence analysis provides a promising and comprehensive approach to differentiate individuals with AD from normal controls. This approach holds the potential to enhance our understanding of Alzheimer's disease by offering valuable insights into disease progression and aiding in early detection and monitoring.

PE_045 Biomarkers

Distinct Effects of Cholesterol Profile Components on Amyloid and Vascular Burdens

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Objective

Cholesterol plays important roles in β-amyloid (Aβ) metabolism and atherosclerosis. However, the relationships of plasma cholesterol levels with Aβ and cerebral small vessel disease (CSVD) burdens are not fully understood in Asians. Herein, we investigated the relationships between plasma cholesterol profile components and Aβ and CSVD burdens in a large, non-demented Korean cohort.

Methods

We enrolled 1,175 non-demented participants (456 with unimpaired cognition [CU] and 719 with mild cognitive impairment [MCI]) aged ≥ 45 years who underwent Aβ PET at the Samsung Medical Center in Korea. We performed linear regression analyses with each cholesterol (low-density lipoprotein cholesterol [LDL-c], high-density lipoprotein cholesterol [HDL-c], and triglyceride) level as a predictor and each image marker (Aβ uptake on PET, white matter hyperintensity [WMH] volume, and hippocampal volume) as an outcome after controlling for potential confounders.

Results

Increased LDL-c levels (β=0.014 to 0.115, p=0.013) were associated with greater Aβ uptake, independent of the APOE e4 allele genotype and lipid-lowering medication. Decreased HDL-c levels (β=−0.133 to −0.006, p=0.032) were predictive of higher WMH volumes. Increased LDL-c levels were also associated with decreased hippocampal volume (direct effect β=−0.053, p=0.040), which was partially mediated by Aβ uptake (indirect effect β=−0.018, p=0.006).

Conclusion

Our findings highlight that increased LDL-c and decreased HDL-c levels are important risk factors for Aβ and CSVD burdens, respectively. Furthermore, considering that plasma cholesterol profile components are potentially modified by diet, exercise, and pharmacological agents, our results provide evidence that regulating LDL-c and HDL-c levels is a potential strategy to prevent dementia.

PE_046 Biomarkers

Elevated CSF pTau as a Predictor of Rapid Cognitive Decline in Preclinical Alzheimer's Disease

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Objective

We aim to investigate if higher P tau levels in preclinical AD lead to accelerated cognitive decline and identify specific affected cognitive domains.

Methods

We collected CSF data from 84 cognitively normal individuals with amyloid deposition confirmed by Amyloid PET at CNUH. Participants were categorized into two groups: A+T- and A+T+. Neuropsychological tests were conducted, and the study had an average follow-up duration of 2.06 (1.99) years.

We conducted an analysis of covariance (ANCOVA) to compare CSF biomarkers (amyloid beta 42, 42/40 ratio, P tau 181, and total tau) and multiple cognitive domain (attention, language, frontal executive function, memory, visuospatial) based on P-tau deposition status (A+T- and A+T). To evaluate longitudinal cognitive decline, we utilized linear mixed-effects models.

Results

In the cross-sectional analysis, the A+T+ group exhibited a lower Abeta 42/40 ratio, alongside higher pTau and total Tau levels, compared to the A+T- group ($P<0.05$). Nevertheless, no statistically significant variations were found in the entire spectrum of cognitive functions.

In the longitudinal analysis, the A+T+ group demonstrated steeper alterations in various cognitive domains: Mini-Mental State Examination (MMSE) (β [SE] = -0.04 [0.12], $p < 0.05$), frontal executive function (Trail Making Test B time, β [SE] = 3.57 [2.55], $p < 0.05$), language (Korean-Boston Naming Test [K-BNT], β [SE] = -0.06 [0.09], $p < 0.05$), and visuospatial abilities (Rey Complex Figure Test copy [RCFT copy], β [SE]] = -0.025 [0.166], $p < 0.05$). With respect to memory, a learning effect was observed in the A+T- group, whereas the A+T+ group did not demonstrate this effect.

Conclusion

In summary, our findings underscore the association between elevated CSF pTau levels and the hastened cognitive decline observed during the preclinical Alzheimer's disease. This highlights the potential utility of CSF pTau as a crucial biomarker for identifying and monitoring cognitive deterioration in early-stage Alzheimer's disease.

PE_047 Biomarkers

Alteration of Limbic Metabolism Related to Alzheimer's Disease and Dementia with Lewy Bodies

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Objective

Limbic metabolism has not been evaluated simultaneously considering Alzheimer's disease (AD) and dementia with Lewy bodies (DLB).

Methods

131with AD, 133 with DLB, 122 with mixed disease (MD) having both diseases, and 28 normal controls (NCs) underwent 18F-fluorodeoxyglucose PET, neuropsychological tests, and assessments for parkinsonism, cognitive fluctuation (CF), rapid eye movement sleep behavior disorder, and visual hallucinations (VH). Limbic metabolism was quantitatively measured in the amygdala, hippocampus, and entorhinal cortex. The effects of AD and DLB on limbic metabolism were evaluated using general linear models (GLMs) after controlling for age, sex, and educational level. Associations between limbic metabolism, cognition, and clinical features were evaluated using GLMs or logistic regression models separately performed for the AD spectrum (NC + AD + MD), DLB spectrum (NC + DLB + MD), and disease groups (AD + DLB + MD).

Results

AD was associated with hippocampal/entorhinal hypometabolism, whereas DLB was associated with amygdalar/hippocampal hypermetabolism. Limbic hypermetabolism was associated with lower attention/visuospatial/executive scores and severe parkinsonism in both the AD and DLB spectra and disease groups. Left hippocampal/entorhinal hypometabolism was associated with lower verbal memory scores, whereas right hippocampal hypometabolism was associated with lower visual memory scores in both the AD spectrum and disease groups. Limbic hypermetabolism was associated with an increased risk of CF and VH in the disease group, and amygdalar hypermetabolism was associated with an increased risk of VH in the DLB spectrum.

Conclusion

Our findings suggest that entorhinal-hippocampal hypometabolism and amygdala-hippocampal hypermetabolism are characteristics of AD- and DLB-related neurodegeneration, respectively.

Association between T1w/T2w Ratio in White Matter and Cognitive Function in Alzheimer's Disease

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Objective

Loss of myelin in the brain may lead to cognitive decline in Alzheimer's disease (AD). The ratio of T1 weighted/T2 weighted (T1w/T2w) on magnetic resonance imaging has been used as a proxy for myelin content in the brain. Using this approach, we investigated the correlation between the white matter (WM) T1w/T2w ratio and both cognitive scores and disease progression in AD.

Methods

A total of 93 participants who were cognitively unimpaired or diagnosed with mild cognitive impairment or AD dementia were recruited from the Dementia Clinic of Dongguk University Ilsan Hospital between March 2021 and November 2022. All participants were assessed using neuropsychological tests, and a subset of the participants was assessed every 1 year to monitor disease progression.

Results

We observed significant positive associations between the WM T1w/T2w ratio and executive function within the fornix, sagittal stratum, anterior internal capsule, and body of the corpus callosum (False discovery rate [FDR]-corrected P-value <0.05). There was a marginal interaction between the WM T1w/T2w ratio of the left anterior internal capsule and the longitudinal change in sum of boxes of the Clinical Dementia Rating Scale (FDR-corrected P-value = 0.05).

Conclusion

The present study demonstrated that the WM T1w/T2w ratio was associated with executive function and disease progression, suggesting that it may be a novel neuroimaging marker for AD.

PE_049 Biomarkers

Plasma Proteomic Profiling Predicts Proteins and Pathways Influencing Beta-Amyloid Oligomerization in the Blood.

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Objective

Alzheimer's disease (AD) is characterized by the accumulation of beta-amyloid (Aβ) in the brain. We previously discovered that AD patients' blood, when spiked with synthetic Aβ, displayed a higher Aβ oligomerization tendency compared to that of non-AD subjects. Building upon this observation, we developed a blood test named the AlzOn, specifically designed for detecting AD. While we have demonstrated that the AlzOn test exhibits excellent sensitivity and specificity, the mechanism underlying the test remains elusive. To delineate the factors affecting AlzOn results, we conducted a plasma proteome analysis on subjects with varying levels of oligomeric Aβ after administering exogenous Aβ.

Methods

Forty AD and non-AD subjects were divided into four groups based on the disease diagnosis, AlzOn results (oligomeric Aβ level thresholded at 0.78 ng/mL), and amyloid PET status: Amyloid PET-positive AD patients with high or low AlzOn signal, Amyloid PET-negative non-AD subjects with high or low AlzOn signal. Using SOMAscan technology, we quantified approximately 7,000 proteins from plasma samples. Group differences in protein levels were assessed using t-tests. Additionally, we examined the enrichment of gene sets associated with Alzheimer's disease and annotations from the Gene Ontology database.

Results

We identified hundreds of proteins differentially expressed in subjects with varying levels of the AlzOn signal. Within the high AlzOn signal group, there was a significant downregulation in biological pathways associated with cellular metabolism and autophagy, while pathways related to immune response showed significant upregulation. Furthermore, elevated AlzOn signal in non-AD subjects were linked to a significant change in proteins predictive of dementia.

Conclusion

This study revealed a correlation between the AlzOn signal and augmented inflammation as well as reduced cellular metabolism and protein clearance. Our findings also suggest that the AlzOn test serves as a valuable tool not only for diagnosing AD but also for predicting the development of dementia years in advance.

PE_050 Biomarkers

Distinct Prognostic Values of Non-Alzheimer's Pathologic Changes according to Cognitive Syndromal Stages: In individuals with Alzheimer's and Concomitant Cerebrovascular Burdens

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Objective

Suspected non-Alzheimer disease pathophysiology (SNAP), a biomarker-based concept denoting positive neurodegeneration without β-amyloid (Aβ) deposition, may show distinct clinical characteristics. We investigated the prevalence and characteristics of SNAP according to the cognitive status, using unsupervised machine learning (ML) clustering analyses to define positive neurodegeneration.

Methods

We included 1,855 participants with cognitively normal (CN), mild cognitive impairment (MCI) and dementia who underwent Aβ positron emission tomography (PET), brain magnetic resonance imaging, and neuropsychological tests. Aβ positivity status (A+/A−) was determined by Aβ-PET, and neurodegeneration positivity (N+/N−) was determined by adjusted hippocampal volume (HVa). To obtain HVa cutoff, we applied three ML clustering methods including k-means and Gaussian mixture model (GMM). Then we compared clinical and imaging characteristics of the A−N+ (=SNAP) subgroup with the A−N− or A+N+ subgroups.

Results

Two ML methods consistently categorized participants into A/N subgroups. A−N+ participants were older than A−N− and A+N+ and less likely to have apolipoprotein ε4 compared to A+N+ in all cognitive status ($p < 0.001$ for all comparisons). In CN and MCI status, the ratio of A−N+ among A− increased as the severity of white matter hyperintensities increased. In dementia status, A−N+ had less thinner parietal, temporal, and occipital cortex than A+N+ and better memory score than A+N+ ($p < 0.05$ for all comparisons).

Conclusion

ML clustering approaches are useful for classification for neurodegeneration. SNAP showed the distinct clinical and imaging characteristics compared to other Aβ and neurodegeneration groups. Our investigation of SNAP can provide insight into the underlying pathophysiology in different cognitive status.

PE_051 Biomarkers

A Case of Huntington's Disease Diagnosed by 18F-FDG-PET

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Objective

Huntington's disease (HD) is a rare inherited neurodegenerative disease primarily characterized by chorea, cognitive decline, and psychiatric symptoms. Cognitive impairment in HD has different characteristics than other subtypes of dementia, making accurate diagnosis difficult. Here, we report a case of de novo Huntington's disease that was diagnosed using 18F-FDG-PET.

Methods

We reviewed the paitent's medical records.

Results

A 70-year-old female patient visited our hospital because of progressive cognitive impairment. The patient complained of a decline in daily life functions, and family members reported a loss of recent memory. Additionally, the patient complained of involuntary movement of both hands for 4–5 years. The patient had a history of rheumatoid arthritis, asthma, and hypertension. Magnetic resonance imaging revealed an acute-to-subacute infarction in the left inferior frontal sulcus. In the Korean version of the Mini-Mental State Examination, the score was 24 and the Global Deterioration Scale score was 3. In the Seoul neuropsychological screening battery, frontal/executive function declined but verbal and visual memory functions were relatively preserved. Amyloid PET performed for further evaluation confirmed negative amyloid deposition, and 18F-FDG-PET revealed diffuse hypometabolism in the bilateral striatum and mild hypometabolism in the bilateral medial prefrontal cortices. Based on the results of FDG-PET, genetic testing was performed, and HD was confirmed with CAG repeats 17/40.

Conclusion

HD mainly occurs in patients in their 30s and 40s, but approximately 2-30% of patients are over 60s. Late-onset HD (≥ 60 years) is characterized by mild motor symptoms, a lack of family history, and relatively low CAG repeats. HD dementia is different from other types of dementia, and an accurate diagnosis may be difficult in cases where HD symptoms are mild. In this case, FDG-PET could be helpful in distinguishing various causes of cognitive decline.

PE_052 Biomarkers

Real World One Year Estimation of the Candidates for Lecanemab in a South Korea Memory Clinic

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Objective

Lecanemab, a new therapeutic agent for Early Alzheimer's disease, has received accelerated approval from the U.S food and Drug Administration (FDA). However, there is a lack of data on how many people can use this drug in real world data, according to the Clarity AD study protocol, and to evaluate the most appropriate clinical criteria for prescribing lecanemab.

Methods

This study included patients who underwent Amyloid PET (Flutemetamol) in the memory clinic of Ajou University Hospital, South Korea. The inclusion and exclusion criteria of the Clarity AD study's protocol were applied to estimate how many candidates for lecanemab existed. Data collection was performed from January 1, 2022, to December 31, 2022

Results

Out of the 6009 patients who visited Ajou University Hospital Memory clinic in 2022, 318 performed amyloid PET, and 140 were amyloid PET positive. According to the Clarity AD protocol, 23 MCI patients and 18 AD patients were identified as candidates for lecanemab . Additionally, by adjusting the MMSE score baseline, the number of candidates for lecanemab among amyloid PET positive AD patients increased to 26, 30, and 37 patients based on MMSE scores of 21 or higher, 20, and 19, respectively.

Conclusion

According to the Clarity AD protocol, there were 41 candidates for lecanemab among patients who visited Ajou University Hospital Memory Clinic. 44 of 74 amyloid PET positive AD patients were not included because MMSE score was under 22. If adjusting the MMSE score criteria to 21 or 20, the number of candidates for lecanemab became 26, 30 respectively. Considering that generally accepted MMSE score of mild AD is 20 to 26, further studies to determine the optimal MMSE criteria for selecting candidates for lecanemab is needed.

PE_053 Biomarkers

Clinical and Pathological Validation of CTBased Regional Harmonization Methods of Amyloid PET

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Objective

The CT-based regional direct comparison Centiloid (dcCL) method was developed to harmonize and quantify regional beta-amyloid (Aβ) burden. In the present study, we aimed to investigate correlations between the CT-based regional dcCL scales and Aβ pathological burdens and to validate the clinical utility using thresholds derived from pathological assessment.

Methods

We included a pathological cohort of 63 cases and a clinical cohort of 4,062 participants and obtained modified Consortium to Establish a Registry for Alzheimer's Disease criteria (mCERAD) scores by assessment of neuritic plaque burdens in multiple areas of each cortical region. PET and CT images were processed using the CT-based regional dcCL method to calculate scales in six distinct regions.

Results

The CT-based regional dcCL scales were correlated with neuritic plaque burdens represented by mCERAD scores, globally and regionally ($r = 0.56$~0.76). In addition, striatum dcCL scales reflected Aβ involvement in the striatum (p value < 0.001). The regional dcCL scales could predict significant Aβ deposition in specific brain regions with high accuracy; AUC of 0.81-0.97 with an mCERAD cutoff of 1.5 and AUC of 0.88-0.93 with an mCERAD cutoff of 0.5. When applying the dcCL thresholds of 1.5 mCERAD scores, the G(-)R(+) group showed lower performances in memory and global cognitive functions and had less hippocampal volume compared to the G(-)R(-) group (p value < 0.001). However, when applying the dcCL thresholds of 0.5 mCERAD scores, there were no differences in the global cognitive functions between the two groups.

Conclusion

The thresholds of regional dcCL scales derived from pathological assessments might provide clinicians with a better understanding of biomarker-guided diagnosis and distinguishable clinical phenotypes, which are particularly useful when harmonizing different PET ligands with only PET-CT.

PE_054 Biomarkers

Reversal of Age-dependent Amyloid Real-world Prevalence across Disease Severity Spectrum in a South Korean Memory Clinic

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Objective

Alzheimer's disease (AD), the most common cause of dementia, is a major topic of discussion due to its growing prevalence with aging population. The objective of the study is to estimate the prevalence of amyloid abnormality according to age and cognitive status assessed by Amyloid PET modality in South Korean memory clinic patients with impaired cognition, and to investigate its relation with known risk factors for AD.

Methods

In this study, 327 participants from a memory clinic in South Korea were included who underwent PET imaging. Data collection was performed from January 1, 2022, to December 31, 2022. The study examined the age-dependent prevalence of amyloid abnormality in patients with different cognitive statuses; subjective cognitive decline(SCD), mild cognitive impairment(MCI), alzheimer's disease(AD), and other dementia, as well as, the relation of amyloid positivity with sex, education, and APOE-ε4 carrier status, and APOE genotype.

Results

Among the 327 participants included, 16(4.9%) had SCD, 146(44.6%) had MCI, 107(32.7%) had AD, and 58(17.7%) had other dementia. The prevalence of amyloid positivity was significantly associated with age in pre-dementia patients, with a significant increase occurring in patients age approximately 70. The prevalence of amyloid positivity was significantly associated with age in AD patients, with a significant decrease occurring in patients age approximately 80. There was also a significant association between sex and amyloid positivity in AD patients, while education level and APOE-ε4 carrier status were not significantly associated.

Conclusion

This study found that older age was associated with a decline of amyloid positivity in AD dementia, and an increase of amyloid positivity in pre-dementia patients, in real-world clinic data from Korea. Sex and APOE genotype were also found to be associated with amyloid positivity in AD patients. These findings may be useful in the clinical determination of diagnosis and treatment for patients with impaired cognition.

PE_055 Biomarkers

Elevated Plasma Axon Guidance Molecule is Early Stage of Alzheimer's Disease-Specific and Associated with Amyloid and Tau Pathology

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Objective

There is no biomarker that can detect early-stage Alzheimer's disease to this day, and we want to find a biomarker that could be used in an early diagnosis kit.

Methods

To test whether plasma growth-associated protein 43 (GAP-43), axon guidance molecules (NTN1, NTN4), and brain-derived neurotrophic factor(BDNF) concentration are elevated in Healthy control (n= 10), subjective cognitive decline(SCD) Aβ-negative (nSCD–= 6), SCD Aβ-positive (nSCD+= 2), mild cognitively impaired(MCI)Aβ-negative (nMCI–= 1), MCI Aβ-positive (nMCI+= 6), early stage of AD dementia Aβ-positive (nAD= 10), and its associations with other hallmarker of AD, we examined the plasma GAP-43, NTN1, NTN4, and BDNF measurements of 36 participants.

Results

Associations were investigated between plasma GAP-43, NTN1, NTN4, BDNF, and clinical diagnosis, Aβ/tau/neurodegeneration (AT(N)) status, blood biomarkers of AD, cognitive measurements, and brain neuroimaging findings. Blood plasma NTN4 levels were increased in patients with AD dementia (mean, 229.08 pg/ml) compared with healthy control (mean, 24.18 pg/ml) and MCI (mean, 57.86 pg/ml) (P value) groups. Plasma NTN4 correlated with apolipoprotein E (APOE) e4 variant and Aβ-positive.

Conclusion

Furthermore, when Aβ and tau are abnormally increased in primary hippocampal neurons via PFFs or viral infection, NTN4 and GAP43 are reduced in neurons, but the opposite is true in neuronal media. The findings suggest that plasma NTN4/GAP-43 may predict disease progression in Alzheimer's disease involving amyloid and tau molecules.

PE_056 Biomarkers

Distinct Cerebral Cortical Microstructural Changes in Idiopathic Normal-Pressure Hydrocephalus

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Objective

The aim of the study is to evaluate idiopathic normal-pressure hydrocephalus (INPH)-related cortical mean diffusivity (MD) abnormalities.

Methods

We investigated cortical MD utilizing surface-based diffusion tensor imaging analysis in three groups: INPH patients, Alzheimer's disease (AD) patients, and healthy controls. Forty-two INPH patients, 51 AD patients, and 23 healthy controls were imaged with MRI, including three-dimensional T1-weighted MR images, for automated surface-based analysis across the entire brain.

Results

Compared with age- and gender-matched healthy controls, INPH patients showed a statistically significant reduction in MD in the high convexity of the frontal, parietal, and occipital cortical regions. In clusters of lower MD in INPH patients, INPH patients, when compared to AD and control groups, showed a statistically significant decrease in average MD values. Additionally, a significant increase in MD, mainly in the ventromedial frontal cortex, ventrolateral frontal cortex, supramarginal gyrus, and temporal cortical regions, was observed in the INPH group relative to the control group. In clusters of higher MD in INPH patients, INPH patients, when compared to AD and control groups, showed a statistically significant increase in average MD values. In clusters of higher MD in INPH patients, AD patients, when compared to controls, showed a statistically significant increase in average MD values. The mean MD of clusters of lower MD in INPH patients compared with healthy controls yielded an area under the curve of 0.857, differentiating INPH from AD.

Conclusion

A distinctive pattern of cortical MD changes was found in INPH patients. The mean MD for clusters of lower MD in INPH patients compared with healthy controls distinguishes INPH from AD with good diagnostic sensitivity and specificity. Our findings suggest microstructural changes in cortical integrity can help differentiate INPH and AD in elderly patients.

PE_057 Biomarkers

Association of Cerebrospinal Fluid (CSF) Synaptosomal-Associated Protein 25 (SNAP-25) and Cognitive Functions in Alzheimer Disease

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Objective

Synapses are crucial for cognitive functions such as memory and learning, and their impairment is a hallmark of Alzheimer's disease (AD). Cerebrospinal fluid synaptosomal-associated protein 25 (SNAP-25) has been investigated in the context of AD due to its potential association with cognitive functions. Research suggests that alterations in SNAP-25 levels in CSF may provide insights into the synaptic dysfunction observed in AD. The objective of this study was to examine the association of CSF SNAP-25 and cognitive functions in AD.

Methods

A systematic review search through Pubmed/MEDLINE, Scopus, Cochrane Library, and EBSCO was conducted to find this topic. The studies were selected and critically appraised. Data were then analyzed and summarized descriptively.

Results

A study by Kivisäkk P et al. (2022) observed the levels of SNAP-25 were found to be higher in Alzheimer's disease (AD) subjects with dementia compared to those with Mild Cognitive Impairment (MCI) in an unadjusted analysis. SNAP-25 levels were higher in asymptomatic AD (163±47 pg/ml) and AD MCI (151±51 pg/ml) compared to healthy controls (HC) (97±36 pg/ml) ($pAdj<0.01$ and $pAdj=0.00005$, respectively). Specifically, the levels of SNAP-25 levels were at 180±73 pg/ml in AD subjects with dementia. This indicates an increase in these synaptic proteins in AD with dementia ($p<0.05$). Another study by Zhang H et al. (2018) concluded that CSF levels of SNAP-25 were found to significantly predict the conversion from MCI to AD. This suggests that higher levels of these proteins may be associated with a greater risk of progressing to AD from MCI (HR 2.47).

Conclusion

CSF levels of SNAP-25 may have utility as biomarkers for identifying individuals at higher risk of converting from MCI to AD and for understanding the rate of progression in Alzheimer's disease.

Genetic Analysis of Method, Kit and Device for Risk Assessment of Alzheimer's Dementia

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Objective

Alzheimer's is a disorder that affects cognitive function, where sufferers can experience problems with memory, behavior, and the ability to think. Genetic analysis is an important force in evolution as it allows natural selection to increase or decrease frequency of alleles already in the population. DNA arrays capable of simultaneously measuring expression of thousands of genes in clinical specimens from affected and normal individuals have the potential to provide information about superior characteristics gene from organism. Genes can be used as markers for cell recruitment and activation molecules. This study aims to evaluate the genetic of method, kit and device for risk assessment of alzheimer's dementia.

Methods

Data obtained from 23 sequences of method, kit and device for risk assessment of alzheimer's dementia on secondary data form on https://www.ncbi.nlm.nih.gov/ and selected articles journal evaluated (2019-2023). The phylogeny analysis of variations and relationships of DNA sequences was inferred using the UPGMA method and the evolutionary distances were computed using the Maximum Composite Likelihood method using MEGA11 software.

Results

Based on the tree analysis of 23 sequences were divided into 3 main groups, namely cluster A consisting of 16 specimens, cluster B consisting 6 specimens, and cluster C consisting of 1 specimens. The optimal tree with the sum of branch length = 978.20062095 is shown. This grouping is based on the existence of a similar genetic makeup equation with a high bootstrap value indicating the degree of kinship between specimens and the strength of the philogenous trees. Specimens that are in the same cluster show a degree of close kinship. On the other hand, specimens from different clusters display distant kinship.

Conclusion

The genetic analysis for risk assessment of alzheimer's dementia have highly variation. Information about kinship can be used as an informative source to assembly of superior genes in living of human cells.

PE_059 Biomarkers

Bibliometric Analysis on Brain Aging Biomarkers

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Objective

Brain aging is a complex biological process with significant implications for cognitive health and the rising prevalence of age-related neurological diseases. Brain aging biomarkers present the prospect of earlier detection, monitoring, and intervention in various disorders. The objective of this study was to provide a thorough assessment of the growing landscape of brain aging biomarkers in the Scopus database from 2013 to 2023.

Methods

In this study, the Scopus database was extensively explored to conduct a bibliometric analysis of the most recent global publications on brain aging biomarkers from 2013 to 2023. VOSviewer software version 1.6.19 was applied to analyze co-authorship and keyword co-occurrence networks.

Results

A total of 2,074 scholarly papers on brain aging biomarkers were discovered in the Scopus database from 2013-2023. The findings revealed a significant rise in the number of publications on brain aging over the last ten years, indicating increased interest and research effort in the topic. The co-authorship network analysis identified numerous countries that have made major contributions to the advancement of brain aging biomarkers. The United States, China, the United Kingdom, Germany, and Italy were the most prolific contributors to brain aging, according to the geographical distribution of research output. The most commonly studied biomarkers, according to keyword co-occurrence analysis, were "Tau", "Amyloid beta", "Apolipoprotein E", "Brain-derived neurotrophic factor (BDNF)", and "SIRT1".

Conclusion

In conclusion, several important protein biomarkers reflecting hallmarks of brain aging have been identified. This bibliometric analysis serves as a valuable compass pointing biomedical researchers in the direction of a deeper understanding of brain aging and the pivotal role of biomarkers in assessing the critical component of human health. The attempt to decipher the complexities of brain aging and identify reliable biomarkers continues to be an essential endeavor, poised to influence the future of aging research and medical treatment.

PE_060 Biomarkers

Clinical Utility of Plasma Alzheimer's Biomarkers across Asian Neurodegenerative Dementias: Cross-sectional Study in Large Multi-center Cohort

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Objective

In the present study, we explored the correlation between blood-based and imaging biomarkers in large Korean cohort of 2,988 participants across the clinical AD spectrum (cognitively unimpaired, mild cognitive impairment, or dementia of AD type), subcortical vascular cognitive impairments, and frontotemporal dementia.

Methods

All participants underwent amyloid PET and their plasma samples were analyzed using single molecular assay including amyloid beta 42/40 ratio, phosphorylated tau 231, glial fibrillary protein, and neurofilament light chain. Aβ positivity were determined based on klunkCL>20.

Results

The numbers of study participants were 2,988 including 675 in CU, 1434 in MCI, 600 in DAT, 187 in SVCI and 92 in FTD. The Spearman rho between plasma biomarkers and KlunkCL in the total group were -0.5 for Aβ42/Aβ40 ratio, 0.56 for p-tau231, 0.52 for GFAP (all p <0.001). In all groups, the Aβ (+) groups showed lower plasma Aβ42/Aβ40 ratio (all p <0.001), and higher p-tau231 (CU, MCI, DAT, and SVCI, p <0.001; FTD, p=0.012) and higher GFAP levels (CU, MCI, DAT, and SVCI, p <0.001; FTD, p=0.003) than the Aβ (-) groups. Aβ42/Aβ40 ratio, p-tau231, and GFAP discriminated Aβ status in CU and MCI with very good accuracies (AUC>0.8 for Aβ42/Aβ40 ratio, p-tau231, and GFAP). NfL levels showed the highest AUC differentiating SVCI (0.797 for clinical SVCI, 0.768 for Aβ (-) SVCI) and FTD (0.887 for clinical FTD, 0.889 for Aβ (-) FTD) from Aβ (-) CU, followed by GFAP. All of Aβ42/Aβ40 ratio, p-tau231, GFAP, and NfL at baseline were associated with steeper increase in CDR-SB in MCI (all p <0.001), while GFAP (p=0.034) and NfL levels (p=0.012) also demonstrated significant association with CDR-SB change in CU.

Conclusion

Our findings suggested that plasma AD biomarkers showed very high accuracies in prediction of Aβ positivity, differential diagnosis, and prediction of cognitive decline across Asian diverse dementia groups.

PE_061 Biomarkers

Brain Metabolic Resilience in Alzheimer's Disease: A Predictor of Cognitive Decline and Conversion to Dementia

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Objective

AD patients with similar pathological burdens may differ in clinical severity, and the concept of resilience has been introduced to explain this phenomenon. Previously, the clinical impact of cognitive resilience (CR) and brain resilience (BR) have been studied. However, the impact of preservation of brain glucose metabolism for a given amount of pathologic burden, or metabolic resilience (MR), remains to be studied. We aimed to quantify and investigate the clinical impacts of MR based on the amount of conserved brain glucose metabolism.

Methods

From the ADNI database, participants with MRI data, cognitive scores, CSF biomarkers, 18F-Florbetapir PET and 18F-Fluorodeoxyglucose (FDG) PET, were included in the study. We quantified the resilience variables, MR, BR, and CR, using partial least squares path modeling. Linear mixed-effect regression was used to determine the effect of each resilience on longitudinal changes in cognition. Cox propositional hazards regression was used to identify how well each resilience predicts MCI to AD conversion.

Results

A total of 848 participants were included in this study. All resilience metrics were associated with slower cognitive decline. Results from the ANOVA test showed that the additional inclusion of MR improved the performances of the linear mixed effect models. In survival analysis, all resilience variables were negatively associated with the risk of conversion to dementia. In line with the results of the linear mixed effects models, the additional inclusion of MR into the models with different resilience variables increased the C-index.

Conclusion

Our findings suggest that MR is a valuable predictor of future cognitive decline and conversion to dementia. Although hippocampal atrophy and cerebral hypometabolism are both biomarkers of neurodegeneration, FDG PET may complement MRI by capturing biologically different aspects of neurodegeneration. Also, despite the decreased clinical application of FDG-PET, it may be useful as a prognostic marker.

PE_062 Biomarkers

fNIRS Signal as a Potential Biomarker for White Matter Hyperintensity Progression in Patients with Subcortical Vascular Cognitive Impairment

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Objective

White matter hyperintensities (WMH) are a common cause of subcortical vascular cognitive impairment (SVCI). Many individuals with WMH are asymptomatic in the early stages, necessitating the development of reliable biomarkers for early detection and WMH progression monitoring. This study aims to investigate the association between fNIRS signals during mental and physical activities and WMH volume. Additionally, it explores the relationship between fNIRS signals and WMH progression, suggesting fNIRS as a potential biomarker.

Methods

We recruited 27 patients with mild cognitive impairment (MCI) presenting WMH. Data from fNIRS and MRI scans were collected during their first visit. Ten of them underwent fNIRS and MRI scans in a second visit two years later. WMH volume analysis used volBrain lesionBrain 1.0 (https://www.volbrain.net). ROC curve analysis determined a WMH cutoff value of 1.555 (normalized), classifying patients into SVCI and control groups. We compared fNIRS data during cognitive tests and physical activities between SVCI and control groups at the first visit and in the two-year follow-up.

Results

Statistically significant differences in WMH volume ($P<0.001$) existed between the SVCI and control groups. In the initial visit, fNIRS signals exhibited significant changes in the left prefrontal cortex during cognitive tests and physical activities. In the two-year follow-up, fNIRS signals revealed significant bilateral prefrontal cortex changes during cognitive tests and physical activities, with an increase in WMH volume.

Conclusion

Our results suggest that fNIRS signals have the potential to serve as biomarkers for WMH progression.

PE_063 Biomarkers

Assessing Hippocampal Atrophy as a Biomarker for Alzheimer's Disease in Indonesian Seniors

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Objective

Alzheimer's disease (AD) is a growing concern in Indonesia, with an aging population. This study aims to investigate hippocampal atrophy as a potential biomarker for early AD detection in Indonesian seniors.

Methods

We conducted a cross-sectional study with 150 participants aged 60 and above, including 75 AD patients and 75 age-matched controls, in Indonesia. All participants underwent high-resolution structural magnetic resonance imaging (MRI). Hippocampal volumes were quantified using advanced image analysis software. Cognitive assessments, including the Mini-Mental State Examination (MMSE), were administered to all participants.

Results

The prevalence of AD in our Indonesian cohort was 18.7% (95% CI: 13.6% - 23.8%). The AD group exhibited significantly smaller hippocampal volumes compared to controls ($p < 0.001$). The average hippocampal volume in the AD group was 2,345 mm^3 (95% CI: 2,210 mm^3 - 2,480 mm^3), while in the control group, it was 3,150 mm^3 (95% CI: 3,075 mm^3 - 3,225 mm^3). Hippocampal volume demonstrated a strong negative correlation with MMSE scores ($r = -0.75$, $p < 0.001$) in the AD group.

Conclusion

This study demonstrates the potential of hippocampal atrophy as a specific and sensitive biomarker for Alzheimer's disease in Indonesian seniors. Smaller hippocampal volumes were strongly associated with AD and correlated with cognitive decline. Early detection of AD using MRI-based hippocampal assessment could facilitate timely interventions and support for affected individuals in Indonesia's aging population.

Early Detection of Alzheimer's Disease Progression Using Multi-Modal Machine Learning

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Objective

Alzheimer's disease (AD) presents a formidable challenge to individuals and healthcare systems worldwide, underscoring the critical importance of early detection for timely intervention. This study aims to develop a highly specific machine learning model that combines neuroimaging data from structural MRI scans and cerebrospinal fluid (CSF) biomarker profiles to predict AD progression in individuals with mild cognitive impairment (MCI).

Methods

We meticulously gathered a cohort of 200 MCI-diagnosed individuals who underwent longitudinal MRI scans and CSF biomarker analysis over a 4-year period. Neuroimaging data were processed to extract regional brain volumes, cortical thickness, and white matter integrity measures. CSF biomarkers included Aβ42, tau, and p-tau levels. Our approach employed an ensemble of advanced machine learning techniques, incorporating gradient boosting and deep neural networks, to integrate multi-modal data and capture intricate relationships. To assess model performance, we utilized a stratified 5-fold cross-validation, calculating specificity, positive predictive value (PPV), negative predictive value (NPV), and F1-score.

Results

Our multi-modal machine learning model achieved remarkable specificity, with a rate of 96.3% (95% CI: 94.8% - 97.8%), PPV of 95.7% (95% CI: 94.1% - 97.2%), NPV of 97.1% (95% CI: 95.8% - 98.4%), and an F1-score of 96.0% (95% CI: 94.5% - 97.5%). These results underscore the model's exceptional accuracy in identifying MCI individuals who will progress to AD. Furthermore, our model identified key neuroimaging features and CSF biomarkers influencing AD progression, shedding light on the underlying pathophysiological mechanisms.

Conclusion

Our study combines neuroimaging and CSF biomarkers in a multi-modal machine learning model, achieving exceptional accuracy in predicting Alzheimer's disease (AD) progression in individuals with mild cognitive impairment (MCI). These results support early detection and personalized interventions for AD. Identifying key biomarkers enhances our understanding of disease progression and highlights the importance of utilizing multi-modal data and advanced machine learning in AD research and clinical practice.

PE_065 Biomarkers

Elevated Aβ Oligomerization of Blood Plasma is Associated with Albuminome Profile in Alzheimer's Disease.

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Objective

In Alzheimer's disease (AD), beta-amyloid (Aβ) oligomer is identified as a major neurotoxic agent that contributes to neuronal degeneration and the accumulation of Aβ plaques within the brain. Recently, we discovered that the level of Aβ oligomerization was substantially increased in the plasma of AD patients when synthetic Aβ was introduced. This discovery led us to develop an AD diagnostic tool called 'AlzOn'. However, the molecular mechanisms of AlzOn have not been investigated. To elucidate the diagnostic activity of AlzOn, the blood plasma albuminome of both non-AD and AD patients was analyzed.

Methods

To investigate the impact of albuminone on AlzOn test signal, the blood plasma albuminome was depleted by immunoprecipitation, and the level of oligomeric Aβ was assessed by AlzOn. The albuminome from non-AD or AD patients' plasma was isolated by immunoprecipitation and the global proteome expression of them was evaluated by liquid chromatography tandem mass spectrometry (LC-MS/MS).

Results

After depleting the albuminome, the increment of Aβ oligomerization was not detected in AD compared to non-AD plasma. However, isolated albuminome of AD plasma upregulated Aβ oligomerization. Notably, LC-MS/MS data demonstrated substantial differences in the protein expression between non-AD and AD patients. A total of 370 proteins were identified; 8 proteins (2% of the total) were increased more than two-fold and 123 proteins (33% of the total) were decreased more than two-fold. Additionally, 42% of the top 50 abundant proteins of plasma albuminome were relevant to AD.

Conclusion

This report highlights the crucial role of plasma albuminome on Aβ oligomerization and the diagnostic specificity of the AlzOn system.

PE_066 Biomarkers

Investigating Hub Genes and Key Pathways Implicated in Alzheimer's Disease Using Bioinformatics Analysis

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Objective

Alzheimer's disease (AD) is a progressive, neurodegenerative disease that is characterized clinically by a progressive decline in cognitive function. However, despite the clinical understanding of AD, there is still a need to investigate potential diagnostic biomarkers, including the exploration of hub genes as therapeutic targets and candidate biomarkers. This study emphasizes the significance of identifying AD-related hub genes for the development of novel strategies against the disease.

Methods

To explore the molecular intricacies of AD, the gene expression profiles from the GSE122063 dataset in the Gene Expression Omnibus (GEO) were obtained, and differentially expressed genes were identified. Subsequently, enrichment analysis employing Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analyses was conducted to investigate the important regulated signaling pathways. Moreover, a protein-protein interaction (PPI) network was constructed using the cytoHubba plug-in of Cytoscape to identify potential hub genes.

Results

The pathway enrichment analysis revealed the presence of several significant pathways. The upregulated genes predominantly highlighted pathways such as the glutamatergic synapse, chemical synaptic transmission, calcium ion binding, and the neuroactive ligand-receptor interaction. In sharp contrast, the downregulated genes showed pathways like the plasma membrane, inflammatory response, systemic lupus erythematosus, and enzyme binding. By conducting the PPI network for upregulated genes, we identified pivotal hub genes: BDNF, GRIN2A, GAD1, PVALB, SNAP25, SST, CALB1, SLC32A1, GAD2, and SLC17A6. On the other side, for the downregulated genes, the hub genes that emerged were PTPRC, CD163, TLR4, FCGR2A, ITGB2, CD44, TLR2, CCL2, CD86, and CXCL1.

Conclusion

Our research provides valuable insights into the strong association between the identified hub genes and the diagnosis of AD. This study not only presents a new viewpoint on the molecular mechanisms underpinning AD but also emphasizes the considerable therapeutic potential of these hub genes as viable targets for treatment.

PE_067 Biomarkers

VR-EP-EEG-MRI Digital Biomarkers: Multi-modal Machine Learning Model for Detecting Mildcognitive Impairment

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Objective

As mild cognitive disease (MCI) is the last stage to prevent conversion to Alzheimer's disease, early detectionof patients with MCI is crucial. Clinical studies have reported that multi-modal biomarkers are useful for earlydetection of MCI. Biomarkers include virtual reality (VR), evoked potential (EP), electroencephalogram (EEG)and magnetic resonance imaging (MRI). Although single modal biomarkers are also valid to early detect MCI,the combination of multi-modal biomarkers could offer complementary information for cognitive impairment.In this study, we developed a multi-modal machine learning model using digital biomarkers VR, EP, EEG, andMRI and assessed its accuracy to early detect MCI.

Methods

Thirteen healthy controls and thirteen MCI patients were recruited. All participants conducted VR, EP, EEG, andMRI tasks. For the classifier, a decision tree model was trained with aforementioned features, to discriminateMCI patients from healthy controls. Accuracy of the model was assessed by four-fold validation.

Results

The decision tree model with all multi-modal biomarkers?VR, EP, EEG, MRI reached the highest performancefor classification between healthy controls and MCI patients (accuracy: 84.62%, sensitivity: 92.31%, andspecificity: 76.92%). On the other hand, model with single modal biomarkers reached lower performance,including VR, EP, EEG and MRI.

Conclusion

In conclusion, multi-modal biomarkers VR, EP, EEG, MRI showed the highest accuracy for detecting MCIpatients. This meant that multi-modal biomarkers could provide complementary information for cognitivefunction of MCI patients. In single modal biomarkers, VR and MRI biomarkers performed best for detection ofMCI patients, as consistent

PE_068 Biomarkers

Exploring Hub Genes and Critical Pathways Involved in Vascular Dementia Development

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Objective

Vascular Dementia (VaD) is the second most common form of dementia among the elderly, following Alzheimer's disease (AD). It is characterized by decline in cognitive functions, particularly executive functioning, due to cerebral ischemia or infarction. However, VaD is poorly understood, which hampers the progress in comprehending the underlying mechanisms of the disease and developing effective treatments. This study aims to analyze the gene network of VaD patients compared with normal cognitive to identify disease biomarkers.

Methods

The gene expression profile files of GSE122063 data were acquired from the Gene Expression Omnibus (GEO) dataset, followed by the identification of differentially expressed genes. To gain a deeper understanding of the roles and interactions of these genes, the enrichment analysis was performed to investigate the regulated signaling pathways, utilizing Gene Ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway enrichment analyses. Furthermore, a protein-protein interaction (PPI) network was constructed using the cytoHubba plug-in of Cytoscape to identify hub genes.

Results

The pathway enrichment analysis unveiled numerous significant pathways. The upregulated genes showed significant involvement in pathways related to extracellular space, metabolic pathway, G-protein coupled receptor signaling pathway, and extracellular matrix structural constituent. Conversely, the downregulated genes were associated with notable pathways such as plasma membrane, inflammatory response, integral component of membrane, and protein binding. Through the PPI network analysis, NMU, TAC1, PRKACB, SST, GAD2, CRH, and ADCYAP1 were identified as hub genes among the upregulated genes. In contrast, CD163, PTPRC, FCGR3A, TLR2, C5AR1, CCL2, ITGB2, ILA1, FCGR2A, and CCR5 were identified as hub genes among the downregulated genes in the comparison between normal cognitive and VaD patients.

Conclusion

Overall, our study provides evidence for a strong correlation between the identified hub genes and the development of dementia, offering novel insights into the underlying mechanisms involved.

PE_069 Biomarkers

Development of A Neuron-Selective Probe Incorporating into Live Neuronal Membranes

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Objective

Primary neuronal cultures become a standard model for investigating the development of the mammalian central nervous system at the single-cell level. In particular, mixed cultures involving neurons, astrocytes, and microglia have been established as platforms for drug discovery targeting neuro-inflammation and neuro-degeneration. To facilitate these applications, we developed a neuron-membrane selective probe, which allows for the real-time monitoring of dynamic neuronal processes over prolonged periods of culture.

Methods

As the first neuron-selective probe, NeuO has been used to label neurons. While NeuO exhibits superior selectivity for neurons, it does have limitations when used as a neuron tracer. Firstly, its rapid efflux prevents long-term neuronal tracking. Secondly, NeuO is suboptimal for assessing neurite outgrowth. To develop a long-term staining neuron-probe, a series of NeuO derivatives were synthesized, each bearing an alkyl side chain (C0~C14). The neuron-staining capabilities were evaluated using rat primary hippocampal and cortical neurons, and NeuM was identified as having the best neuron-trafficking properties. We identified membrane localization through high-resolution image analysis and subcellular-fraction and elucidated the mechanism through molecular dynamics simulations.

Results

Among the NeuO derivatives, NeuM exhibited the best neuron-staining properties, including neuronal retention time, fluorescence intensity, and neurite-stainability by targeting neuronal cell-membrane. NeuM autonomously assembles into micellar structures, which leads to the quenching of its fluorescence. Upon exposure to neurons, NeuM micelles were selectively internalized into neuronal endosomes via clathrin-mediated endocytosis. Through the endocytic recycling pathway, NeuM micelles integrate into a neuronal membrane, dispersing fluorescent NeuM molecules in the membrane.

Conclusion

NeuM molecules integrated into neuronal cell-membrane, visualizing the entire neuronal structure including neurites. Owing to this membrane-trafficking mechanism, NeuM exhibited a superior selectivity to live neurons, not labeling dying neurons or cell debris.

PE_070 Biomarkers

Gingitracker-1: A Fluorescent Probe Labeling the Active Site of Gingipains of P. gingivalis

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Objective

P.gingivalis, an oral pathobiont, plays a key role in the pathogenesis of periodontitis, mainly by its cysteine proteases, gingipains. In this study, we aimed to develop a small-molecule fluorescent gingipain sensor, Gingitracker-1, to facilitate P.gingivalis diagnosis.

Methods

P.gingivalis along with control bacteria A.actinomycetecomitans and F.nucleatum were cultured. Bacterial phenotype, levels of gingipains, and LPS were evaluated by scanning electron microscopy and ELISA respectively. For initial screening, the fluorescence response of our in-house thiol-reactive probes was observed in each bacterial-conditioned medium. The detection of gingipains by Gingitracker-1 was confirmed using bacterial culture, and purified enzymes. Native PAGE analysis was utilized to detect the covalent linkage between Gingitracker-1 and gingipains, and possible interactions at active sites were predicted by docking studies. TD-DFT calculations determined the fluorescent properties of Gingitracker-1. The inhibitory potential of Gingitracker-1 was evaluated through activity inhibition and bacterial growth inhibition assays. The P.gingivalis cell's ultrastructure was observed through transmission electron microscopy. The clinical application of Gingitracker-1 was explored on human teeth and dental plaque acquired from one healthy control and three periodontitis patients.

Results

Gingitracker-1 showed significantly increased fluorescent response exclusively when exposed to P.gingivalis C.M and cells. Gingitracker-1 selectively detected recombinant gingipains, Kgp, and RgpB by forming a covalent bond with catalytic cysteine in the active site. Moreover, these covalent interactions within the gingipain's binding pocket enabled Gingitracker-1 to inhibit gingipain's proteolytic activity, ultimately leading to growth inhibition of P.gingivalis and reduction in its capsule thickness. Finally, when Gingitracker-1 was applied to periodontitis-affected human teeth, fluorescently labeled gingipains attached to dental plaque could be readily visualized under UV light without requiring any microscopic aid.

Conclusion

Gingitracker-1, through its ability to form a covalent bond with cysteine in the active site of gingipains, offers a promising solution for precise gingipain targeting, making it a valuable diagnostic tool with potential therapeutic applications.

PE_071 Biomarkers

The effect of Neuroimaging Biomarkers on Gait Patterns in the Patients with Alzheimer's Disease

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Objective

Although ongoing research is investigating the association between gait parameters and Alzheimer's disease (AD), a comprehensive link has not been definitively established. In this study, we investigated the association between gait patterns and neuroimaging biomarkers in AD.

Methods

We prospectively included 33 cognitively unimpaired (CU) individuals, 20 patients with MCI due to AD, and 43 patients with AD dementia at the Memory Disorder Clinic of Wonju Severance Christian Hospital between January 2022 and May 2023. Participants underwent brain magnetic resonance imaging (MRI), 18F-florbetaben PET, neuropsychiatric tests, and APOE genotyping. Gait was evaluated using a 5.79-m long walkway. We conducted a comparative analysis using Pearson correlation to examine the relationships between gait parameters and several variables, including cortical thickness and regional Standardized Uptake Value Ratios (rSUVR).

Results

After controlling for age, sex, and duration of education, the MCI group exhibited distinct gait patterns compared to the CU group. Specifically, the MCI group displayed lower velocity, reduced step length, and decreased swing %. The gait patterns of the Dementia (DEM) group were characterized by even more pronounced decreases in velocity, step length, and swing percentage in comparison to the CU group. Decreased gait velocity and step length was associated with greater Aβ burden in prefrontal, sensorimotor, parietal, lateral temporal, occipital, and anterior cingulate cortices and precuneus. Decreased step length was associated with greater Aβ burden in the prefrontal, inferior parietal, lateral temporal, occipital, anterior cingulate cortices and precuneus after multiple region-wise correction. Gait velocity and step length was associated with cortical thickness in the lateral temporal, inferior parietal, entorhinal, parahippocampus, insular cortices and precuneus.

Conclusion

Our study has revealed significant correlations between gait parameters and Aβ, and cortical thickness in AD.

Machine Learning Model for Mild Cognitive Impairment based on Gait and MRI Images

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Objective

Within mild cognitive impairment (MCI), a lower level of cognitive function is associated with a higher likelihood of progressing to dementia. Additionally, gait disturbance and structural changes in brain MRI reflect cognitive levels. Therefore, we aimed to classify MCI based on cognitive levels using gait parameters and brain MRI imaging data.

Methods

Eighty patients diagnosed with MCI from three dementia centers in Gangwon-do, Korea were recruited for this study. We defined MCI as a Clinical Dementia Rating global score of 0.5 or higher, with a memory domain score of 0.5 or greater. The patients were classified as having either higher or lower MMSE group based on their Mini Mental Status Examination z-scores. We trained a machine learning model using gait parameters and MRI data parameters.

Results

CNN resulted in the most performant classifier in separating MCI with lower MMSE (L-MCI) from MCI with higher MMSE (H-MCI), and its performance was maximized when using feature patterns that included multimodal features (GAIT + gray matter set). Left fusiform gyrus thickness was the strongest predictor.

Conclusion

Machine learning incorporating gait and gray matter parameters achieved the highest accuracy in distinguishing L-MCI from H-MCI.

PE_073 Biomarkers

A Deep Learning Approach with Analysis of Acoustics and Speech for Developing MCI Prediction Model

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Objective

The possibility of non-invasive early diagnosis was proposed by developing an artificial intelligence model to predict the onset of MCI by focusing on the impact of cognitive dysfunction on the acoustic characteristics of speech.

Methods

By analyzing speech signals (autocorrelation function according to delay time) of conversation sounds of multiple MCI patients and normal people in DementiaBank, detailed changes in speech patterns were acoustically investigated. In addition, President Reagan's four speeches given at five-year intervals were analyzed to investigate trends in changes in each parameter. Speech data from a total of 80 normal people and patients diagnosed with MCI were analyzed using Tau1 and Phi1, which represent the time to the first peak (pitch) and pitch strength, respectively, and τe, which represents the effective duration of the signal. Additionally, President Reagan's speech data from the time his cognitive function was normal to the time he developed disability was also analyzed.

Results

Statistical significance was found in the speech data of MCI patients and Reagan at the time of onset of cognitive dysfunction based on ACF parameters compared to the control group. This suggests that decline in cognitive function affects the periodicity and energy characteristics of speech. MCI prediction performance was improved by constructing an artificial intelligence model that independently extracts important features of voice audio data that are improved over hand-crafted features.

Conclusion

MCI was diagnosed through an AI model based on the acoustic characteristics of vowel utterances. Through continuous data collection, it is possible to predict the onset time and further establish a systematic treatment strategy to detect various types of dementia early.

PE_074 Biomarkers

APOE4 Genetic Influence on Blood Biomarkers and Amyloid Pathology in Subjective Cognitive Decline

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Objective

Blood biomarkers are gaining prominence in the diagnosis and monitoring of Alzheimer spectrum disorders. The APOE4 genetic risk factor plays a pivotal role in disease progression and brain pathological alterations. This study examined the influence of APOE4 on various blood biomarkers and amyloid pathology burden in individuals with subjective cognitive decline (SCD).

Methods

104 SCD subjects from SCD cohort, comprising 46 males and 58 females (average age: 70.6 years, education: 11.5 years, MMSE score: 27.2), were categorized into two groups based on their APOE4 genetic status: 23 APOE4 positive and 81 APOE4 negative. Blood biomarkers, including serum Aβ40, Aβ42, Aβ42/40 ratio, Glial Fibrillary Acidic Protein(GFAP), neurofilament light(NFL), and pTau181 were quantified using the Single Molecule Array (Simoa) method. Concurrently, the Global SUVR was determined using flurobetaben amyloid PET.

Results

Notable differences between the APOE4 positive and negative groups were observed. Specifically, Aβ42(pg/mL) 6.53±1.33 vs. 7.54±2.25 (p=0.044), Aβ42/40 ratio 0.061±0.007 vs. 0.071±0.011 (p=0.001), GFAP(pg/mL) 182.99±62.86 vs. 116.27±54.84 (p=0.001), NFL(pg/mL) 30.84±10.57 vs. 22.63±12.16 (p=0.004), pTau181(pg/mL) 43.04±19.97 vs. 25.64±6.99 (p=0.001), and Global SUVR 1.62±0.28 vs. 1.18±0.09 (p=0.001). No significant difference was identified in Aβ40 levels.

Conclusion

The presence of APOE4 profoundly impacts most blood biomarker values, even at the SCD phase. Future studies are anticipated to elucidate the clinical implications of these biomarkers in the progression of SCD.

PE_075 Biomarkers

Prevalence of β-Amyloid Positivity in Dementia Syndromes in Korea: Impact of Age and APOE Genotypes

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Objective

When recommending Aβ therapies for diverse populations, it is crucial to consider the ethnicity-specific characteristics of amyloid-β (Aβ). Our study aimed to investigate the prevalence of Aβ positivity (+) and the longitudinal trajectories in relation to risk factors in dementia syndromes in Korea.

Methods

We recruited 6,634 participants from multiple centers in Korea with Aβ PET scans and followed 4,808 participants over time. They were diagnosed with Alzheimer's disease-related cognitive impairment (ADCI), subcortical vascular cognitive impairments (SVCI), or frontotemporal dementia (FTD). They were categorized into three cognitive stages: cognitively unimpaired (CU), mild cognitive impairment (MCI), and dementia. We estimated Aβ+ frequencies using Clopper-Pearson method and used multivariable logistic regression to assess the odds of Aβ+ in relation to age and APOE genotype.

Results

In our cross-sectional study, we observed the odds of Aβ+ among ADCI participants as follows: CU, 21.0; MCI, 49.1; and dementia, 80.5. In SVCI, the odds were: CU, 20.0; MCI, 34.0; and dementia, 40.1. For FTD, the odds were 13.1. Among ADCI participants, Aβ+ prevalence increased with age in the non-demented group (CU: odds 1.10; MCI: 1.03) and decreased with age in the dementia group (odds 0.95). On the other hand, SVCI and FTD had more Aβ+ with increasing age. The APOE ε4 allele was a significant risk factor for Aβ+ in all cognitive stages of ADCI and in the MCI and dementia groups of SVCI. In our longitudinal study involving ADCI participants, the effects of APOE genotypes were significant in Aβ+ participants but not in Aβ– participants.

Conclusion

Our findings provide valuable insights into the associations between Aβ+ and risk factors including age and APOE genotype in dementia syndromes in Korea. These results imply the need for customized Aβ-targeted therapies across different ethnic groups.

PE_076 Biomarkers

Comparison of Enlarged Perivascular Spaces in Early-Onset and Late-Onset Alzheimer Disease-related Cognitive Impairment

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Objective

We examined whether there were differences in the presence of centrum semiovale-enlarged perivascular spaces (CSO-ePVS) and basal ganglia-ePVS (BG-ePVS) among patients with Alzheimer's disease-related cognitive impairment (ADCI) based on their age of onset.

Methods

Between July 2015 and February 2022, we identified 133 patients with clinically diagnosed AD dementia and 106 patients with mild cognitive impairment (MCI) who visited the Dementia Clinic at the Neurology Department of Pusan National University Hospital. Out of a total of 239 patients with cognitive impairment, 155 with positive amyloid-PET results were included. Among these, 43 had early-onset ADCI (EOADCI) and 112 had late-onset ADCI (LOADCI). We measured ePVS, lacunes, white matter hyperintensities and microbleed.

Results

Patients with LOADCI exhibited higher prevalence of hypertension, lacunes, white matter hyperintensities, and BG-ePVS than those with EOADCI. BG-ePVS showed a significant correlation with age at onset and the number of lacunes, whereas CSO-ePVS did not exhibit any association.

Conclusion

The higher prevalence of BG-ePVS in patients with LOADCI might be attributable to vascular risk factors (hypertension) and cerebral small vessel disease (CSVD). These findings support the hypothesis that BG-ePVS are associated with CSVD and vascular risk factors, whereas CSO-ePVS is associated with cerebral amyloid angiopathy.

PE_077 Biomarkers

Influence of Sleep Quality, Risk of Obstructive Sleep Apnea and Sleep Deprivation on Cortical Oxygenation in Elderly Individuals

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Objective

Poor sleep quality, obstructive sleep apnea (OSA) and sleep deprivation are risk factors for cardiovascular diseases and cognitive impairment. Cerebral blood flow and its regulation are affected by pathological condition commonly observed in the elder population, such as dementia, history of stroke, diabetes mellitus and hypertension. The aim of this study was to investigate the influence of sleep quality, OSA risk and total sleep time (TST) of prior night in level of activation of the frontal cortex using functional near-infrared spectroscopy

Methods

We investigated 204 participants without cognitive impairment between the ages of 60 and 85 years. All patients functional near-infrared spectroscopy (fNIRS) along with cognitive tasks, including digit span, semantic verbal fluency task, stroop test, to investigate hemodynamic response in the fontal cortex of patients with depression compared to a healthy elderly group. The Pittsburgh Sleep Quality Index (PSQI) for sleep quality, STOP-BANG questionnaire for risk of OSA, and TST of prior night which reported by participants was assessed.

Results

In poor sleep quality group (PSQI<5), reduced hemodynamics during the Stroop task compared to control group in all channel average (Mean accΔHbO2 of 0.11μM in poor sleep quality group versus -0.12 μM in control, $p<0.05$) and right channel average (Mean accΔHbO2 of 0.01μM and -0.03 μM, $p<0.05$). In sleep deprived group (TST<5), reduced hemodynamics during the verbal fluency test was observed in right channel average (Mean accΔHbO2 of 0.024 in sleep deprived group versus 0.01 μM in control, $p<0.05$). There was no significant difference between high risk of OSA group (STOP-BANG>5)

Conclusion

Poor sleep quality and sleep deprivation (<5 hours) may be an important factor that influences cortical oxygenation in the elderly population.

PE_079 Biomarkers

Functional Connectivity Changes between Tau-accumulated Regions and Whole Brain in Alzheimer's Disease Continuum with Affective Symptoms

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Objective

Neuropsychiatric symptoms (NPS) are common in the Alzheimer disease (AD) continuum. However, there has been little research on NPS at various levels, from the regional molecular level to the whole-brain network level. In this study, we investigated the neural correlates of NPS, especially focusing on affective symptoms, with regional tau accumulation and functional connectivity (FC).

Methods

We used data of 77 patients who are amyloid-positive and have preprocessed positron emission tomography (PET) images with AV-1451, resting state fMRI (rsfMRI), and T1 from the Alzheimer's Disease Neuroimaging Initiative (ADNI) dataset. Also, among four factors of NPS, affective scores were evaluated with scores of depression and anxiety. We obtained standardized uptake value ratio (SUVR) of tau per ROI using PETSurfer and found seed regions whose SUVR is correlated with affective score. Then, we preprocessed rsfMRI and analyzed seed-to-voxel FC with CONN 2022a. We compared FC between patients without affective symptoms (nAS, n=52) and with affective symptoms (AS, n=25) controlling for age, MMSE, sex, and education.

Results

We found 28 regions showing a significant correlation between SUVR and affective score. ($p<0.05$) Among these regions, left isthmus of cingulate gyrus and right middle temporal gyrus have lower connectivity with supramarginal and angular gyrus of the contralateral hemisphere in AS. Meanwhile, left medial orbitofrontal cortex has higher connectivity with left temporal pole and left parahippocampal gyrus in AS. Also, right lingual gyrus has higher connectivity with left precentral and postcentral gyrus in AS. (voxel threshold: $p < 0.001$ (p-uncorrected), cluster threshold: $p<0.05$ (cluster-size p-FWE corrected))

Conclusion

Functional network changes with tau-accumulated regions can explain affective symptoms in the AD continuum. In AS, tau-accumulated regions have decreased connectivity with regions mainly in default mode network (DMN). They also have increased connectivity with somatomotor network and with DMN overlapping with parts of salience network and allocortex, presumably by compensation.

PE_080 Biomarkers

Advancing Alzheimer's Diagnosis: Creating the Gold Standard pT217 Antibody for Enhanced Sensitivity

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Objective

While numerous blood biomarkers have been proposed for Alzheimer's disease, only a few have demonstrated definitive diagnostic value. Recently, a set of phosphorylated Tau proteins, particularly pT217, have emerged as promising candidates with superior diagnostic performance. Given the development of pT217 antibodies by major global pharmaceutical companies, our goal is to create the best-in-class pT217 antibody, establishing it as the gold standard for diagnostics.

Methods

To address common practical challenges encountered in applying antibodies to patient blood samples, such as matrix effects, we implemented specific strategies from the initial screening of antibodies targeting pT217. We then compared the performance of our various antibody clones against those of other companies.

Results

Our antibody clones exhibited a threefold enhancement in the lower limit of quantification (LLOQ) for pT217 Tau fragments compared to antibodies from Company-L. Additionally, the LLOQ for different lengths of pT217 Tau fragments was improved fourfold with our antibody clones when contrasted with Company-L's antibodies. These results unequivocally underscore the significantly higher sensitivity of our antibody candidates compared to those from Company-L.

Conclusion

In conclusion, our study has demonstrated the successful development of pT217 antibodies with superior sensitivity in comparison to global competitors' pT217 antibodies. These antibodies exhibit robust and specific binding to the pT217 Tau peptide, a pivotal component in Alzheimer's disease diagnosis and research. The heightened sensitivity of our antibodies positions them as strong contenders in advancing Alzheimer's disease diagnostics, potentially enabling earlier and more accurate disease detection. These findings hold substantial promise for enhancing early Alzheimer's disease diagnosis and contributing to the development of more effective treatment strategies.

The Power of Voice Using a Deep Neural Network Model for Alzheimer's Disease Detection

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Objective

This study used voice data to distinguish between normal cognition and cognitive impairment or Alzheimer's disease (AD) dementia. Voice, reflecting cerebral functions, holds the potential for analyzing and understanding brain function, especially in the context of cognitive impairment and Alzheimer's disease.

Methods

The study involves three groups: Normal Cognition (NC) with 52 subjects, Mild Cognitive Impairment (MCI) with 110 subjects and Alzheimer's Disease Dementia (ADD) with 59 subjects. The study extracted voice features using Mel-frequency cepstral coefficients (MFCCs) and Chroma.

Results

The deep neural network (DNN) model showed promising performance, with an accuracy of roughly 81% in ten trials in predicting ADD, which increased to an average value of about 82.0±1.6% when evaluated against unseen test dataset.

Conclusion

While the results did not demonstrate the level of accuracy necessary for a definitive clinical tool, they provide a compelling proof-of-concept for the potential use of voice data in cognitive status assessment. The DNN algorithms using voice offer a promising approach to early detection of AD, which could improve the accuracy and accessibility of diagnosis and ultimately lead to better outcomes for patients.

PE_083 Biomarkers

A Reproducible Self-supervised Deep Neutral Network with Dual Attention Module for Alzheimer's Disease Classification

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Objective

Alzheimer's disease is one of the most common types of neurodegenerative disease, characterized by the accumulation of amyloid-beta plaque and tau tangles. Recently, deep learning approaches have shown promise in Alzheimer's disease diagnosis. In this study, we propose a reproducible model that utilizes a 3D convolutional neural network with a dual attention module for Alzheimer's disease classification.

Methods

The 1.5 T T1-weighted MRI images were collected from the public database of Alzheimer's Disease Neuroimaging Initiative (ADNI). The ADNI, initiated in 2003 by Principal Investigator Michael W. Weiner, collected brain images and clinical assessments from thousands of participants across North America. For our study, we selected 403 Alzheimer's disease patients (AD) and 653 cognitive normal patients (CN). The Australian Imaging, Biomarker & Lifestyle Flagship Study of Ageing (AIBL) and the Open Access Series of Imaging Studies 1 (OASIS-1) were used as independent datasets to evaluate the generalizability of our method.

Results

We evaluated our proposed method on the largest Alzheimer's disease database, ADNI, and verified its generalizability on other independent datasets, namely AIBL and OASIS1. We achieved an Alzheimer's disease classification accuracy of 96.30%, a sensitivity of 93.76%, and a specificity of 97.95%. Furthermore, our proposed method demonstrated good generalizability performance in AIBL and OASIS1 datasets. The high attention scores in the hippocampus and medial temporal lobe, as revealed by an explainable AI, highlight the interpretability and reliability of our model.

Conclusion

These results indicate that our proposed approach has competitive performance and generalizability when compared to recent studies in the field.

PE_084 Biomarkers

Lesion-network Mapping for Post-stroke Cognitive Impairment

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Objective

To overcome the difficulty of obtaining functional neuroimages directly from acute stroke patients, researchers have developed a new "indirect lesion-network mapping." This new method has successfully mapped some peculiar stroke symptoms, such as aphasia and post-stroke pain. However, whether this method can produce sensible mapping results for post-stroke cognitive impairment remains unclear.

Methods

A total of 1,431 patients were enrolled from two university hospitals. They underwent a neuropsychological test within one-year post-stroke. We used the Verbal Learning Test to examine memory performance and the trail-making test-A and digit symbol coding task to assess the processing speed. We classified the patients into two groups— cognitively-impaired (CI) (< -2.0 standard deviation) and cognitively-unimpaired (CU) (> -1.0 SD)—based on the task performance. We calculated the lesion-affected networks based on patients' stroke lesions and the normative functional network data from the Human Connectome Project-Aging cohort, n = 687. Then, we obtained and compared the lesion network maps for patients with versus without cognitive impairment.

Results

348 patients showed impairment in the memory task, while 247 patients demonstrated impairment in the speed-of-processing task. For both tasks, the conventional lesion-network mapping approach produced highly similar results between the CI versus CU groups—both groups were localized to the major hubs of the large-scale functional networks, such as mid-cingulate and insular cortices. However, the mapping results became more sensible when we contrasted the lesion-network maps between the CI versus CU groups. For example, the memory impairment was localized to the functional network including the left medial and anterior temporal, inferior, and dorsolateral frontal cortices, whereas the speed-of-processing impairment was localized to the network including both occipital and anterior temporal cortices.

Conclusion

We suggest additional analysis steps to the conventional lesion-network mapping, including the contrast analysis, which can help improve the results' specificity and sensitivity when targeting post-stroke cognitive impairment.

PE_085 Clinical Manifestations

Unveiling Alzheimer's Disease Characteristics and Follow up Changes in Heterogeneous Mild Cognitive Impairment over 5 Years

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Objective

To investigate cognitive and pathological (amyloid and tau) changes of mild cognitive impairment (MCI), the heterogenous disease entity, in a long-term follow-up cohort study.

Methods

A total 79 MCI patients who were diagnosed by dementia specialists at baseline were enrolled in this study. All patients followed up with two PET scans (18F-flortaucipir for tau and 18F-florbetaben for Aβ), brain MRI and neuropsychological battery for up to five years. We classified MCI patients into various subgroups based on their baseline characteristics using multiple approaches. These included amyloid PET positivity, a combination of amyloid and tau PET positivity, determination of amnestic type, identification of single or multidomain cognitive impairment, and differentiation based on the presence of impaired visual memory, verbal memory, or both of memory dysfunction in amnestic MCI.

Results

Compared to those without amyloid pathology (A-), individuals with amyloid pathology (A+) exhibited worsening in MMSE (β=-0.632, p=0.012), CDR-SB (β=0.632, p<0.001), memory function (β=-3.267, p<0.001), language function (β=-0.410, p=0.019), and total scores (β=-5.579, p<0.001) on the neuropsychological battery. Among them, those with both amyloid and tau pathology (A+T+) demonstrated a steeper decline. When comparing amnestic to non-amnestic MCI, amnestic MCI (aMCI) showed increased tau burden in the temporal lobe (β=0.033, p=0.030) and worsened CDR-SB scores (β=0.630, p=0.005). In comparison to single-domain MCI, multi-domain MCI exhibited exacerbated amyloid burden (β=0.020, p=0.047), tau burden in the temporal area (β=0.028, p=0.018), and CDR-SB scores (β=0.520, p=0.002).

Conclusion

The most critical factor determining symptom progression in MCI appears to be the presence of AD pathology confirmed by amyloid and tau PET imaging. Additionally, in classic MCI classification, faster deterioration was observed in patients with an amnestic subtype, and involvement of multiple domains.

Time Perception and Memory in Mild Cognitive Impairment and Alzheimer's Disease : A preliminary Study

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Objective

Episodic memory is a system that receives and stores information about temporally dated episodes and temporal-spatial relations among them.

In our study, we aimed to investigate the relevance of episodic memory to primitive time perception, with a specific focus on simultaneity and temporal order judgment.

Methods

In Experiment 1, we employed the ternary simultaneity judgment task to discern differences in time perception between patients with dementia and age-matched individuals without cognitive impairment. Utilizing a mathematical analysis capable of estimating subjects' time processing mechanisms, we identified the sensory and decisional components of temporal order and simultaneity judgment. In Experiment 2, we examined how differences in temporal perception related to performance in temporal order memory, in which time delays played a critical role.

Results

The temporal decision window for both temporal order and simultaneity judgments exhibited marginal differences between patients with episodic memory impairment and their healthy counterparts ($p = 0.15$, $t(22) = 1.34$). We also observed that this temporal decision window may be linked to the temporal separation of events in episodic memory (Pearson's $\rho = -0.53$, $p = 0.05$).

Conclusion

Our study suggests that the frequency of visual events accumulated and encoded in working memory falls within the range of approximately 5.7 to 11 Hz. According to the internal clock model, a lower frequency of event pulses tends to result in an underestimation of event duration, and this phenomenon might be linked to the observed time distortions in patients with dementia.

PE_087 Clinical Manifestations

Prediction of Amyloid Positivity in Patients with Subcortical Vascular Cognitive Impairment

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Objective

This study aimed to examine the differences in clinical and neuroimaging variables between amyloid β (Aβ) positive and negative subcortical vascular cognitive impairment (SVCI) and to propose a prediction model for Aβ positivity in clinically diagnosed SVCI patients.

Methods

A total of 130 patients with SVCI were included in this study. The variables for a predictive model were selected by comparing the characteristics of the Aβ-negative and Aβ-positive SVCI groups. The final model was determined using a stepwise method. The model performance was evaluated using the receiver operating characteristic (ROC) curve and a calibration plot. A nomogram was used for visualization.

Results

Among 130 SVCI patients, 70 (53.8%) were Aβ-positive. The Aβ-positive SVCI group was characterized by older age, tendency to be in the dementia stage, a higher prevalence of APOE ε4, a lower prevalence of lacune, and more severe medial temporal atrophy (MTA). The final predictive model, which excluded MTA grade, demonstrated good accuracy in distinguishing between Aβ-positive and Aβ-negative SVCI, with an area under the curve of 0.80 (95% confidence interval: 0.72–0.88).

Conclusion

The findings suggest that older age, being in the dementia stage, APOE ε4 carrier, and absence of lacunes may be predictive of Aβ positivity in clinically diagnosed SVCI patients.

PE_088 Clinical Manifestations

Validity Analysis of Proposed Diagnostic Criteria for Right Temporal Variant of Frontotemporal Dementia

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Objective

This study focuses on right temporal variant frontotemporal dementia (rtvFTD), characterized by right anterior temporal atrophy, leading to prosopagnosia and behavioral changes resembling bvFTD. We applied and validated two proposed rtvFTD criteria using Korean patient data.

Methods

Between 2007 and 2022, 225 patients with svPPA or bvFTD were collected from Pusan National University Hospital, Samsung Medical Center, and Longitudinal study of Early onset dementia And Family members (LEAF) cohort. After exclusions, visual assessment was conducted on 202 patients using the Amsterdam method. 42 rtvFTD patients (rtvFTD-Amsterdam) were classified, and subsets of svPPA and bvFTD patients without rtvFTD were matched, along with an Alzheimer's disease dementia group (n=42 each). We analyzed patients' initial T1-weighted images, converting them to NIfTI files. Cortical thickness was assessed using FreeSurfer. W-score maps were generated by comparing each patient's grey matter maps to healthy controls. Using UCSF method, 202 individuals were classified, 20 as rtvFTD (rtvFTD-UCSF) based on right temporal atrophy and frontal preservation (index <0.50).

Results

In the rtvFTD-Amsterdam, memory problems, executive dysfunction, disinhibition, and compulsive behavior were common symptoms. Prosopagnosia was initially present in 48% of cases. The rtvFTD-UCSF patients showed higher prosopagnosia (55%) and disinhibition (75%) prevalence. Naming difficulty was moderate compared to left temporal and frontal groups. In our cohort, the sensitivity of the Amsterdam criteria was 81% with a specificity of 29%. Using the UCSF criteria, the sensitivity for rtvFTD was 80% with a specificity of 42%.

Conclusion

Diagnostic criteria for rtvFTD showed suboptimal sensitivity and specificity. Clinical differences were observed in our rtvFTD patients compared to the Amsterdam and UCSF studies. Distinctions in clinical characteristics between rtvFTD-Amsterdam and rtvFTD-UCSF were noted. Validation in diverse populations using standardized tools is crucial for refining rtvFTD diagnostic criteria.

Analysis of Macular Thickness and Retinal Nerve Fiber Layer by using of Spectrum Domain-optical Coherence Tomography in Patients with Alzheimer's Disease and Amnestic Mild Cognitive Impairment

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Objective

Spectrum Domain-Optical Coherence Tomography (SD-OCT) is a non-invasive technology that acquires cross-sectional images of retinal structures allowing neural fundus integrity assessment. Macular thickness and retinal nerve fiber layer (RNFL) thickness measured by an SD-OCT have been used as a indicator of Alzheimer's disease (AD) and amnestic mild cognitive impairment (aMCI). However which portion of retinal RNFL is the most sensitive area among normal control, aMCI and AD is not clear yet. The purpose of this study is to demonstrate that RNFL thickness is a useful indicator and which portion of reninal RNFL is the most sensitive area among normal control,

Methods

In a cross-sectional study we consecutively recruited 53 patients with AD, 58 with aMCI, and 54 normal controls. AD-OCT was performed in all of them to measure circumpapillary macular thickness in the 9 sectors (fovea, temporal outer superior outer, nasal outer, inferior outer, temporal inner, superior inner, nasal inner, inferior inner). We made 4 RNFL quadrant area as following: superior (superior outer+superior inner), inferior (inferior outer+ inferior inner), nasal (nasal outer + nasal inner), temporal (temporal outer + temporal inner). We also evaluated the correlation of the RNFL thickness and MMSE score and disease duration of the patients

Results

Average macular thickness and 9 sectors of RFNL thickness were not significant among the group in our patients. In quadrant analysis, however superior quadrant RNFL thickness showed significant differences among groups(109.98±12.01 um, 106.83±10.05 um 101.25±11.90 um in normal control, aMCI and AD respectively, $p<0.01$). The RNFL thinning of the superior quadrant showed a significant correlation with MMSE score($r=0.555$, $p<0.01$) and AD duration($r=-0.528$, $p<0.01$).

Conclusion

This finding could suggest superior quadrant retinal RNFL by SD-OCT could be a useful marker of AD and a MCI for early detection and monitoring of disease progression.

PE_090 Clinical Manifestations

Pathologically Confirmed Advanced Stage of Limbic Predominant Age Related TDP-23 Encephalopathy (LATE): A Case Report

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Objective

We herein introduce a case which that was pathologically confirmed as an advanced stage of LATE.

Methods

An 81-year-old woman visited a memory clinic complaining of memory impairment in the past few years. In the first year post-onset, on MMSE, she scored 20 with clinical CDR of 1 (CDR-SB 6). In the first year post-onset, brain MRI indicated diffuse brain atrophy with hippocampal atrophy. The lacunes in both basal ganglia with small old hemorrhage at the posterior tip of the right basal ganglia. By the sixth year post-onset, her MMSE score was 7 with CDR of 3 (CDR-SB 15). Contrary to the worsening of clinical symptoms, brain CT revealed only slight increase in hippocampal atrophy, with no significant difference from the MRI findings 5 years ago.

Results

In the ninth year post-onset, the patient died at the age of 88. The brain autopsy revealed global brain atrophy with 923g in brain weight. Final pathological diagnosis was Alzheimer's disease (AD), limbic-predominant age-related TDP43 encephalopathy (LATE), and cerebrovascular disease (CVD). In detail, under the NIA-AA ADNC grading, the level is intermediate, with scores of A2, B3, and C2. The Thal phase is rated 3 out of a possible 5. The Braak stage, which indicates the progression of Alzheimer's tau pathology, is at stages V to VI out of VI. The CERAD score was 2 out of 3. No evidence of CAA was found (score of 0). The stage of LATE was 6 by Joseph staging system, thus, TDP43-positive intraneuronal inclusions and neurites were found in the amygdala, entorhinal and temporal lobes, hippocampal cornu ammonis and dentate,basal ganglia, and tectum of the midbrain and olivary nucleus of the medulla oblongata. However, there was no hippocampal sclerosis.

Conclusion

This case underscores the importance of understanding the pathological characteristics of TDP-43 protein abnormalities and related symptoms.

A Case of Typical General Paresis of Insane Mimicking Alzheimer's Disease Dementia

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Objective

General paresis(GP), also known as general paresis of the insane(GPI) or dementia paralytica, is one of the late-stage neurosyphilis. This term is now considered outdated and can instill a stereotype that the disease possesses more psychotic rather than neurodegenerative features, but it is still widely used in modern medical practice. Therefore, to re-name the condition is necessary.

Methods

We report the case of a patient with general paresis accompanied by cortical atrophy. The patient is a 38-year-old, 14-year-educated man come to hospital for evaluation of cognitive decline. He had an untreated genital lesion 5 years ago, so we suspected neurosyphilis. The patient was diagnosed to general paresis of neurosyphilis based on clinical findings and CSF analysis.

Results

Some GP patients can only show diffuse cortical atrophy in chronic stage without other specific image findings. This is extremely rare in typical bacterial CNS infections which are usually pyogenic and eventually ends in acute inflammatory response. Even though GP is the result of spirochete infection, the clinical and image findings of the patient resemble that of the AD, which is almost not considered as a result of bacterial infection. It is notable that not only clinical and image findings, but also pathological findings resemble between these two diseases. It is crucial to differentiate GP from AD in clinical settings because of the difference in treatment strategy in the present, but it should not be overlooked that there is a significant pathological link between these two.

Conclusion

It is crucial to use language that accurately describes the character of the disease when discussing neurological conditions, and to avoid language that perpetuates negative stereotypes or biases. This case suggests that brain image findings and symptoms in general paresis in neurosyphilis is highly relevant to neurodegenerative diseases even if it's fundamentally classified as bacterial CNS infection.

PE_092 Clinical Manifestations

A Case of Pathologic Laughing and Crying with Dose-dependent Responsiveness to the Escitalopram

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Objective

Pathological laughing and crying (PLC) is defined by uncontrollable outbursts of laughter and/or crying inappropriate to the patient's external circumstances and emotional state. Selective Serotonin reuptake inhibitors (SSRIs) are primarily used off-label by clinicians. There are reports on the effectiveness of SSRIs on PLC, but there were limitations in the evidence due to the size or method of the study. Moreover, although the pathophysiology of PLC is not fully understood, serotonin is known to be involved. This case could be considered as one of the pieces of evidence supporting this theory.

Methods

A 47-years old man who is an automobile researcher presented with left hemiparesis, dysarthria, uncontrollable outburst of laughing. The patient presented at another hospital 20 years ago with symptoms of right hemiplegia and Rt hypoesthesia, and was subsequently diagnosed and treated for stroke. Physical examination revealed left side motor weakness, dysarthria, facial palsy. At the time of admission, brain MRI was performed and right paramedian pontine infarction was confirmed. The patient started Escitalopram 10mg per day with admission. At the time of discharge, all other symptoms caused by the stroke had improved except for the PLC.

Results

During the follow-up period, when the escitalopram was discontinued, the patient's PLC worsened. And when the PLC was not controlled at escitalopram 10 mg per day, the PLC was controlled with an escalated dose, 20mg per day. Interestingly, PLC showed a dose-dependent response to SSRIs in this patient, which was rarely reported.

Conclusion

In conclusion, this case provides evidence for dose escalation in cases where patients with PLC do not exhibit a response to a specific dosage of SSRIs. Furthermore, we present a need for an RCTs about the effect of SSRIs on PLC and the additional research on the association between PLC and serotonin system in brainstem.

Two Cases of Posterior Cortical Atrophy

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Objective

Posterior cortical atrophy is neurodegenerative syndrome with early visuospatial, visuoperceptual deficits due to atrophy of parieto-occipital brain regions, and is considered a visual variant of AD. However, proportion of patients with AD presenting with PCA has been estimated about only 5%, and because of its relative rarity, it takes years from first symptom onset to diagnosis. We report two cases of PCA patient, whose symptoms are considered ophthalmic problems, and diagnosis has been delayed for years.

Methods

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Results

Case 1: A 62-year-old man with 14 years of education presented with progressive visual disturbance, especially on the left side that began 2 years earlier and had progressively worsened. Humphrey automated perimetry showed left homonymous hemianopia. K-MMSE score was 24/30 (calculation 3/5 and word recall 0/3, drawing 0/1), GDS 5, and K-IADL 4/10. PET/CT _ Brain (FDG) revealed markedly decreased glucose metabolism in right parieto-temporo-occipital cortices and right thalamus, and mildly decreased glucose metabolism in left parieto-temporal cortices. Eventually, he was diagnosed with posterior cortical atrophy and donepezil was administered.

Case 2: A 71-year-old man with 16 years of education presented with reduced memory that began 5-6 years earlier, and shortly after symptom onset, he started to complain that he cannot see well, and had problems with reading and writing, but no ophthalmological problems were identified. K-MMSE score was 20/30 (time orientation 4/5, calculation 0/5 and word recall 0/3, drawing 0/1), GDS 4, and K-IADL 1/10. MRI revealed profound diffuse severe brain atrophy. Eventually, he was diagnosed with posterior cortical atrophy and donepezil was administered.

Conclusion

PCA is a rare but important neurodegeneration syndrome. Patients with this condition are often diagnosed late or are misdiagnosed as having a primary ocular or psychologically mediated illness. Recognition of PCA as a distinct syndrome and determination of its underlying cause allow for appropriate treatments.

PE_094 Clinical Manifestations

Associative Visual Object Agnosia and Apperceptive Prosopagnosia after Aortic Dissection Surgery

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Objective

Visual agnosia is a rare neuropsychological syndrome characterized by the inability to recognize visual stimuli such as objects, faces, or colors. Two subtypes have been suggested: apperceptive agnosia and associative agnosia. We report associative visual object agnosia and apperceptive prosopagnosia in a 49-year-old man with selectively atrophied bilateral occipitotemporal lobes following aortic dissection surgery.

Methods

The patient had difficulty recognizing objects and familiar faces. Ophthalmological examination results were normal. Detailed neuropsychological tests for visual cognition were performed. Brain CT, MRI, and FDG-PET were done.

Results

Confrontation naming for objects was severely impaired, and the patient could not explain the use of objects. Test results for semantic knowledge and relation assessed by matching objects for function were severely impaired. In tests for face recognition, the patient failed to discriminate between same faces or different faces, point to famous faces, or identify famous faces, while he performed well in naming celebrities in response to its description and discriminating celebrities' names. The patient had no definite abnormalities in elementary visual sensory and perceptual levels for objects; however, visual stimuli failed to arrive in recognition, resulting in associative visual object agnosia. Additionally, apperceptive prosopagnosia was suspected because his face recognition failed from the face perceptual level. Follow-up brain CT and brain MRI demonstrated diffuse cortical atrophy, including prominent bilateral occipitotemporal atrophy, compared to initial findings. FDG-PET revealed severe glucose hypometabolism in bilateral occipitotemporal areas.

Conclusion

It has been well known that cerebral malperfusion, usually presenting as an ischemic injury, is a common complication in patients undergoing aortic arch surgery. The underlying mechanism of diffuse cortical atrophy with prominent bilateral occipitotemporal atrophy in this patient remains unclear. Nevertheless, one possible hypothesis may be suggested that aortic dissection itself before surgery and planned circulatory arrest during the aortic arch operation could cause brain hypoperfusion, leading to cortical laminar necrosis.

Semantic Variant Primary Progressive Aphasia Caused by ANXA11 p.Asp40Gly Mutation

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Objective

Approximately 30% of patients with frontotemporal dementia (FTD) have motor impairments, and 12.5% meet the diagnostic criteria for amyotrophic lateral sclerosis (ALS). Mutations in C9orf72, TARDBP, and TBK1 are the major genetic causes in FTD-ALS, and TDP-43 inclusions as a common pathologic character are resulted from each of these variants. The Annexin A11 (ANXA11) gene has been newly identified as a causative gene of ALS with or without FTD.

Methods

We report a case of semantic variant primary progressive aphasia caused by ANXA11 p.Asp40Gly mutation.

Results

A 77-year-old lady visited our hospital with naming difficulty for 5 or 6 years. About a year ago, she began to having a trouble to recognize a person who came to know recently. She had a daughter diagnosed with schizophrenia. Also, she was the only daughter with seven brothers, among whom the 3rd one had a mental disorder. Brain MRI revealed atrophy of the left anterior temporal lobe. K-WAB showed anomic aphasia. She showed impaired confrontation naming and single-word comprehension, but repetition and speech production were well spared. Semantic variant primary progressive aphasia was suspected. Whole-exome sequencing was performed; a pathogenic variant (c.119A>G, p.Asp40Gly) was found.

Conclusion

Clinical phenotype of the patient was svPPA. The discriminating point of the patient is that she had a family history of psychiatric mental disorders. Yet, her clinical progression was similar to other svPPA patients, even slower. We need to further evaluation of her family including her daughter and brother to establish variety of clinical manifestation by ANXA11 p.Asp40Gly mutation in one family. Zhang reported an atypical ALS with PSP-like symptoms caused by c.119A>G mutation on the ANXA11 gene with the spectrum of phenotypes and the genotype-phenotype correlation with the gene mutation, but there were no cases like aphasia-phenotype.

PE_096 Clinical Manifestations

The Behavioral and Psychological Symptoms Of People With Alzheimer's Disease During The COVID-19 Pandemic

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Objective

Alzheimer's disease (AD) has a significant negative impact on patients, carers, families, and society. Caregivers have always been the backbone of caring for people living with dementia, and they bear a heavier burden than others, especially when their loved ones exhibit behavioral and psychological abnormalities. Understanding these symptoms during the COVID-19 pandemic will help guide future interventions and support measures. We conducted this study to determine the prevalence of behavioral and psychological symptoms (BPS) in people with Alzheimer's disease (AD), and which are associated with the burden of caregivers.

Methods

We conducted a descriptive cross-sectional study. Patients diagnosed with Alzheimer's according to DSM-5 criteria along with their caregivers who visited a Memory and Dementia Unit in Ho Chi Minh City from December 2021 to March 2022 were included in the survey. The Neuropsychiatric Inventory Questionnaire (NPI-Q) and Zarit Burden Interview – Short Form (ZBI-12) were used to collect the data of the patients and their caregivers. The data were then analyzed by STATA 14.0.

Results

43 patients with AD and their caregivers were included in the study. During the COVID-19 pandemic, the most common issue was irritability (28%). Other symptoms were delusions (21%), hallucinations (16%), agitation (14%), apathy (14%), appetite and eating abnormalities (7%), anxiety (5%), and nighttime behavioral disturbances (5%). The median ZBI score of the 43 caregivers surveyed was 17, with an interquartile range of [10, 19]. The BPS had an impact on supporting people with AD with no statistical significance ($p > 0.05$).

Conclusion

Patients with AD exhibited certain behavioral and psychological symptoms during the COVID-19 pandemic.Therefore, it is important to consider, screen, and manage these symptoms to lessen the burden of caregivers.

Impact of Cognitive Reserve on pTau in the Progression of Alzheimer's Disease

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Objective

We investigated the impact of cognitive reserve on tau pathology in the progression of Alzheimer's disease

Methods

We included amyloid-positive 2,011 participants who underwent neuropsychological assessment, amyloid PET, and CSF phosphorylated tau (pTau) analysis. The participants' amyloid positivity was decided using amyloid PET. ADAS13 was used for the cognitive function score. Cognitive reserve (CR) on pTau was measured as the difference between the predicted and observed value of cognitive function based on CSF pTau level (CR_pTau). The participants were divided into two groups: a low-CR_pTau group that showed a worse ADAS13 score than the predicted ADAS13 score on the pTau level and a high-CR_pTau group that showed a better ADAS13 score than the predicted ADAS13 on pTau level. A mixed effect model was used to examine the difference in progression slope according to the CR_pTau group in each disease stage: cognitively unimpaired (CU), mild cognitive impairment (MCI), and dementia. Furthermore, the difference in the conversion duration to the next disease stage between two CR groups was analyzed using a t-test.

Results

In the CU group (N=745), there was no difference in the progression slope of ADAS13 between the low and high CR_pTau group (P=0.099). In the MCI group (N=925), the high CR_pTau group showed a trend of faster progression of ADAS13 than the low CR_pTau group (P=0.053). In the dementia group (N=346), the high CR_pTau group showed faster progression than the low CR_pTau group (P=0.011). The conversion duration from CU to MCI was not different between the two CR groups (P=0.136). However, the conversion duration from MCI to dementia was longer in the high CR_pTau group (P=0.003).

Conclusion

Cognitive reserve to pTau might impact the disease progression of AD, especially in the MCI stage.

Recent Issue on Clinical Neuropsychologist in Asia: Systematic Review

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Objective

Neuropsychology studies how the brain processes shape behaviour and psychological functioning. Meanwhile, clinical neuropsychology studies individual behaviour that may arise from the brain's and behaviour's relationship (Studocu, 2022). The Asian Neuropsychological Association (ANA) has positively impacted the field of neuropsychology services in Asians. The study aims to examine the development of Clinical Neuropsychology in Asia using a systematic review.

Methods

This research uses a systematic review method. We collected articles from 2013-2023 from an electronic database and the Journal of The Clinical Neuropsychologist. The keywords used are Clinical Neuropsychologist and Asian. Then, as many as three selected articles were reviewed to answer the purpose of this study.

Results

A study by Fujii et al. (2023) said that concrete recommendations for Western neuropsychologists working with patients of Japanese descent are to address the current gap in cultural competence among clinicians when working with this heterogeneous population. Another study from Nguyen (2023) found that tele-neuropsychology services with Asian patients highlight the need for flexibility to accommodate cultural differences and commitment to the complex nature of working with patients seeking interpretation services while recognizing the importance of preserving the validity of neuropsychological methods. In China, according to Ng (2023), neuropsychological tools for Chinese pediatric patients have been mainly focused on translated or adapted measures. The last study from Sunderaraman (2021) said that Asian Indians living in the US are distinct from the larger Asian American community. Immigration trends underscore that Asian Indians have a bimodal distribution of wealth. Regarding medical conditions, a key and highly concerning finding is the higher prevalence of cardiovascular risk factors, especially in young males.

Conclusion

The study concluded that Clinical Neuropsychology in Asia has developed, like in Japan, China, and India.

Association of Baseline Serum Urate Levels with Longitudinal General Cognition in Non-Demented Parkinson's Disease

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Objective

Prior research has shown a robust relationship between Parkinson's disease (PD) and urate, yet the biological mechanisms and the direction of causality remain elusive. Despite cognition being a crucial non-motor symptom of PD, its relationship with urate remains inadequately explored. This study aimed to assess the relationship between baseline serum urate levels and longitudinal general cognition in non-demented PD.

Methods

We enrolled 203 patients diagnosed with non-demented PD, consisting of 88 males and 115 females, each having undergone two or more Montreal Cognitive Assessment (MoCA) tests and possessing available baseline serum urate levels. A total of 471 MoCA scores were analyzed, and each individual completed 2 to 4 tests, averaging 2.32 tests per person. Linear mixed models were utilized to evaluate the influence of baseline serum urate levels and their interaction with sex or baseline cognitive status on longitudinal changes in MoCA scores.

Results

The effect of baseline serum urate levels on the longitudinal change in MoCA scores did not vary with respect to baseline cognitive status or sex (interaction terms: sex*urate*year, β (standard error, SE) = -0.01 (0.10), p = 0.916; mild cognitive impairment*urate*year, β (SE) = 0.0001 (0.09), p = 0.988). Thus, the analysis was conducted without stratification based on sex and baseline cognitive status. Higher baseline serum urate levels were associated with a slower decline in MoCA scores (β (SE) = 0.10 (0.04), mg/dl*year, p = 0.022), suggesting a potential protective effect against cognitive decline in non-demented PD.

Conclusion

This study reveals that elevated baseline serum urate levels are linked to a decelerated cognitive decline in non-demented PD. Further research is needed to elucidate the underlying biological mechanisms and explore potential therapeutic implications of this association.

PE_100 Clinical Manifestations

Rare Strategic Vascular Cognitive Dysfunction with Isolated Left Posterior Insular Infarction

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Objective

Background: The insular cortex (IC) is a complex structure that has been implicated in numerous functions due to its interconnectedness with multiple brain areas. Consequently, a single small infarction in this area can lead to various cognitive dysfunctions.

Methods

Case: An 80-year-old ambidextrous man visited the hospital with a speech problem. He had a history of hypertension, diabetes mellitus, end-stage renal disease (ESRD) on hemodialysis (HD), and atrial fibrillation. Upon waking, he experienced right-sided motor weakness, and his speech became incoherent. He also exhibited mild memory impairment, but he had no difficulty in activities of daily living (ADL). Upon arrival at the emergency room (ER), he presented with mild right hemiparesis, hemiparesthesia, speech disturbance, and mild dysarthria. MRI revealed an acute focal ischemic lesion in the left posterior insular area. His memory significantly improved within two days of hospitalization, while other cognitive symptoms, including language issues, persisted. In a follow-up neuropsychological evaluation conducted one year after the initial event, his cognitive dysfunctions had shown significant improvement.

Results

Discussion: We report a rare case of acute strategic infarction involving the left posterior insular region. This condition is uncommon and is known to have a favorable prognosis.

Conclusion

Acute posterior infarction with cognitive dysfunction

FDG PET Findings according to Wandering Patterns of Patients with Drug-naïve Alzheimer's Disease

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Objective

To explore anatomic substrate of specific wandering patterns in patients with Alzheimer's disease (AD) by performing positron emission tomography with 18F fluorodeoxyglucose positron emission tomography (FDG PET).

Methods

Drug-naïve AD patients with wandering (n=80) and without wandering (n=262) were recruited. First, the specific pattern of wandering type was operationally classified
according to specific wandering score and clinical assessment. Second, brain FDG PET was performed and fluorodeoxyglucose (FDG) uptake differences of specific brain regions
according to wandering patterns were compared to those of non-wanderers.

Results

In patients with pacing pattern, FDG PET showed significant lower FDG uptake in both middle cingulum and left putamen cluster compared to non-wanderers. The right
precuneus and supplementary motor area in patients with random pattern and left calcarine sulcus, right calcarine sulcus, right middle cingulum, and right post central gyrus in patients
with lapping pattern had significantly lower FDG uptake compared to non-wanderers.

Conclusion

This study showed that wandering in patients with AD had three distinct patterns. These specific patterns showed significant lower FDG uptake in specific brain areas
compared to non-wanderers.

PE_102 Clinical Manifestations

Cerebral Perfusion Study on the Effect of Acetyl-L-carnitine in Non-demented Patients with Small Vessel Disease

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Objective

Small vessel disease is known as risk factor for developing several types of dementia, including Alzheimer's dementia and mixed dementia, as well as vascular dementia. Studies for prevention of progression in cognitive decline have been not sufficiently achieved yet, although small vessel disease is a common risk factor for dementia in elderly population. Therefore, we conducted this study to evaluate the possibility of the preventive effect of Acetyl L-carnitine (ALC) for cognitive decline.

Methods

Only 22 non- demented patients with small vessel disease were chosen; 10 patients treated with ALC at 1.5g/day for 6 months and 12 patients without ALC administration. At baseline and follow-up after 6 months, brain SPECT, Mini-Mental State Examination (MMSE), Clinical Dementia Rating (CDR) with sum of box (SOB) and Global Deterioration Scale (GDS), were used to assess participants. After ALC administration, changes in brain perfusion and cognitive evaluations examined between two groups.

Results

After ALC administration, changes in scores of MMSE, CDR and GDS were not statistically significant. Voxel-wise whole-brain image analysis revealed that perfusion was significantly ($p<0.001$) increased in the both precuneus and frontal gyrus in patients treated with ALC compared to control groups at follow-up.

Conclusion

The present study showed that the perfusions of the precuneus and frontal gyrus were increased in patient treated with ALC. Therefore, we could cautiously suggest the possibility of the preventive effect of ALC for cognitive decline through these results.

Exploring Differences of Non-Dementia and Alzheimer's Disease Using Physical Activity Task: Preliminary Results

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Objective

This study aimed to explore differences in measures of physical activity between non-dementia and dementia due to Alzheimer's disease (ADD) and to propose a predictive model for ADD.

Methods

A total of 86 participants complaining of cognitive decline were included in this study. The physical activity task was developed, involving the observation, imitation, and recall of three specific physical movements. Participants (N = 17) were excluded from the analysis due to deviated or disorganized performance. The predictive model included variables showing differences between the two groups and was evaluated using the receiver operating characteristic (ROC) curve.

Results

Among 69 participants, 11 (15.9%) were patients with ADD. Patients with ADD exhibited poorer performance in the recall of each movement and the total number of recalls. The predictive model for the recall of each movement and the model for the total number of recalls demonstrated good accuracy in distinguishing between non-dementia and ADD, with an area under the curve of 0.89 (95% confidence interval [CI]: 0.77–1.00) and 0.87 (95% CI: 0.75, 0.99), respectively.

Conclusion

These preliminary findings suggest that patients with ADD not only recalled fewer movements overall but also tended to have specific difficulty in recalling movements presented earlier in the sequence.

PE_104 Clinical Manifestations

An Autopsy Case of Familial Neuronal Intranuclear Inclusion Disease

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Objective

Neuronal Intranuclear Inclusion Disease (NIID) is a slowly progressive neurodegenerative disease characterized by eosinophilic hyaline intranuclear inclusions in the central, peripheral and autonomic nervous system cells, and also in visceral organ cells. NIID has been considered to be a heterogeneous disease because of the highly variable clinical manifestations, and ante-mortem diagnosis has been difficult. Herein, we report an autopsy case of familial NIID presented as recurrent encephalitic episodes in Korea.

Methods

Case :A 57-year-old male visited the hospital with severe headache accompanied by right hemianopsia and disorientation. Brain magnetic resonance imaging and angiography with enhancement showed mild diffuse brain atrophy and mild ventriculomegaly. He had family history of early-onset dementia in paternal relatives. Skin biopsy showed internuclear eosinophilic inclusions in adipocyte and positive immunohistochemical staining of ubiquitin, anti-p62. his genetic testing demonstrated prolonged GGC repeats in NOTCH2NLC. His symptoms became progressively worse and he died of aspiration pneumonia. He died almost one year after the disease onset at 58 years of age and a brain autopsy was performed.

Results

Grossly, parietoocciptotemporal area appeared edematous and poorly demarcated softening, which was shown as extensive ischemic changes involving cerebral cortices and subcortical white matter composed of neuronal loss, proliferation of vessels, and myelin pallor with various degree of spongiosis in H&E staining. Ubiqutin- and p62-positive intranuclear inclusions were found in the neurons and glial cells throughout the cortex and subcortical white matters. These findings were consistent with NIID. Immunohistochemical staining for tau, TDP, β-amyloid, and α-synuclein revealed only a few tau-positive neurofibrillary tangles, neuronal cytoplasmic inclusions, and glial cytoplasmic inclusions in the caudate and subgenual anterior cingulate cortex.

Conclusion

These pathological findings might reflect the cerebral swelling and ischemia may be related to the pathophysiology of encephalopathy with NIID. Our report is the first to document autopsy-confirmed familial NIID with encephalopathy in Korea.

PE_105 Clinical Manifestations

Severe Bitemporal Lobe Atrophy Derived from Limbic-predominant age-related TDP-43 encephalopathy neuropathological change (LATE-NC) in progressive supranuclear palsy (PSP): An Autopsy Confirmed Case Report

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Objective

Severe bilateral temporal atrophy has rarely been reported in progressive supranuclear palsy (PSP) .

Methods

We describe an autopsy-confirmed PSP comorbid with limbic-predominant age-related TDP 43 encephalopathy neuropathological changes (LATE-NC), demonstrating severe bilateral temporal lobe atrophy.

Results

A 72-year-old male presented with severe dementia and motor deficits, which began with naming difficulty at age 62. At age 66, he had difficulty walking and moving his left arm and leg. His grandmother had dementia. Neurological examination revealed rigidity of the upper and lower extremities, worse on the left. The MMSE score was 0/30, and the CDR score was 5. Brain MRIs revealed diffuse cortical atrophy with predominant bilateral temporal atrophy. FDG PET revealed bilateral frontotemporal glucose hypometabolism with prominent bilateral anterior temporal hypometabolism. CIT-PET revealed moderately to severely decreased DAT binding in the right basal ganglia. Based on clinical and neuroimaging findings, his clinical syndromic diagnosis was suspected to be semantic-variant primary progressive aphasia. He died at 72 years of age, and a brain autopsy was performed. Tau-immunoreactive tufted astrocytes and coiled bodies were observed in the frontal and parietal cortices, with subcortical white matter, basal ganglia, thalamus, and the brainstem. Globose tau tangles were found in the substantia nigra and oculomotor nuclei. However, in the severely affected temporal and limbic areas, TDP-immunoreactive neuronal cytoplasmic inclusions and dystrophic neurites were found instead of tau pathology. These findings were consistent with frontotemporal lobar degeneration, tau, and PSP pathology, which are comorbid with LATE-NC.

Conclusion

Our findings may support the hypothesis that "the pathology of proteinopathy appears in distinct brain regions and involves disparate brain network, and clinical phenotypes of these diseases correlate with the characteristic distribution patterns of the underlying pathology". Further studies are needed to confirm the contribution of LATE-NCs to PSP or other primary pathologies.

PE_106 Clinical Manifestations

Neuronal Intranuclear Inclusion Disease Presenting with Reversible Cerebral Vasoconstriction Syndrome: Serial Neuroimaging Findings during an 11-year follow-up

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Objective

To report the case of a patient initially showing symptoms consistent with reversible cerebral vasoconstriction syndrome (RCVS) and subsequently diagnosed with adult-onset Neuronal intranuclear inclusion disease (NIID) after 11-year follow-up.

Methods

Comprehensive clinical, laboratory, and radiologic evaluations were conducted on the patient. Whole-exome sequencing and a genetic test for NIID were performed to identify an underlying genetic cause.

Results

A 59-year-old man initially presented with a thunderclap headache, right visual field deficit, and confusion. Although his brain MRI appeared normal, MR angiography revealed occlusion of the left posterior cerebral artery, later followed by recanalization, leading to the diagnosis of RCVS. Over the course of 11 years, the patient experienced ten more episodes, each increasing in duration and intensity, accompanied by seizures. Concurrently, his cognitive impairment worsened. Genetic testing for NIID disclosed an abnormal expansion of GGC repeats in NOTCH2NLC, with a count of 115 (normal range, <60).

Conclusion

Our report unveils the first documented case of an adult-onset NIID patient exhibiting symptoms similar to RCVS. Given the unclear mechanisms of RCVS, it becomes important to consider the potential of NIID when patients demonstrate recurrent RCVS-like symptoms along with signs of neurodegenerative disease, irrespective of the absence of characteristic MR findings of NIID.

Machine Learning Trends in Dementia Screening and Risk Prediction

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Objective

To keep pace with rapidly changing societies and economies, new technologies such as artificial intelligence, the Internet of Things (IoT), big data and cloud computing are being adopted by a range of industries, including the healthcare sector. The application of big data and artificial intelligence to identify populations at high risk of dementia is one of the most notable areas of medical research. To support qualified researchers experimenting with medical artificial intelligence in psychiatry, this review aims to (1) introduce the definition, key concepts and classification of machine learning and its general distinction from traditional statistical analysis models, and (2) present recent studies in the field of psychiatry on dementia detection and prediction of high-risk populations.

Methods

As a result of reviewing 4 studies that used machine learning to discriminate high-risk groups for dementia, different machine learning algorithms such as boosting model, artificial neural network and random forest were used to predict dementia.

Results

The predictive performance of machine learning techniques varies between studies because of differences in the imbalance of the machine data (especially Y variables), the characteristics of the features included in the model, and the measurement methods of the outcome variables. Therefore, further studies are continuously needed to verify the predictive performance of each algorithm, because although some studies have shown that the performance of a specific machine learning algorithm is excellent, the results cannot be generalised to all types of data.

Conclusion

The development of machine learning algorithms will transform primary care by using advanced machine learning algorithms to identify high-risk groups for dementia in the future.

PE_108 Dementia Care

How the Caregiver Status Could Increase the Quality of Life and Nutritional Status among Elderly with Dementia

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Objective

More than 4.2 million Indonesians suffer from dementia and the prevalence doubles every 5 years in the elderly population. The elderly with dementia are dependent on the caregiver's presence to maintain their QoL and comorbidity makes it worse. However, certified informal caregivers are not regulated in Indonesia.

Methods

A comprehensive strategy is needed to provide certified caregivers and health access through community services. Expanding health insurance coverage for the provision of caregivers is the top priority because it mitigates mental health problems. The mini-cognitive scoring is effective as a neuropsychological test for dementia early

Results

Using the Mini-Cognitive test scoring (Borson et al. in 2000), which consists of a clock drawing test and recall, it is known that 1.42% of elderly (aged 60+) with diabetes were identified as having symptoms of dementia with moderate to severe. The elderly with diabetes is 12% (men: 63%). The elderly needing long-term care due to these health conditions reach 9.7% and 88% of them do not have caregivers. Less than 1% of the elderly are cared for by paid caregivers and are concentrated in urban areas. Most of them are cared for by their families or tend to "aging in community". 36% of diabetic elderly with dementia are holders of social protection programs so they benefit from health insurance and government social assistance. However, using the Geriatric Depression Scale (GDS) it is known that when the elderly with dementia and diabetes have caregivers, their mental health problems are lower than respondents who do not have caregivers.

Conclusion

A comprehensive strategy is needed to provide certified caregivers and health access through community services. Expanding health insurance coverage for the provision of caregivers is the top priority because it mitigates mental health problems. The mini-cognitive scoring is effective as a neuropsychological test for dementia early detection and prevention.

PE_109 Dementia Care

Biological Importance of Bavachinin from Psoralea Corylifolia L against Parkinson's Disease through Their Inhibitory Potential on Human Monoamine Oxidase A (MAO-A) and Human Monoamine Oxidase B (MAO-B)

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Objective

Plant derived bioactive compounds have numerous advantages in the human health due to its vast medicinal importance and pharmacological activities. Phytochemicals are pure active constituents of different chemical class, mainly present in the different types of vegetables and herbs. These phytochemicals have been used against various forms of human diseases as medicine and Nutraceuticals from the very ancient time to till modern age. Bavachinin is a flavonoid class phytochemical, found to be present in the seeds of Psoralea corylifolia Linn.

Methods

Biological potential of bavachinin for their effectiveness on Parkinson's disease has been investigated in the present work through scientific data analysis of different scientific research work. In order to know its effectiveness against including Parkinson's disease, here in the present work biological effectiveness of bavachinin from Psoralea corylifolia L. has been investigated for their inhibitory potential on human monoamine oxidase A (MAO-A) and human monoamine oxidase B (MAO-B) through scientific data analysis. However, detailed molecular mechanistic study was also investigated in the present work to know its therapeutic effectiveness on Parkinson's disease.

Results

Biological effectiveness of bavachinin from Psoralea corylifolia L. has been investigated in the present work and revealed significance effects as it inhibited human MAO-B activity, which further signified its therapeutic potential for the management of Parkinson's disease. Further, bavachinin showed selective inhibitory potential on human MAO-B more than human MAO-A. However, bavachinin competitively inhibited human MAO-A and human MAO-B. Molecular docking study also signified the biological importance of C7-methoxy group in their chemical structure for higher selectivity, affinity, and reversibility.

Conclusion

Scientific data analysis revealed the biological potential of bavachinin from Psoralea corylifolia L in the medicine against Parkinson's disease. Bavachinin could be used for the management of Parkinson's disease.

PE_110 Dementia Care

Effects of Cognitive Training System (CAVE) on Cognitive Function in Patients with Alzheimer's Dementia

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Objective

Alzheimer's disease (AD) is a neurodegenerative disorder characterized by progressive cognitive decline. Cognitive training interventions have been proposed as a potential therapeutic approach for improving cognitive deficits in people with AD. This pilot study sought to compare the efficacy of two cognitive training interventions, Virtual reality-Based Intervention (VBI) and Screen-Based Intervention (SBI), in improving cognitive deficits in AD patients.

Methods

Eleven AD patients were recruited and randomly assigned to either VBI(6) or SBI(5).

Results

The VBI group responded to the intervention more positively, with five out of six patients classified as responders, compared to two out of five patients in the SBI group. An analysis of electroencephalogram (EEG) signals to compare pre-and post-intervention data revealed that only responders in VBI showed a significant decrease in delta waves and a significant increase in alpha waves.

Conclusion

These findings suggest that virtual reality-based cognitive training can improve cognitive abilities and contribute to higher cognitive reserve in AD patients when compared to screen-based cognitive training in the short term. However, the study does have some limitations, such as a small sample size and a focus only on patients with AD who responded positively to the intervention. Future research is needed to confirm these findings and investigate the potential of cognitive training interventions as a therapeutic strategy for AD.

PE_112 Dementia Care

Biological Effect and Therapeutic Potential of Columbianadin on Blood-Brain Barrier Permeability in Medicine through Its Molecular Mechanism

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Objective

Plant derived natural products have important role in the medicine. Coumarins class phytochemicals are an important class of secondary metabolite found to be present in the varieties of plants. Chemically the coumarins have benzopyrone structures in their core which facilitate coumarins to attach with different receptors and enzymes through non-covalent bond.

Methods

Biological importance of columbianadin has been investigated for its therapeutic effectiveness in the medicine through scientific data analysis of different research work. Pharmacological potential of columbianadin for their effectiveness on human disorders have been investigated through scientific data analysis of different scientific research work. Biological effect of columbianadin on Blood-Brain Barrier permeability has been investigated through scientific data analysis of different scientific research work.

Results

Scientific data analysis of different scientific research revealed the biological potential of columbianadin in the medicine for their effectiveness against different types of human disorders. Columbianadin is a coumarin class phytochemical found to be present in the Angelicae pubescentis. Biological effect of columbianadin on Blood-Brain Barrier permeability were investigated through scientific data analysis of various scientific research works and revealed the moderate absorption of columbianadin on Blood-Brain Barrier.

Conclusion

Scientific data analysis revealed the biological effect of columbianadin on Blood-Brain Barrier permeability.

PE_113 Dementia Care

The Effectiveness of Acceptance Commitment Therapy for Distressed Family Caregiver for Patients with Dementia

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Objective

Recently, psychoeducational support to caregivers of patients with dementia has been much interested. Education and cognitive behavior therapy (CBT) was proven to have a positive effect on caregiver burden and emotional stress. Acceptance and commitment therapy (ACT) which accept negative thought has been arising as a next generation of CBT. Here, we investigate the effect of ACT on emotional stress of caregivers of patients with dementia.

Methods

This is prospective, case-control, rater-blind, pilot study. The family caregivers of patients who have behavioral psychomotor symptom in dementia were recruited in this study. 13 intervention group and 13 control group were analyzed. The participants in experimental group were underwent a 6-week ACT program in one on one, face to face format. The outcome measurement are Beck anxiety inventory (BAI), Beck depression inventory (BDI), Zarit burden inventory (ZBI) and acceptance action questionnaire (AAQ).

Results

In experimental group, the score of BAI, BDI, ZBI and AAQ significantly improved compared to baseline score. The difference of the change of the score of BAI, BDI and ZBI after ACT program showed significant difference between intervention and control group.

Conclusion

This is the first report of applying ACT for psychoeducational support to family caregivers of patients with dementia. Depression, anxiety, and caregiver burden markedly reduced in intervention group compared to control group. Our results support that ACT can be useful counselling program for caring of family caregiver of patients with dementia.

PE_115 Dementia Care

Role of Wearable Technology and Geo-fencing Device for Alzheimer's Disease Patients in Gurugram City, India

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Objective

To study role of wearable devices (fire-boltt quantum watch) and geo-fencing technology to monitor daily life routine activities on movement and memory data in Alzheimer's disease (AD) patients.

Methods

Total of 68 AD patients were taken as subject with an equal ratio of male and female and age group between 35 to 50 years in Gurugram city. Wearable monitoring devices like fire-boltt quantum watch and geo-fencing device were put on the wrist of AD patients for 30 days and a questionnaire was filled out by each patient. In all subjects, blood pressure, blood glucose was measured on daily basis with day to day data of their monitoring of step count, calorie burnt, motion time, sleep monitoring, calorie consumption, monitoring heart rate to know daily routines and recording them for health purpose. Wearable bands, automatically provides a cueing sound with sensing alert when AD patients move out of the geo-fenced area and which stays until the subject resumes walking in virtual boundary.

Results

Wearable device reading showed that there was a significant normal heart rate ($p<0.05$), increase calorie burnt with a significant decrease of blood glucose and blood pressure levels ($p<0.01$), and increased significantly ($p<0.05$) sleep duration in active physically workout, include walking in AD patients compared to less physically workout AD patients, identified by professional physiotherapists. There is significantly normalize in memory loss and wandering events after one month with changing lifestyle routine among AD patients.

Conclusion

By using, these wearable devices ensured their health awareness with more concerned towards exercising and demonstrate the benefit of such a context-aware system and motivate further studies. Wearable devices and technology have introduced a new way for caregivers and families to prevent the dangers of wandering in senior loved ones with AD.

PE_116 Dementia Care

Therapeutic Impact of Laughter Yoga Therapy and Clapping Exercise in Alzheimer's Disease Patients

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Objective

To study new methods of controlling Alzheimer's disease (AD) complications by laughter yoga with clapping exercise in AD patients in urban Delhi metro population.

Methods

For this purpose, we used laughter yoga, which includes respiratory laughing and fun exercises. Using a cross-sectional design, which includes age, family history of AD, exercise status and waist circumference, memory task, fasting glucose and glycosylated hemoglobin (HbA1c), MRI, CT scan were recorded for 68 aging patients (subject) between 70-85 years old. A combination of biomarkers assessed through imaging and cerebrospinal fluid (CSF) yields better diagnostic accuracy. The three CSF biomarkers consistently studied and validated are Aβ42 (A), phosphorylated tau (p-tau; T) and total tau protein (t-tau; N). The patients were randomly divided into two groups, control or experimental (n=10 per group). A 30-minute lecture was followed by 30-minute intense laughing workout with clapping exercise included in the program. After completing exercises, post-evaluation of anxiety and sleep quality of patients in both groups were conducted using questionnaires.

Results

After 30 days laugher yoga and clapping exercise therapy showed that there was a significant normal HbA1c levels ($p<0.05$), increase calorie burn with a significant decrease of blood glucose and blood pressure levels ($p<0.01$), and increased significantly ($p<0.05$) sleep duration in active physically workout AD patients. MRI and CT scan data compare to normal levels with changes in life style and increase movement with memory improvement with therapy in AD patients, identified by professional physiotherapists. There is significant normalization in Aβ42, phosphorylated tau and total tau protein memory loss ($p<0.05$) after one month with changing lifestyle routine among AD patients.

Conclusion

Our study indicated the importance of daily opportunities for laughter yoga with clapping exercise in patients with AD. The results of such studies will be useful for delaying of the aging process and development of new drugs for AD.

Perceived Barriers and Facilitators in Providing Care for Older Adults with Advanced Dementia: A Lived Experiences of Senior-year Nursing Students

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Objective

Dementia has become a major public health concern worldwide due to the rapid increase in the prevalence rate and the number of dementia-related deaths in acute care, long-term care facilities, and community-based environments. However, it is unclear whether nursing education programs are adequately preparing nursing graduates to provide care for older adults with advanced dementia. This study was conducted to explore the perceptions and experiences of senior-year nursing students in providing direct and indirect care for patients with advanced dementia.

Methods

This descriptive qualitative study followed Colizzi's phenomenological research method. The data were collected from three groups of fifteen senior-year nursing students through face-to-face, in-depth focus group interviews. The data obtained were analyzed by thematic text analysis as described by Braun and Clarke. Interviews were decoded until all data were exhausted, and themes were extracted by grouping related codes.

Results

Three major themes were identified in the participants' experiences: the complexity of care, feelings of unpreparedness and helplessness, and eagerness to implement changes. Participants felt that it was much more difficult to care for older adult patients with advanced dementia, due to communication barriers. They consistently revealed practical, therapeutic, and behavioral challenges associated with providing direct and indirect care for patients with advanced dementia. They expressed feelings of self-insufficiency. However, participants claimed that, although it was challenging to care for this patient population, they were more eager to learn about better nursing care plans and to implement changes to provide better care.

Conclusion

The findings indicate that senior-year nursing students have internalized aspects of dementia care principles and developed critical thinking skills. However, it also provides further evidence of the complexity of caring for those with advanced dementia. Thus, the findings suggest enhancing the nature and quality of nursing education in advanced dementia care.

PE_118 Dementia Care

Evaluating the Efficacy of Music Therapy in Managing Agitation and Anxiety among Indonesian Dementia Patients

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Objective

Dementia-related behaviors, such as agitation and anxiety, present considerable challenges in dementia care in Indonesia. Existing pharmacological interventions often come with adverse effects, necessitating innovative and culturally specific alternatives. This study investigates the precise impact of music therapy on managing agitation and anxiety in Indonesian dementia patients. The primary objective of this research was to assess the effectiveness of a structured music therapy program in reducing agitation and anxiety levels among individuals with dementia in Indonesia.

Methods

A randomized controlled trial was conducted involving 120 Indonesian dementia patients aged 60 and above, residing in care facilities. Participants were randomly assigned to either a 12-week structured music therapy group or a control group receiving standard care. Agitation and anxiety levels were assessed at baseline and at the end of the intervention period using validated instruments, including the Cohen-Mansfield Agitation Inventory and the Cornell Scale for Depression in Dementia. Statistical analysis included analysis of covariance (ANCOVA) with a significance level set at $p < 0.05$.

Results

The structured music therapy group exhibited a remarkable 52% reduction in agitation levels (95% CI: 48-56%) and a 46% decrease in anxiety levels (95% CI: 42-50%) compared to the control group. Notably, no adverse effects or complications were reported among the participants in the music therapy group.

Conclusion

Our study underscores the effectiveness of culturally tailored music therapy for reducing agitation and anxiety in Indonesian dementia patients, improving their quality of life. Importantly, this intervention is safe and suitable as a non-pharmacological adjunctive therapy in dementia care. Integrating music therapy into standard protocols offers a unique approach to addressing these challenging behaviors in Indonesia.

PE_119 Dementia Care

Implementation of Theory of Planned Behavior as Psychosocial Factors in the Prevention of Young Onset Dementia (YOD): Case Study in Indonesia

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Objective

The increase of dementia worldwide is estimated to reach 153.8 million cases in the next 30 years. LMICs have a high crude estimate, 764.3 per 100,000 populations, especially in Indonesia, which has a big contribution to the fast growth of dementia patients' number. It worsens with the adult worker having a bad lifestyle. This study aims to examine the associations between psychosocial factors (PF) and lifestyle risk behavior to prevent the increase of Young Onset Dementia (YOD) in the middle-aged population in Indonesia.

Methods

This study employs quantitative research by collecting online survey data from 143 adults in Indonesia from several areas. The questionnaire is adapted from the Theory of Planned Behavior (TPB) and Mini-Mental State Examination (MMSE). Then, this study adopts the PLS-SEM to examine data.

Results

This study has results for all the variables measured. First, middle-aged worker attitudes and subjective norms have a positive association with the intention to change their lifestyle with coefficients 0.211 (p-value 0.010) and 0.549 (0.000) respectively. It can be interpreted that environment and community can trigger the changing of lifestyle to prevent YOD. Meanwhile, Perceived Behavior Control does not correlate with the intention of changing the lifestyle with coefficients 0.115 (p-value 0.129). It is related to low self-esteem that cannot motivate them to change the habit. Lastly, middle-aged worker intention has a positive correlation with behavior with a coefficient of 0.619 (0.000). After having the support variable, it is shown that the support from the community and environment then intention can be the main reason for working adults' lifestyle by doing regular exercise and eating healthy food to prevent young onset dementia.

Conclusion

To conclude, our findings support that PF contributes to the changing behavior for the prevention way for YOD, especially with minimum work-life balance, food nutrition, and less sleep time in Indonesia.

Biological Potential and Therapeutic Application of Karanjin on Brain Related Disorders in Medicine through Its Molecular Mechanism

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Objective

Flavonoids are non-nutritive parts of plants, basically categorized in the polyphenolic compounds found to be present in the different plant material in the nature. Due to their medicinal application and biological importance in the medicine such as antioxidant, anticancer, antitubercular, antibacterial, antiallergic, antimicrobial, anti-inflammatory and antidiabetic potential, it has been used for different purpose in the medicine.

Methods

Karanjin is an important plant chemical found to have hypoglycemic, antifungal, insecticides and antifeedent activity in the medicine and also commercially used in the cosmetic and sun-screen preparations. In order to know the medicinal importance of karanjin in the medicine, here numerous scientific data has been collected and analyzed in the medicine. Biological potential of karanjin on brain related disorders has been investigated in the present work through scientific data analysis of various scientific research works.

Results

Scientific data analysis of various research works revealed the medicinal importance of karanjin in the medicine. Scientific data analysis revealed the biological importance of karanjin on brain related disorders as karanjin showed decrease the transfer latency time in dose dependent manner and escape latency time in Morris water maze method. Scientific data analysis revealed significant reduction in amnesia compared to standard and vehicle control.

Conclusion

Scientific data analysis revealed the biological potential of karanjin on brain related disorders.

The Influence Nonpharmacologic Approaches in Managing Dementia-related Behaviour

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Objective

Dementia is a disease that causes a decrease in memory and thinking. This condition impacts the sufferer's lifestyle, social skills and daily activities (Alodokter, 2023). The most common types of dementia are Alzheimer's disease and vascular dementia. Apart from therapy, support from family or relatives is needed to maintain the patient's quality of life. Various approaches are used to manage dementia-related factors, including nonpharmacologic approaches. This study aim to examine the reliability of nonpharmacologic approaches in managing dementia-related behaviour.

Methods

This research uses a systematic review method. We collected articles from 1995-2023 from an electronic database (pubmed.gov, springer, science direct, Gleneagles). The keywords used were dementia-related behaviour, management, and nonpharmacologic approaches. Then, as many as three selected articles were reviewed to answer the purpose of this study.

Results

Carlson et al. (1995) found that nonpharmacologic approaches can help alleviate behavioural problems and improve the overall care of elderly patients with dementia. These results are supported by Karlin et al. (2014) the results support the feasibility and effectiveness of STAR-VA for managing challenging dementia-related behaviours in veterans in real-world nursing home settings. Karel et al. (2016) also report on the efficacy of an interdisciplinary, nonpharmacological intervention for managing challenging behaviours among Veterans with dementia following expanded implementation in the VA healthcare system. In nonpharmacologic approaches, understanding caregiver readiness and factors associated with its change may be essential considerations in nonpharmacologic interventions (caregiver-related factors were related to initial readiness, financial stability, therapeutic engagement, and perceived benefits enhanced probability of change) (Gitlin and Rose, 2013).

Conclusion

The results of this study conclude that nonpharmacologic approaches are perfect for use in the management of dementia-related behaviour. Both in terms of feasibility and effectiveness and understanding caregiver readiness and associated factors.

PE_122 Dementia Care

Investigation of TDP-43 Pathological Aggregation and Mislocalization with the Help of TDP43-BiFC Cell Line

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Objective

The primary pathology of TDP-43 proteinopathies involves the translocation of TDP-43 from the nucleus to the cytoplasm. Common methods, such as tagging TDP-43 with green fluorescent protein (GFP), prove unsuitable for visualizing TDP-43 translocation. To overcome this limitation, we employed the Bimolecular Complementation technique to establish the TDP43-BiFC cell line.

Methods

To visualize TDP-43 aggregation and mislocalization, we developed a TDP43-BiFC cell line and validated it by treating it with various activators at concentrations of 1, 3, and 10μM. Time-dependent visualization of TDP43 mislocalization was assessed with selected activators at 1, 3, 6, 12, 24, 36, 48, and 60-hour time points by Operetta CLS machine and Leica microscope. TDP-43 accumulation and aggregation were confirmed through immune-blot analysis.

Screening for TDP-43 aggregation inhibitors was performed using a Thiol-reactive drug library at concentrations of 1, 3, and 10 μM, along with a TDP-43 pathology activator at 3 μM. Selected compounds underwent dose-dependent treatment.

Results

In order to visualize TDP-43 aggregation and mislocalization in living cells, a stable TDP43-BiFC cell line was established. To validate the cell model, TDP43-BiFC cells were treated with various pathological conditions activators. A different TDP-43 activation phenotype was observed and one of the TDP-43 pathological modification was identified as a main contributing in TDP-43 aggregation and mislocalization. SDS-resistant and non-resistant TDP-43 TDP-43 oligomers were detected by immune-blot analysis, leading us to the conclusion that disulfide bonds may play an essential role in TDP-43 aggregation as well.

Having established a connection between TDP-43 aggregation and the formation of TDP-43 disulfide bonds, we conducted a systematic screening of the Thiol reactive drug library. Effective compounds were selected, and their IC50 values were quantified.

Conclusion

Results suggest a potential connection between TDP-43 aggregates and disulfide bonds. Furthermore, one of the TDP-43 post-translational modification appears to be a key in TDP-43 mislocalization and aggregation.

Managing Dementia with a Non-pharmacological Approach

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Objective

Dementia is a clinical syndrome characterized by mental, personality, affect, and socialization disorders. Dementia can reduce the quality of life and increase the burden of caregiving and medications. Treatment of dementia with drugs (pharmacology) has side effects on patients, while non-pharmacological treatment can increase the happiness and well-being of dementia patients. Therefore, this research focuses on managing dementia through a non-pharmacological approach.

Methods

This research uses a qualitative approach with the library research method, data was collected through journal articles, health websites, and general articles available online.

Results

Non-pharmacological measures are carried out to manage the behavioral and psychological symptoms of dementia patients, this is because the side effects are minimal. Management of dementia using a non-pharmacological approach includes the following things: 1) Regular structured routine. 2)Non-pharmacological interventions 3) Physical exercise, 4) Music therapy, art therapy, and animal-assisted therapy, 5) Environmental modification, 6)Caregiver education and support programs.

Conclusion

non-pharmacological approaches have an important role in managing the behavioral and psychological symptoms of dementia, and provide alternatives for unmet needs such as physical discomfort, unmet basic needs, restricted independence, frustration with communication, and unfamiliar environments or situations

PE_126 Dementia Care

Physical Fitness Variations based on Cognitive Function in the Elderly

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Objective

The relationship between cognitive decline and physical fitness in aging is a prominent research focus. While both domains have been individually studied, their combined dynamics in the elderly are less understood. Our study aimed to identify disparities in physical fitness based on cognitive function, offering insights for integrated interventions in the geriatric population.

Methods

A total of 88 elderly participants (average age 70.61 ± 5.15 years) were enrolled in the study. Cognitive function was assessed using the Mini Mental State Examination (MMSE) and Clinical Dementia Rating (CDR). Physical fitness parameters evaluated included muscular strength (grip strength), muscular endurance (30-sec chair sit-to-stand), flexibility (sit and reach), dynamic balance (timed up and go; figure 8 walking), cardiopulmonary endurance (2-min walk), and coordination (T-wall test).

Results

When comparing physical fitness factors based on cognitive function levels, elderly individuals with cognitive impairment (MMSE score < 27) demonstrated significantly lower levels in sit and reach (p

Conclusion

Elderly individuals with cognitive impairments, as measured by MMSE and CDR, show marked deficits in select physical fitness metrics. These findings highlight the close relationship between cognitive health and physical fitness, suggesting the need for integrated interventions.

PE_127 Dementia Care

Perspectives about Life-Sustaining Treatment and Physician-Assisted Suicide among Dementia Caregivers in Korea

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Objective

Given the aging trend in Korea, the increasing number of patients with dementia has broadened discussions on life-sustaining treatment (LST) and physician-assisted suicide (PAS). This study was conducted to understand caregivers' perceptions of these issues, considering Korea's unique cultural backdrop. The study aims to serve as a foundation for future educational initiatives for medical professionals, medical students, and caregivers as well as for policy amendments.

Methods

This study was conducted from August 23 to September 24, 2023, and employed a dual-method approach to collect data from 1,932 dementia caregivers in Korea. A 34-item survey was used. The data were analyzed using SPSS 22.0, with the application of frequency analysis and the related-sample McNemar change tests.

Results

Of the responding caregivers, 74.4% were female, and 30.5% were aged 40–49 years. 56.0% cared for their parents or in-laws, with the majority of care (52.7%) occurring in their homes. A significant inclination (71.2%) toward LST withdrawal was observed, linked with alleviating patient suffering. Regarding LST decisions for patients with dementia, 45.1%, 75.3%, 61.1%, and 68.9% of the caregivers, respectively, favored discontinuation of artificial nutrition, approved of kidney dialysis, were receptive to do-not-resuscitate orders, and preferred a natural death. The corresponding percentages for patients with terminal-stage disease were 59.0%, 59.5%, 73.7%, and 74.8%. McNemar tests confirmed significant decision-making differences between these two groups of caregivers. Although 64.8% of the caregivers were familiar with PAS, opinions on the issue varied, with 40.2% being undecided.

Conclusion

In Korea, caregivers' ethical decision-making regarding end-of-life care showed marked differences between decisions for patients with dementia and those for patients with terminal-stage disease. Perspectives on PAS varied considerably, emphasizing the urgent need for culturally sensitive guidelines and expanded education. To our knowledge, this is the first study to investigate the perceptions of Korean dementia caregivers regarding LST. Further research is needed on caregivers' decision-making regarding LST for patients with dementia.

PE_128 Dementia Care

Reversible Stupor with Triphasic Waves after Polytherapy with Levetiracetam and Lamotrigine in a Dementia Patient with Seizure: A Case Report

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Objective

Epilepsy is a commonly combined neurological disorder in elderly dementia patients. Often the seizure event is mistaken for the general aging process or signs of dementia. Non-convulsive status epilepticus (NCSE), in particular, is difficult to diagnose due to without prominent motor signs and symptoms. This case involves a dementia patient with NCSE, admitted for an altered mental state, developed stupor after polytherapy of antiepileptic drugs (AEDs), but significantly improved after switching to monotherapy.

Methods

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Results

A 75-year-old female with dementia, previously medicated, was admitted due to altered consciousness. Before admission, she was immobile and dependent on others for daily activities, but alert and able to communicate. On admission, she was in a stupor and unresponsive to stimuli (Glasgow Coma Scale score, 10). Initial tests including diffusion magnetic resonance imaging (MRI) and various blood-chemistry tests were nonspecific. However, the electroencephalography (EEG) showed multifocal sharp waves and generalized sharp and wave complexes. Under the diagnosis of NCSE, intravenous levetiracetam was administered, and then she improved to an alert state with nearly normal background activities with only rare bifrontal sharp waves on EEG. Lamotrigine was added for further improvement, but it worsened her condition to a deep stupor and the EEG showed triphasic waves. We concluded that she had developed toxic encephalopathy due to polytherapy. After switching the treatment to lacosamide monotherapy, she gradually regained consciousness with improved EEG findings. She was eventually discharged with AEDs as part of her ongoing treatment.

Conclusion

Generally, seizures in dementia patients respond well to AEDs. However, the treatment of seizures in this group is challenging due to various factors such as different pharmacokinetics, an increased risk of drug-drug interactions, and combined morbidities. Additionally, AEDs could potentially worsen neuropsychological and cognitive dysfunction in these patients. Consequently, the selection of AEDs for dementia requires a more delicate and careful approach.

PE_129 Dementia Care

Patient and Caregiver Demographic and Clinical Factors Associated with Care Burden in Early Onset Dementia

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Objective

Early-onset dementia is often predicted to have a greater care burden than late-onset dementia. We explored which factors determine care burden in early-onset dementia.

Methods

Two hundred fifty five caregivers whose patients participated in a longitudinal study of early onset dementia and family members (LEAF) were asked to respond to questionnaires associated with caregiver features and care burden as follows: CAS-K (Korean Version of Caregiver Activity Survey), ZBI (Zarit Burden Interview), SF-36v2® (Short-Form Health Survey 36 version 2). Correlation and linear regression analyses were conducted to clarify the factors affecting care burden, using commercial software (SPSS 23.0; SPSS Inc. Chicago, IL, USA).

Results

A total of 255 caregivers were divided as three groups depending on the clinical diagnosis of the patient who they care for (EOAD 181; FTD 53; other EOD 21). Mean age of caregivers was 54.5±25.3 years and the proportion of female was 54.9%. The general burden for caregivers was higher and the time spent by the caregivers was more amongst patients with lower education years, lower score of mini-mental state examination (MMSE, -0.381, $p<0.001$), higher clinical dementia rating (CDR, 0.359, $p<0.001$) or CDR sum of boxes (0.418, $p<0.001$), decreased level of activities of daily living (ADL, basic -0.334, $p<0.001$; instrumental 0.527, $p<0.001$), higher geriatric depression scale (GDS, 0.245, $p<0.001$) and higher body mass index(BMI, 0.149, $p<0.05$). Caregivers with a high Beck depression inventory (BDI, 0.218, $p<0.001$) spent more time caring for patients. The general care burden was greater in younger caregivers (-0.142, $p<0.05$) and for caregivers with lower average monthly income(-0.166, $p<0.001$), decreased physical function (-0.142, $p<0.05$) or mental health (-0.150, $p<0.05$), more physical (-0.313, $p<0.001$) and emotional role limitation (-0.464, $p<0.001$).

Conclusion

This study is expected to have implications in that it also reviews the economic status of caregivers and ongoing personal and social changes according to the care burden. Demographic and clinical factors of patients and caregivers predict care burden in early-onset dementia. This suggests that it is possible and necessary to attempt to reduce care burden through adjustment and support for related factors.

PE_130 Neuropsychological Assessment

Development of a Parkinson's Disease Dementia Prediction Model based on Machine Learning Technique

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Objective

The aim of this study was to provide baseline data for the earliest detection of Parkinson's disease (PD) and to develop a model for the prediction of Parkinson's disease (PD) and Parkinson's disease with dementia (PDD) based on a neuropsychological test using a national survey.

Methods

289 Parkinson's disease patients (110 PDD and 179 MCI) aged 60 years or older were included in the study. The independent association of each neuropsychological test with PD was determined using optimal scale regression.

Results

Regression coefficient, standard error by bootstrap (n=1,000), quantification index, odds ratio and 95% confidence intervals were used to present the results of the analysis. Even after adjustment for all tests (PD motor symptoms and neuropsychological tests), K-MMSE (b=-0.52, SE=0.16) and H&Y staging (b=0.44, SE=0.19) were significantly ($p<0.05$) effective models for differentiating PDD from PD-MCI. According to the results of the study, there were 10 K-MMSE optimal categories and 7 H&Y staging categories.

Conclusion

The results of this study suggest that among various neuropsychological tests, the optimal classification scores of the MMSE-K and H&Y staging could be used as a useful screening test for early differentiation of PDD from PD-MCI.

Digital Biomarker for Classification of Mild Cognitive Impairment in Older Adults

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Objective

Mild Cognitive Impairment (MCI) indicates cognitive decline with preserved daily functioning, increasing dementia risk. Early diagnosis and continuous monitoring are important, but hospital visits and complex examinations can be burdensome. Mobile app-based cognitive tests offer efficient alternatives, considering biomarkers hard for humans to detect. We aimed to develop classifiers differentiating MCI from normal group with digital biomarkers of Alzguard, a mobile cognitive assessment tool.

Methods

We recruited 62 MCI and 91 cognitively normal participants, dividing them into younger group (59 individuals) and older group (94 individuals) to address age-related cognitive variations. Age threshold was determined by the multi-classification model targeting age and cognitive status such as 'younger-mci'. We constructed a series of models, starting from age 68 and increasing by one year, finally selecting age 70 as the appropriate threshold. At 70, we observed a decrease in the importance of age, which had been the most significant feature in the other models, while other features gained greater importance.
Alzguard tasks cover five cognitive domains: Attention, Memory, Language, Executive, and Calculation, measured through digital biomarkers of keystrokes, speech, and eye movement. We developed younger and older models respectively. Feature selection included the Mann-Whitney U test and RFECV. Furthermore, k-fold cross-validation and random search techniques were used to prevent overfitting and optimize hyperparameters.

Results

In cognitive performance, language showed a significant difference between MCI and Normal individuals in older group, but not in younger group. With XGBoost, accuracy of the younger model was 91.7%, with AUC of 94.3%, while the older model achieved accuracy of 89.5% and AUC of 96.6%.

Conclusion

Using digital biomarkers from Alzguard, we obtained high score values for accuracy and AUC. And we discovered the necessity of separating groups with appropriate age threshold because cognitive assessment and digital biomarker values vary with age, even among individuals with the same MCI condition.

PE_132 Neuropsychological Assessment

Eye-Tracker Assessment of the Impact of Donepezil on Visuospatial Abilities in Mild Cognitive Impairment: Preliminary Findings

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Objective

Cholinesterase inhibitors (ChEIs) have been shown to reduce cognitive decline over the long term in patients with Alzheimer's disease (AD). However, there is limited evidence to suggest that ChEIs influence cognitive test results in patients experiencing mild cognitive impairment (MCI) due to AD. Traditional evaluation criteria, including cognitive tests may not be sufficiently responsive to detect subtle therapeutic effects in MCI patients. We propose a randomized controlled trial to assess the effect of donepezil with MCI due to AD.

Methods

Our study enrolled 16 participants with MCI (8 in each arm, donepezil vs. control), who had amyloid positron emission tomography (PET)-positive results. We employed eye-tracking metrics and digital pen data during the execution of the simplified Rey Complex Figure (RCFT). Eye-tracking was recorded during the copying of the simplified RCFT. After standard gaze mapping, we quantified eye-tracking metrics such as the number and duration of fixations in the perception and working areas. The primary outcome measure involves evaluating alterations in the ratio of the number of fixations (working space/perceptual space) using the simplified RCFT, from baseline to the 12-week mark, as evaluated through eye-tracking metrics. Statistical analyses for primary outcome was applied on the donepezil and control groups between the baseline session and follow-up session using paired-Wilcoxon test.

Results

Eye-tracking metrics showed that the ratio (working space/perceptual space) of the visit count (P=0.036), total visit duration (P=0.025), total fixation duration (P=0.036), and first fixation duration (P=0.025) were significantly increased in the follow-up visit compared to the baseline visit in the donepezil group. And the metrics in the control group showed no significant changes.

Conclusion

This research suggests the potential utility of eye-tracking metrics as valuable digital biomarker for detecting subtle alteration.

Facial Emotion Recognition Deficits in Individuals with Mild Behavioral Impairment

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Objective

Mild behavioral impairment (MBI) is a recently recognized concept, characterized by the emergence and persistence of diverse neuropsychiatric and behavioral symptoms in late life. Recent research has indicated that emotional and social functions may be affected during the pathophysiologic course of Alzheimer's disease (AD) before the onset of cognitive impairment, indicating its role as a precursor to dementia. Detecting these transitional changes in older adults could be helpful in identifying individuals at the highest risk of disease progression. We aimed to investigate the cross-sectional relationship between MBI and facial emotion recognition, using data available in Korea, among individuals with preclinical AD. Additionally, we aimed to compare the associations between MBI and deficits in social cognition.

Methods

Using the MBI-checklist (MBI-C) scores obtained from caregivers of individuals with subjective cognitive decline (SCD) and mild cognitive impairment (MCI), we categorized those with BMI based on a threshold of 6.5 for SCD and 8.5 for MCI. We assessed and compared their performance on the Korean version of the Florida Facial Affect Battery (K-FAB) between individuals with MBI and those without.

Results

Among the 74 participants with SCD and MCI, 31 were categorized as having MBI, and were compared with 43 without MBI. Individuals with MBI had lower educational levels (7.5±4.0 years in those with MBI vs. 10.0±5.2 years in those without MBI, p=0.026). Statistically significant deficits were observed in facial identity discrimination (p=0.031) and facial affect discrimination (p=0.041) in K-FAB. Specifically, MBI subjects showed differences in the recognition of happy and sad emotions in the FAB subtest 4 (facial affect selection) (p=0.026 and 0.013, respectively).

Conclusion

Our study revealed that Individuals with MBI experience difficulties in differentiating facial expressions of emotion and facial identity. It suggests the significance of MBI as a potential early marker of disease progression.

PE_134 Neuropsychological Assessment

Diagnostic Performance of a Tablet Computer-based Cognitive Screening Test for Identification of Amnestic Mild Cognitive Impairment

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Objective

We investigated the performance of the computerized cognitive screening test (Inbrain Cognitive Screening Test; Inbrain CST) in the diagnosis of aMCI and compared its performance to that of the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease (CERAD) test (CERAD-K), a comprehensive and pencil-and-paper NP test.

Methods

The participants were recruited as part of a prospective, community-based cohort study for MCI (PREcision medicine platform for mild cognitive impairment on multi-omics, imaging, evidence-based R&;BD; PREMIER). All participants were assessed using the CERAD-K and the Inbrain CST. The Inbrain CST comprised seven subtests that assessed the following five cognitive domains: attention, language, visuospatial, memory, and executive functions. Seventy-six participants underwent brain magnetic resonance imaging and [18F]-flutemetamol positron emission tomography (PET). We evaluated the diagnostic performance of the Inbrain CST for the identification of aMCI by comparing the findings with those of CERAD-K. We also determined the characteristics of aMCI patients as defined by the CERAD-K and Inbrain CST.

Results

All participants were assessed using the CERAD-K and the Inbrain CST. The Inbrain CST comprised seven subtests that assessed the following five cognitive domains: attention, language, visuospatial, memory, and executive functions. Seventy-six participants underwent brain magnetic resonance imaging and [18F]-flutemetamol positron emission tomography (PET). We evaluated the diagnostic performance of the Inbrain CST for the identification of aMCI by comparing the findings with those of CERAD-K. We also determined the characteristics of aMCI patients as defined by the CERAD-K and Inbrain CST.

Conclusion

The Inbrain CST showed sufficient sensitivity, specificity, and positive and negative predictive values for diagnosing objective memory impairment in aMCI. In addition, aMCI patients identified by CERAD-K and the Inbrain CST showed comparable clinical and neuroimaging characteristics. Therefore, the Inbrain CST can be considered an alternative test to supplement the limitations of existing pencil-and-paper NP tests.

Diffusion Tensor Image Assessment in Mild Cognitive Impairment Patients with S-IADL(Seoul-Instrumental Activities of Daily Living)

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Objective

Previous diffusion tensor image (DTI) studies in patients with mild cognitive impairment (MCI) have observed differences between amnestic MCI (aMCI) vs. non -amnestic MCI (naMCI) in brain structures. Recent studies suggested neuropsychological tests are effective in identifying MCI and Alzheimer's disease (AD) more accurately than structural MRI measurement. Here we aimed to investigate correlations between DTI measurements and S-IADL(Seoul-Instrumental Activities of Daily Living) in MCI patients as well as comparing aMCI vs. naMCI.

Methods

We acquired 3D T1-weighted and DTI images from 477 elderly MCI patients (aMCI, n=256; naMCI, n=221), and processed them with FSL and SPM. Brain diffusion MR images were collected at Pusan National University Hospital, with b = 600 s/mm^2 diffusion weighting in 62 directions and one b = 0 image. S-IADL was used to measure each patient's functional activity. Voxel-wise analysis of fractional anisotropy (FA) and mean diffusivity (MD) were conducted using DARTEL in SPM. In voxel-wise analysis, the effects of age, education, MCI subtype, cognitive decline measured with MMSE score were corrected.

Results

Voxel-wise comparison revealed significant difference in FA and MD values between aMCI vs. naMCI. MD was increased in aMCI compared to naMCI in the right parahippocampal gyrus, right uncus, right and left precuneus, right cingulate gyrus, etc. When compared with FA, changes in right lingual gyrus, right precuneus, right parahippocampal gyrus, etc. Functional activity measured with S-IADL was significantly associated with the FA and MD values. FA and MD has significant correlation with S-IADL in various white regions around the corpus callosum.

Conclusion

Impairment in instrumental daily activity was associated with loss of white matter integrity (i.e. decreased FA and increased MD). Combining DTI data with S-IADL scores in individuals, we can identify the microstructural changes in the brain which are not explained by the aging effect or the cognitive decline (measured with MMSE score).

PE_136 Neuropsychological Assessment

The Development of Conversion Scoring System in Neuropsychological Test (Part 1): Cognitive Impairment Screening Test as a Screening Tool for Dementia: The Correlation Study of Subtest Scores with Mini Mental State Examination

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Objective

Cognitive Impairment Screening Test in Korea (CIST-K) is a screening test to detect cognitive decline developed independently and widely used in Korea. However, the validity study with other screening tests has not yet been conducted. The aims of this study were to introduce normative data for CIST-K and assess clinical usefulness by correlation analysis with the Korean version of the Mini Mental State Examination (K-MMSE).

Methods

We enrolled 88 participants from a tertiary university hospital in Korea, including patients with mild cognitive impairment (MCI) and with dementia diagnosed by experienced neurologists. We used CIST-K and K-MMSE to assess the cognitive function of the participants, and the scores of each subtest of the neuropsychological tests were compared.

Results

In multivariate correlation analysis adjusting age, sex, and education level, there was a significant correlation between two tests in frontal, memory, and attention. However, there was not significant correlated between two tests in visuospatial and language functions.

Conclusion

In conclusion, this study demonstrates that some of the subtests in CIST-K can represent the corresponding scores of K-MMSE. However, score of visual and language test of CIST-K score should be careful interpretation. With additional validity study, developing for sensitivity of each subtest is necessary.

PE_137 Neuropsychological Assessment

Association between of Brain Regional Atrophy and Neuropsychological Test Performance in Patients with Definite Alzheimer's Disease

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Objective

The structural changes in the brain are different in normal aging and Alzheimer's dementia. The results of cognitive function tests reflect structural changes in the brain area in AD. We aimed to figure out specific relationships between regional brain volumes and neuropsychological subtest scores in this study.

Methods

Definite AD (confirmed by PET) of 93 patient were retrospectively enrolled. Automated program (QBraVo) was used to measure regional gray matter (GM) volumes of participants. Each score of subset test of SNSB was analyzed for statistical analysis to see regional brain volume's correlations with cognitive functions. Each result of subset test of SNSB was compared with the degree of atrophy of the brain volume.

Results

The COWAT, TMT–e, and K-BNT were strongly correlated with atrophy of GM volume of mainly temporal lobe. Memory functions (SVLT, RCFT recall and recognition test) were correlated a lot to both temporal and frontal regions. Various test reflecting frontal and executive functions did not show significant correlations with frontal regions itself. Specifically, BNT test scores didn't have any correlations with frontal atrophy. Tests reflecting visuospatial capability (RCFT) were also related to interior frontals and temporal atrophies.

Conclusion

In patients with AD, the results of most cognitive function tests were related to the degree of atrophy of the temporal and frontal corteces of the brain. Further research is needed for each neurodegenerative disease to determine how much the cognitive function test results are related to brain atrophy.

The Development of Conversion Scoring System in Neuropsychological Test (Part 2): Correlation Study between Subtest Scores of Seoul Neuropsychological Screening Battery and Consortium to Establish a Registry for Alzheimer's Disease in Korea

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Objective

In Korea, various cognitive function tests are used to diagnose dementia, and the heterogeneous results from these tests conducted on one patient are a major barrier to estimating changes in the patient's cognitive function or conducting any clinical research. This study was designed to gain preliminery results for score conversion between heterogeneous neuropsychological tests.

Methods

We enrolled 88 participants from a tertiary university hospital in Korea, including patients with cognitive unimpaired (CU), with mild cognitive impairment (MCI) and with dementia diagnosed by experienced neurologists. We used the Seoul Neuropsychological Screening Battery (SNSB), and the Consortium to Establish a Registry for Alzheimer's Disease assesment packet in Korea (CERAD -K) to assess the cognitive function of the participants, and the scores of each subtest of neuropsychological tests were compared.

Results

Multivariate analysis revealed a significant correlation between subtests from SNSB and CERAD after adjusting for age, educational level, and sex. Among the various subset tests, Rey–Osterrieth complex figure test (RCFT) and Korean Trail Making Test for the elderly (K-TMT-e) scores in SNSB showed a very high correlation with the test results of language memory, visual memory, and frontal lobe function in CERAD-K. Furthermore, a significant correlation was observed between the language and visual memory tests.

Conclusion

Through this study, it was determined that two cognitive function tests could be used to detect cognitive function for one person and there was significant correlation in result of two tests. RCFT and K-TMT-e tests would be simple tool for estimating cognitive function among patients. Conversion score modeling between SNSB and CERAD-K would be possible through data accumulation in the future.

Sex Differences in Items of Instrumental Activities of Daily Living in Mild Cognitive Impairment and Alzheimer's Disease Dementia

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Objective

Instrumental Activities of Daily Living (IADL) is functional ability based on cognitive abilities. Significant decline in IADL is a key criterion in diagnosing dementia. Mild decline is also seen in the mild cognitive impairment (MCI). In this study, we aimed to find out how MCI and Alzheimer's disease (AD) dementia differ by sex in Korean Instrumental Activities of Daily Living (K-IADL) items.

Methods

K-IADL was used to evaluate IADL. The effects of individual K-IADL items were analyzed by sex using the logistic regression method for the cognitively normal, MCI, and AD dementia groups.

Results

The impact of individual K-IADL items on dementia varied by item, and the highest and lowest frequency items were distinguished. In particular, the K-IADL items that showed functional decline in MCI and AD dementia differed by sex. The magnitude of the impact was also confirmed through the odds ratio for each item.

Conclusion

In previous studies, IADL has been analyzed using total scores. In this study, we found sex differences in the impact of individual K-IADL items in MCI and AD dementia. This suggests that a sex-specific approach to IADL assessment is important not only in AD dementia but also in the MCI.

PE_140 Neuropsychological Assessment

Two Different Patterns of Cognitive Change in SCD Patients: Neuropsychological Perspectives

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Objective

Subjective cognitive decline (SCD) is a condition in which people report a decline in their cognitive abilities, even though objective testing does not show any impairment. This study aims to explore how memory enhancement at 24 months affects the overall trajectory of cognitive decline.

Methods

In this prospective study of SCD, a total of 120 subjects were enrolled as part of a multicenter cohort study for identifying predictors for clinical progression (CoSCo study). Neuropsychological tests were conducted annually. At the 24-month follow-up, we categorized SCD patients based on their memory function, as measured by the Seoul verbal learning test delayed recall z-score. Participants were categorized into two groups based on their memory improvement on the SVLT at 24 months: improved vs. not improved.

Results

Out of 120 patients registered, 107 finished the 24-month assessment. Of these, 80 patients (74.8%) with SCD showed enhanced memory function. At baseline, there was no difference in age, sex, and education level between the two groups, and SCD patients with improved memory function performed better in the trail-making test part B. The memory enhancement group exhibited a steady annual increase in memory function on average, whereas the group with no memory improvement showed an annual decrease in memory function. SCD patients with verbal memory improvement showed significant improvement in other cognitive domains, including the Stroop test, MMSE attention and calculation subtest, and MMSE total score, compared to those without memory improvement.

Conclusion

Our prospective study indicates that SCD patients experiencing memory improvement over a 24-month period had superior executive cognitive function. The pattern of memory improvement is accompanied by a distinct, yet notably positive trend in executive function and general cognition. These findings may inform us about the more closely related cognitive domains and guide plans for cognitive training strategies for patients with SCD in the future.

Remote Neurocognitive Assessment in Clinical Practice: A Pilot Study Using a Mobile Application

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Objective

Neurocognitive test which used as a screening test and a standard for drug insurance is really important for cognitively impaired patients. However, lack of mobility, difficulty to access neurologist in rural area and infectious disease like COVID-19 become obstacles in regular cognitive test follow up especially in elderly. Considering these situations, remote administration of cognitive test can be a useful solution. This study aims to determine the reliability of "untact" mobile application based neurocognitive testing.

Methods

We have developed "DSCogTest", an application which allows to take an Mini-Mental State Examination (MMSE) and Global Deterioration Scale (GDS) virtually. For items which can't be assessed by just orally (e.g. Language : three-stage command, read a written command, Copying : interlocking pentagons), the application provides specialized features which enables rater to check patient's response simultaneously. MMSE and GDS were administered via in-person and were collected on virtual version from consented participants within a minimal 7-day interval. The test-retest reliability was assessed by calculating the intraclass correlation coefficient (ICC).

Results

A total of 28 participants completed both tests. Of the 28 subjects, 10 were MCI, 10 were mild dementia and 8 were moderate dementia patients. The average MMSE total score was 19.1 (SD=6.2) and the average virtually tested MMSE total score was 21.1 (SD=6.5). The intraclass correlation coefficient of total MMSE score was 0.892 and statistically significant ($p<0.001$). The place orientation, attention and language subscore showed moderate correlation. The GDS ICC was 0.920 ($p<0.001$).

Conclusion

Our study found that cognitive test via mobile application is reliable and has the possibility of being used as an alternative of face-to-face test. Still the elderly are not familiar with electronic devices is a problem that needs to be considered.

This study was supported by Korea Institute for Advancement of Technology(KIAT) grant funded by the Korea Government(MOTIE) (P0018061)

PE_142 Neuropsychological Assessment

In-Air-Time during Drawing Tests as a Potential Predictor of Amyloid Positivity in Mild Cognitive Impairment Patients

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Objective

Previous studies showed that digital assessments using digital pen demonstrate a functional equivalence with traditional paper-and-pencil tests and, moreover, are slightly more sensitive in detecting Mild Cognitive Impairment (MCI). The aim of this study is to compare in-air time between amyloid-negative and amyloid-positive MCI patients performing Clock Drawing Test (CDT) and simplified Rey–Osterrieth Complex Figure Test (RCFT).

Methods

A total of 40 MCI patients were recruited; 2 individuals withdrew from the study during its course. Among total 38 participants, 21 were Amyloid-positive MCI and 17 were Amyloid-negative MCI. All Participants performed the CDT and simplified RCFT using digital pen on a tablet in portrait orientation. The digital pen-touch point responses were recorded by the X-Y digital tablet as Cartesian coordinates in pixel units based on placement on the screen, movement, and removal from the screen over time. In the digital pen recording data, points with zero pressure indicate instances when the pen is not touching the surface. We collected these intervals for all participants. Among them, we divided the first in-air-time from the rest, labeling it as "initial-in-air-time," while the others were referred to as "in-air-time." The first time gap represents the time spent conceptualizing before actually beginning the drawing, making it distinct from the remaining time gaps.

Results

Initial-in-air time did not show a significant difference between amyloid-negative and amyloid-positive MCI patients in both CDT and simplified RCFT. In contrast, in-air-time was significantly longer in amyloid-positive MCI patients than amyloid-negative MCI patient in the CDT ($p=0.005$) and in the simplified RCFT ($p=0.015$).

Conclusion

Our results suggested that the in-air-time during the performance of CDT and simplified RCFT may have the potential to predict amyloid positivity in MCI patients.

The Impact of Amyloid-beta on Cognitive Function and Neuroimaging Structure in Lewy Body Diseases

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Objective

Dementia with Lewy bodies (DLB) and Parkinson's disease dementia (PDD) are significant neurocognitive disorders characterized by Lewy bodies, α-synuclein, β-amyloid, and tau pathologies. This study aims to investigate the influence of amyloid beta plaques on cognitive function, clinical symptoms, and neuroimaging differences in Lewy body diseases (LBDs).

Methods

We conducted a retrospective analysis of 26 patients with LBDs (17 with DLB and 9 with PDD). They underwent 18F-florbetaben or flutemetamol positron emission tomography. Based on global standardized uptake value ratios (SUVRs), patients were divided into amyloid-positive (LBDs-Aß+) and amyloid-negative (LBDs-Aß-) groups. We statistically analyzed clinical symptoms, cognitive function, and medial temporal lobe atrophy using independent samples t-test and chi-square test.

Results

In this study of Lewy body diseases (LBDs), subjects were divided into amyloid-positive (LBDs-Aß+) and amyloid-negative (LBDs-Aß-) groups. Demographically, both groups were similar, with no significant differences in age or educational background. While the LBDs-Aß+ group had slightly lower cognitive scores and higher depression scores, these differences were not statistically significant. Clinical symptoms showed no significant variations between the groups, except for impaired visuospatial function in the presence of amyloid beta plaques. Notably, the LBDs-Aß+ group exhibited significant medial temporal lobe atrophy (p=0.047). These findings highlight the potential impact of amyloid plaques on visuospatial function (p=0.038) and structural brain changes in LBDs.

Conclusion

Among patients with LBDs, those with positive amyloid plaques demonstrated severe impairment in visuospatial function and noticeable medial temporal lobe atrophy. These factors could impact cognitive function and patient prognosis, aligning with prior research. While limited by the small size and retrospective design of the patient cohort, these findings emphasize the necessity for larger prospective studies. Such studies can further elucidate the relationship between amyloid plaque presence, cognitive function, and structural brain changes in LBDs.

PE_144 Neuropsychological Assessment

The Cognitive Complexity of IQ Tests Very Strongly Drives the Predictions of Phenotypic Cognitive Scores by Polygenic Cognitive Scores

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Objective

Intelligence is highly heritable and crucial in biomedical research. Recent genome-wide association studies (GWASs) have identified SNPs that account for a modest portion of the heritability of intelligence. There are many studies where cognitive polygenic scores (PGSs) are used to predict scores on intelligence tests; the resulting rs are all over the place. Various unconvincing explanations are offered for this high variability in resulting rs.

The most important difference between intelligence tests is their difference in cognitive complexity. We hypothesize that the predictions of phenotypic cognitive scores by polygenic cognitive scores are a function of the cognitive complexity of the phenotypic cognitive scores.

Methods

We carried out a re-analysis of two large, published studies reporting 1) cognitive polygenic scores and 2) the correlation between cognitive polygenic scores and all the cognitive test scores. We computed the cognitive complexity of the cognitive tests. We then computed the correlation between 1) the cognitive complexity of the cognitive tests and 2) the correlation between cognitive polygenic scores and all the cognitive test scores. A strong positive correlation means that the predictions of phenotypic cognitive scores by polygenic cognitive scores are strongly driven by the cognitive complexity of the phenotypic measures.

Results

The two studies were analyzed and both showed very large correlations, strongly confirming the hypothesis.

Conclusion

Cognitive polygenic scores predict most strongly for difficult IQ tests and least strongly for easy IQ tests. So, we conclude that the predictions of phenotypic cognitive scores by polygenic cognitive scores are strongly driven by the cognitive complexity of the phenotypic measures. A meta-analysis of all the published studies should be carried out.

The Clinical Utility of Cognitive Impairment Screening Test (CIST) in Memory Disorder Clinic

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Objective

The Cognitive Impairment Screening Test (CIST) is developed as a screening tool to detect cognitive impairment in the Community Dementia Reassurance Center, designed to reflect the cultural context of Korea. We aim to assess a utility of the CIST in a memory disorder clinic of hospital, comparing the Korean-Mini Mental State Examination, 2nd Edition (K-MMSE~2) and Seoul Neuropsychological Screening Battery, 2nd Edition (SNSB-II).

Methods

We enrolled 252 participants from a memory disorder clinic of hospital [47 with normal control (NC), 116 with amnestic mild cognitive impairment (aMCI), and 89 with dementia]. Participants underwent CIST, K-MMSE~2 and SNSB-II, and amyloid positron emission tomography imaging. We compared the CIST scores with those from the K-MMST~2 and SNSB-II to obtain validity. Furthermore, to investigate clinical usefulness of the CIST, we compared the scores of the CIST among the three groups and compared the diagnostic power of the CIST to that of the K-MMSE~2 using receiver operating characteristic curve analyses after controlling age, gender, years of education and APOE genotype.

Results

The aMCI showed significantly poor performance in the CIST total and domain scores than NC. There were significant correlations between domain scores of the CIST and K-MMSE~2, as well as corresponding subscores of SNSB-II. The CIST total score can distinguish cognitive impairment from NC, even in the early stages of the disease, such as aMCI [Area Under the Curve (AUC) = 0.879]. The accuracy of the CIST total score in discriminating amyloid positive group from negative one was found to be adequate in not-demented group (AUC = 0.733).

Conclusion

These results indicate that the CIST can detect cognitive impairment and discriminate amyloid pathology adequately in early stage of disease. Therefore, the CIST provides valuable information like a conventional neuropsychological test in the clinical as well as community setting.

PE_146 Neuropsychological Assessment

Clinically Significant Decline in Preclinical and Prodromal Alzheimer's Disease

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Objective

The objective in our study is to determine the minimum clinically important difference (MCID) of neuropsychological assessments which are commonly used in Korea.

Methods

To calculate MCID, we collected data from patients who underwent amyloid PET scans and had two or more neuropsychological assessments. We recruited 215 cognitive unimpaired (CU) β-amyloid (Aβ)− and 80 CU Aβ + patients (pooled mean follow-up time 32 ± 16.52 months). We also recruited 340 mild cognitive impairment (MCI) Aβ − and 340 MCI Aβ + patients (pooled mean follow-up time 25 ± 14.30 months). We used the following tests in the analysis: Korean-Mini Mental State Examination, 2nd Edition (K-MMSE-2); Korean-Boston Naming Test (K-BNT); Rey complex figure copying test (RCFT copy), Seoul Verbal Learning Test delayed recall (SVLT DR); Stroop Test: Color Reading (ST:CR); Controlled Oral Word Association Test (COWAT) animal and phonemic total; and Korean Trail Making Test Part B (K-TMT-B). We calculated and triangulated MCID for each group using both anchor and distribution-based methods. In the anchor method, we defined MCID based on changes in the Clinical Dementia Rating Sum of Boxes score (0.5 for CU and 1 for MCI).

Results

We calculated MCID as follows. It presented in the order of CU Aβ−, CU Aβ+ / MCI Aβ−, MCI Aβ+: K-MMSE~2 1.35, 1.71 / 1.79, 1.86; K-BNT 4.05, 4.01 / 5.21, 4.27; RCFT copy 1.95, 1.57 / 3.10, 3.30; SVLT DR 1.58, 1.42 / 1.83, 1.53; ST CR 13.47, 15.40 / 13.63, 12.50; COWAT animal 3.02, 2.93 / 2.46, 2.41; COWAT phonemic total 6.99, 8.04 / 5.94, 6.00; and K-TMT-B 27.26, 40.80 / 53.35, 51.36.

Conclusion

Our results may provide a criterion to detect clinically meaningful cognitive function changes in clinical practice or clinical trials. However, because we conducted this study in a single center, for generalization we need a multicenter study in the future.

Cognitive Decline During COVID-19: The Effect of Education

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Objective

During the COVID-19 lockdown the older population faced an elevated risk of cognitive decline because of social isolation and depression. In this study we aim to investigate whether cognitive decline progressed more rapidly during the COVID-19 lockdown than before COVID-19. In addition, we examine the protective effect of education on cognitive decline, known as a proxy of cognitive reserve.

Methods

We recruited patients with amnestic mild cognitive impairments (aMCI) who twice underwent neuropsychological tests and divided them into two groups: (a) lockdown patients (LPs, N = 158) from July 2019 to May 2023; and (b) historical controls (HCs, N = 106) from August 2015 to June 2019. We conducted the Seoul Neuropsychological Screening Battery 2nd edition and used the linear mixed effects model to (a) analyze the difference rate of cognitive decline between the two groups and (b) determine whether there was a difference in cognitive decline according to education level.

Results

The level of education was higher in the LPs than in the HCs, and there was no steeper decline in neuropsychological tests in the LPs than in the HCs. To investigate the effect of education on cognitive decline, we selected a lower educated group (≤ 6 years) and a higher educated group (≥ 12 years) from the LPs and HCs. The HCs did not differ in their cognitive decline according to education level. However, in the LPs, the higher education group showed less-steep declines in COWAT and TMT-B than the lower education group.

Conclusion

Our results suggest that the education level of LPs was higher than that of HCs, and their higher education might mitigate the decline of executive functions in LPs. Therefore, these findings suggest that education as a proxy of cognitive reserve would be a protective factor against cognitive decline in aMCI patients during the COVID-19 lockdown.

PE_148 Neuropsychological Assessment

Personality Associations with Cortical Thickness and Resting State Functional Connectivity in Cognitively Normal eElderly

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Objective

Personality is one of the key individual differences that represents person's tendency to think, feel, and, behave and that affects lifestyles. It has been reported that personality is related to brain changes, and cognitive impairment or dementia in older adults. However, studies that include patients with cognitive dysfunction may involve inaccurate self-assessment of personality, and when conducted by caregivers, the rating may include patients' personality changes or abnormal behaviors. This study aimed to learn how personality traits are related to brain structure and function in cognitively normal elderly.

Methods

107 participants (38 men and 69 women, mean age of 66 years) completed the revised NEO Personality Inventory consisting of 240 items. Five personality traits (neuroticism, extraversion, openness to experience, agreeableness, and conscientiousness) were measured from the questionnaire.

Results

After controlling for age, sex, education level, intracranial volume, and other personality traits, results showed that extraversion was positively associated with cortical thickness of the left and right temporal lobes, and the right parietal lobe. Additionally, extraversion tended to be positively correlated with mean cortical thickness of the whole brain (mean CT), and openness had a tendency to be positively correlated with thickness of the right insula. Regarding the resting state functional connectivity, extraversion was positively associated with the cingulo-opercular network (CON), and openness was positively associated with the ventral attention network, while conscientiousness had a negative relationship with the default mode network (DMN). The partial correlations were significantly positive between mean CT and connectivities of the dorsal attention network, frontoparietal network, CON, and DMN.

Conclusion

Extraversion and openness can be considered as protective traits against brain degeneration. Regarding decreased connectivity of DMN in high conscientiousness, discussion is needed in terms of compensation and impairment. The relationship between baseline personality and future cognitive impairment or dementia should be investigated through the longitudinal study.

Chat-bot Based Cognitive Assessment to Screen Cognitive Impairment in older Adults

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Objective

The rise of mobile applications, facilitated by the widespread use of smartphones and integration of advanced technologies, has opened new avenues for cognitive assessment among older individuals. In this context, the utilization of chat-bot-based cognitive screening has gained significant attention due to its user-friendliness and accessibility. This research is focused on exploring the capabilities of a novel mobile application named Chorong, which employs a chat-bot interface for identifying cognitive impairment in older adults.

Methods

A total of 213 normal cognition and 55 with cognitive impairment individuals were recruited. All participants underwent the Korean version of the Mini-Mental Status Examination (K-MMSE) and the Geriatric Depression Scale, in addition to utilizing the Chorong application on the same day. Cognitive impairment was determined based on participant scores falling below -1 standard deviation compared to age, education, and gender- matched norms in the K-MMSE. During the Chorong interaction, participants were tasked with memorizing five items of information and the spatial location of digits both forwards and backwards within a 10-minute session.

Results

Out of the 195 features provided by Chorong, 54 features were utilized to develop a deterministic model for cognitive impairment. A step-wise logistic regression model was employed to classify cognitive impairment in older adults. The key features determining cognitive impairment included age ($p < 0.0001$), total scores of memory recall ($p < 0.01$), total scores of spatial digit span, and reaction time. The ROC curve demonstrated that the model's accuracy was 0.8696, with a sensitivity of 1.00 and and specificity of 0.455.

Conclusion

Our study suggests that the use of this chat-bot-based mobile cognitive assessment, with an accuracy of 0.87, is a useful tool for remotely screening cognitive impairment in older adults. While the sensitivity of the deterministic model is notably high, the enhancement of specificity would require a more extensive dataset.

PE_150 Neuropsychological Assessment

Cognitive Subgroups of Older Adults Living in Rural Korea and Their Characteristics Observed in Structural and Functional Brain Imaging: Results from the Korean Genome and Epidemiology Study (KoGES)-Cardiovascular Disease Association Study (CAVAS)

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Objective

This study aimed to identify distinct cognitive subgroups of older adults living in rural Korea and to investigate the structural and functional brain imaging characteristics of the subgroups.

Methods

A total of 2,245 KoGES-CAVAS participants living in rural areas participated in the study. All participants were administered the Seoul Neuropsychological Screening Battery-Core (SNSB-C) and MRI/fMRI.

Results

The latent profile analysis resulted in four subgroups based on the memory and frontal/executive subtests of the SNSB-C. Group 1 scored higher on both the memory and frontal/executive tests than the other three groups. Group 2 had lower memory scores than Groups 1 and 3, but higher frontal/executive scores than Group 3. Group 3 had lower frontal/executive scores than Groups 1 and 2, but higher memory scores than Group 2. Group 4 scored the lowest of the subgroups on both the memory and frontal/executive tests.

For total brain volume and cortical gray matter volume, Group 4 was significantly smaller than Group 1, Groups 2 and 3 did not differ from Group 1, but Group 2 was significantly larger than Groups 3 and 4. For hippocampal volumes, Groups 1, 2, and 4 had significantly smaller volumes in both the left and right hippocampus, in that order, but Group 3 did not differ from Groups 1 and 2 and had a larger volume than Group 4. For frontal lobe volumes, no differences were found between Group 1 and the other three groups in both gray and white matter, but Group 2 had larger gray and white matter volumes than Group 4.

Conclusion

This study found that older adults living in rural areas were divided into four cognitive subgroups. While the subgroups' overall cognitive function was in the normal range, several brain imaging indices suggested that some subgroups were already showing structural changes in the brain.

Effects of 40 Hz high-definition Transcranial Alternating Current Stimulation (tACS) on Subjective Sleep Quality and Cognition in Neurocognitive Disorder due to Alzheimer's Disease

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Objective

To investigate the effects of gamma-band (40 Hz) high-definition transcranial alternating current stimulation (HD-tACS) on subjective sleep quality and domain-specific cognitive function in patients with mild neurocognitive disorder due to Alzheimer's disease (NCD-AD).

Methods

This study was a double blind, sham-controlled randomized clinical trial. Fifty mild NCD-AD patients were randomly assigned to receive a 4-week course treatment of either HD-tACS, or HD-transcranial direct current stimulation (HD-tDCS), or sham HD-tDCS. Global cognition was assessed by Montreal Cognitive Assessment (MoCA). Subjective sleep quality was assessed by Pittsburgh Sleep Quality Index (PSQI). PSQI total score>5 was defined as sleep disturbances.

Results

The mean score of PSQI was 11.7 in mild NCD-AD patients. Repeated sessions of 40 Hz HD-tACS and HD-tDCS treatments significantly enhanced the subjective sleep quality and cognition. Compared with tDCS, the individuals who received 40 Hz HD-tACS had more improvement on sleep quality (score changes of PSQI: 6.01 vs. 3.72, P<0.001) and cognitive function (MoCA: 2.5 vs 1.56) during a 2-month follow-up period.

Conclusion

Mild NCD-AD patients with sleep disturbances who received 40 Hz HD-tACS had pronounced enhancement in subjcetive sleep quality and global cognition. To identify novel modality of brain stimulation is important toward an effective strategy for comorbidities in preclinical AD.

PE_152 Pharmacological & Non-pharmacological Treatment

Microcurrent as a Novel Therapeutic Approach for Alzheimer's Disease Model

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Objective

This study directly investigated how microcurrent with treatment time affected AD and its impacts by examining the cognitive function and exploring the inflammatory response mechanism.

Methods

Mice were randomly split into eight groups (n = 5 mice/group, Figure 1A): Control (WT-CTL): Normal mice, saline-treated, Normal mice with 3-hour daily microcurrent (WT-3h), Normal mice with 6-hour daily microcurrent (WT-6h), Normal mice with 12-hour daily microcurrent (WT-12h), AD-induced mice (AD-CTL): Mice with Aβ1–42 i.c.v injection, AD mice with 3-hour daily microcurrent (AD-3h), AD mice with 6-hour daily microcurrent (AD-6h), AD mice with 12-hour daily microcurrent (AD-12h). Microcurrent was given to AD mice for 1 month (Figure 1A). Aβ1–42 (100μM ICV injection/mouse) induced AD-like changes in adult mice. Enhanced expression of ionized calcium binding adaptor molecule 1 (Iba-1), glial fibrillary acidic proteins (GFAP), and other inflammatory markers were seen in AD mice brains (Figure 1B). Western blot analysis evaluated biochemical shifts (Figure 1B). Memory and cognitive abilities were gauged via novel object recognition (NOR) and radial arm maze (RAM) tests (Figure 2A, 2B).

Results

The results indicated that a drastic reduction was observed in terms of numbers, as well as the size, of Aβ plaques within Aβ-injected Mouse Model exposed to microcurrent (Figure 3). And they showed improvements in cognitive function after microcurrent compared with untreated Aβ mice ($p < 0.01$, Figure 2). Iba-1, GFAP, and other inflammatory markers were reduced with microcurrent treatment.

Conclusion

Microcurrent treatment removed neurotoxic associated Aβ plaque effectively, resulting in improved cognitive function with disease-modifying biological responses in AD mouse model.

Effect of Tablet-based Cognitive Intervention on Cognition in Patients with Mild Cognitive Impairment: A Pilot Study

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Objective

Growing evidence has shown that cognitive interventions can mitigate cognitive decline in patients with mild cognitive impairment (MCI). However, most previous cognitive interventions have been group-based programs. Group-based programs are not widely used in clinical practice because of their intrinsic limitations. Therefore, we developed a tablet-based cognitive intervention program. This preliminary study investigated the feasibility and effects of a 12-week structured tablet-based program on cognitive function in patients with MCI.

Methods

We performed a single-arm study on 24 patients with MCI. The participants underwent a tablet-based cognitive intervention program five times a week over a 12-week period. The primary outcome was changes in cognitive function, measured using the Korean version of the Consortium to Establish a Registry for Alzheimer's Disease Assessment Packet (CERAD-K). Outcomes were evaluated at baseline, within two weeks of the last program (post-intervention), and at the six-month follow-up session.

Results

The completion rate of the tablet-based program was 83.3% in patients with MCI. The program improved cognitive function based on the CERAD-K total score (p=0.026), which was maintained for at least three months (p=0.004). There was also an improvement in the depression scale score (p=0.002), which persisted for three months (p=0.027).

Conclusion

Our 12-week structured tablet-based program is feasible for patients with MCI. Furthermore, although further studies with a double-arm design are required, the program appears to be an effective strategy for preventing cognitive decline in patients with MCI.

PE_154 Pharmacological & Non-pharmacological Treatment

The Effectiveness of VR-based Cognitive Training Program: A Pilot Study

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Objective

Cognitive training offers a potential therapeutic approach for patients with mild cognitive impairment (MCI) and dementia, especially when medication options are limited. On the basis of the concepts of neuroplasticity and cognitive reserve, a variety of cognitive training programs have been studied in this field. Our study adopted a virtual reality (VR)-based cognitive training system to investigate its effectiveness in patients with MCI.

Methods

We enrolled 32 MCI patients, diagnosed according to Peterson's criteria. Participants underwent a 12-week VR-based cognitive training program, attending twice per week for 50 minutes each session. The program was conducted on an individual basis. At baseline, all patients underwent a computer-based neuropsychological assessment (Inbrain CST) and completed questionnaires on depression (short form of the geriatric depression scale), anxiety (geriatric anxiety inventory), quality of life (Geriatric Quality of Life-Dementia, GQOL-D), and severity of dizziness (University of California Los Angeles Dizziness Questionnaire, UCLA-DQ). Caregivers evaluated the patients' instrumental activities of daily living (Korean Instrumental Activities of Daily Living, K-IADL) and neurobehavioral symptoms (neuropsychiatric inventory, NPI). The assessments and questionnaires were then repeated after all program sessions.

Results

At the 12-week follow-up, 28 patients completed the program. Women were 24/28 (87.5%) were women, and a mean age was 73.21 ± 4.20. Compared to the baseline, neuropsychological tests showed significant improvements in both the total composite score (49.04 ± 9.15 vs. 52.96 ± 9.53, $p<0.0001$) and memory-composite score (51.36 ± 35.98 vs. 66.44 ± 31.40, $p=0.0037$) post the 12-week VR-based cognitive training. However, there were no significant differences between baseline and post-training evaluations regarding depression, anxiety, dizziness, neuropsychiatric symptoms, and instrumental activities of daily living.

Conclusion

Our pilot study showed that the 12-week training led to significant improvements in overall and memory-specific composite scores. Adopting a digital cognitive training program could be a feasible treatment option for patients with cognitive impairment.

The Effect of Home-based Cognitive Training Using Workbook and Tablet PC in Presenile Dementia Patients

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Objective

Although the effectiveness of cognitive training has previously been established, adherence or maintenance to these program is difficult to achieve due to the lack of validated and convenient tools and programs. Furthermore, presenile dementia patients are usually physically normal but their welfare programs are overlooked compared to senile patients. The aims of this study are to evaluate the effects of home-based cognitive training and usefulness of workbook and tablet personal computer focusing on presenile dementia patients.

Methods

We enrolled 48 dementia patients who met the predefined inclusion criteria from two dementia outpatient clinics. Finally, 34 presenile dementia patients (age; 63.03±4.58, 16 men and 18 women, educational attainment; 10.03±4.30 years, CDR sum of box; 3.21±1.97, MMSE; 21.74±5.24, ADAS-Cog_total; 20.12±8.13, K-IADL; 0.43±0.36) were randomly assigned to a 12-week scheduled cognitive training program using either an workbook (W group age; 62.53±4.03, 9 men and 10 women, educational attainment: 10.05±3.05, CDR_SOB; 3.68±2.07, MMSE; 21.42±5.46, ADAS-Cog_total 20.95±8.49, K-IADL; 0.50±0.40) or tablet personal computer (T-group age; 63.67±5.26, men 7 and women 8, Education; 10.00±5.63, CDR_SOB; 2.60±1.71, MMSE; 22.13±5.11, ADAS-Cog_tatal; 19.07±7.81, K-IADL; 0.33±0.29). All patients underwent 1 hour/day for 5 days/week of training with support from their caregiver. During the program, levels of difficulties were adjusted according to rater's regular measurement. Before and after the training program, all patients were tested for MMSE, CDR-SB, IADL and ADAS-Cog.

Results

On ADAS-cog tests, patients showed improvement post training (p=0.021). T group showed more improvement in CDR-SB than W group (P=0.01). In subgroup analyses including subdomain, there were no significant differences between pre and post tests. All patients and caregivers were well-tolerated for 12 weeks.

Conclusion

We suggest that cognitive training using workbook and tablet personal computer is a well-tolerated and comparable tool for presenile dementia patients and their caregivers.

Literature Review on the Memory Intervention of Dementia

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Objective

Memory is controlled in the hippocampus of the brain and belongs to cognitive function and is essential throughout life. However, mild cognitive impairment which gradually decreases cognitive function including memory and dementia which causes overall cognitive impairment make daily performance and social life quite difficult. Therefore, this study aims to identify interventions that promote memory in dementia subjects in Korean society facing super aged and use it as basic data for dementia prevention and rehabilitation.

Methods

This study is a literature review that systematically collected and analyzed intervention papers for 'Dementia Memory' and evaluated research trends, intervention programs, and significant results.
The paper selection process is as follows.
(1)Search source: Korean authorized journal KISS, DND
(2)Search word : KISS 'dementia memory'(228papers) and DND 'memory'(63papers)
(3)Selected papers: 1)Experimental intervention 2) systematically review or
meta-analysis on Intervention 3) diagnosis: Dementia, MCI
(4)exclusion: Duplicate, non-experiment, nonconformity, non-memory(dependent V.)
(5)revalidation and selecting: final 12 papers selected.

Results

<1>The interventions and (dependent variables) that showed a significant increase in memory are as follows.
1.Cognition Program (memory)
2.Cognition-Focused Intervention(long-term memory, retrieval, short-term memory)
3.NeuroFeedbackTraining (NFT) (memory registration)
4.Home based robot cognitive (working memory)
5.Good memory program (K-MMSE)
6.Music-based sling exercise program (memory registration, recall)
7.Group art therapy (memory registration)
8.Spaced-retrieval training (recall maxim time)
9.Combined Cognitivie-Motor learning P (MMSE)
10.Occupation based reminiscene therapy (memory)
11.Step-by-step attention training (memory)
12.Dance therapy program (motor memory performance)
<2> The distribution of memory promotion programs (12papers)
: Cognition Program:4, retrieval training:2, attention training:1, NFT:1, Music-exercise:1, Dance:1, art therapy:1, cognitive T.+Art+Music:1.

Conclusion

The memory interventions for dementia were mainly cognitive training and complex programs. Future research suggests memory verification by measuring significant outcome variables, correlations, and hippocampal volume for each intervention.

Gait Improvement Following Cerebrospinal Fluid Tap Test in Normal Pressure Hydrocephalus Patients with and without Striatal Dopaminergic Deficit

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Objective

Idiopathic normal pressure hydrocephalus (iNPH) is characterized by the classic triad of gait disturbance, urinary incontinence and cognitive impairment. Lumbar puncture (LP) with removal of cerebrospinal fluid (CSF) can improve iNPH symptom and is considered a diagnostic procedure for iNPH. Our study aims to investigate the extent of gait improvement following CSF tap test (TT) in iNPH patients with both normal and reduced striatal dopamine transporter (DAT) uptake.

Methods

Thirty iNPH patients were included in this study based on their magnetic resonance imaging and clinical symptoms. All participants underwent 18 F-N-fluoropropyl-2β-carboxymethocy-3β-(4-iodophenyl)-nortropan (FP-CIT) PET. Reduced DAT uptake was confirmed by nuclear medicine specialist on FP-CIT PET. All subjects underwent LP with removal of 30-50mL of CSF. Walking speed (WS) was compared before and after LP with CSF removal.

Results

Regarding to the 18 F-FP-CIT PET scan, 17 and 4 patients showed normal and reduced striatal DAT uptake, respectively. Among the 17 patients without striatal dopaminergic deficit, 11 (65%) patients showed a response (an improvement of 10% or more in WS) after the TT, while among the 4 patients with striatal dopaminergic deficit, three (75%) patients showed a response after the TT.

Conclusion

In our study, we identified that 19% (4 of 21) of iNPH patients showed reduced striatal dopaminergic deficit and that proportions of improvement after CSF TT were similar between iNPH patients with and without striatal dopaminergic deficit.

Effect of Chewing Gum on Cognitive Function

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Objective

With the support of the Lotte Central Research Institute, we investigated the effect of chewing gum on cognitive function in normal and mild cognitive impairment. In addition, we analyzed the cortical thickness change shown in brain magnetic resonance imaging. Through these results, we suggest the necessity of chewing gum exercise to prevent dementia.

Methods

Among patients who visited Inha University Hospital, Ewha University Hospital, Ajou University Hospital, Bobath Memorial Hospital, and Seongnam Senior Center for health, a total of 94 patients selected who classified as subjective cognitive impairment or mild cognitive impairment in clinical diagnosis. Each institution registers the subjects through competitive registration, and allocates 1:1 to the control group and the intervention group through random allocation by the SAS macro program using the Permitted Block Randomization technique. The gum intervention group is required to chew a non-flavored gum once daily. The gums for the elderly are provided for 12 weeks. The primary end point is evaluated as the change in the total scale index score of the Repetitive Battery for the Assessment of Neurological Status (RBANS). Secondary end point is assessed by changes in cortical thickness shown in brain magnetic resonance imaging.

Results

In the gum chewing intervention group, the total scale index score in RBANS increased significantly compared to the control group. In addition, the change in cortical thickness shown in brain magnetic resonance imaging was difficult to have statistical significance due to a small number, but showed a tendency to improve the effect.

Conclusion

This study shows that chewing gum, which can be easily applied in everyday life, was helpful for maintaining cognitive function. Therefore, it is suggested that chewing gum could be another option to prevent dementia.

Optimization and In-silico Studies of Covalently-acting Tau Aggregation Inhibitors for the Treatment of Alzheimer's Disease.

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Objective

The aggregation and propagation of tau oligomers is a central event in the progression of Alzheimer's disease (AD) and other tauopathies, thus making directly-acting tau aggregation inhibitors a promising strategy for the development of disease-modifying treatment for AD. Recently, levosimendan (LSMD) – a covalently-acting inodilator drug was shown to inhibit tau oligomerization with micromolar potency and disrupt pre-formed tau fibrils. Herein we perform hit-to-lead optimization of LSMD, developing more potent derivatives with better physicochemical properties, and investigate their potential mechanism of fibril disruption.

Methods

Systematic alteration of the LSMD warhead, central ring and head subunits was performed and the aggregation inhibition activity was tested on HEK293 Tau-BiFC cells. The most potent compounds were evaluated based on microsomal stability, CYP and hERG inhibition, AMES toxicity and BBB permeability testing. In silico docking and molecular dynamics simulations on 9-layered tau fibril systems with and without inhibitor molecules were performed to discover their potential binding modes and mechanism of fibril disruption. Lastly, in vivo efficacy of the best compounds was tested on the TauP301L-BiFC transgenic mouse model.

Results

Several compounds bearing the LSMD warhead and optimized central ring and head groups showed improved potency and ADMET properties compared to LSMD. Via computational studies a novel binding site at the top tau fibril layers was discovered adjunct to C322 residue. The electrostatic interaction of the LSMD warhead and positively charged tau residues were crucial for inhibitor binding. Three best LSMD derivatives were evaluated in vivo. The final compounds demonstrated excellent bioavailability and attenuated tau oligomerization in TauP301L-BiFC transgenic mice.

Conclusion

Herein novel tau aggregation inhibitors were developed through systematic optimization of LSMD and their mechanism of action is suggested to be covalent binding to tau C322 residue. These results bring us closer to the development of the first disease-modifying treatment for AD and other tauopathies.

A 12-week Randomized, Blinded Clinical Trial to Compare the Cognitive Function Efficacy of Nutritional Drinks with and without Mature Silkworm Powder

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Objective

This study aims to find out whether mature silkworm ingredients and nutritional beverages can help improve cognitive function, especially in patients with cognitive impairment.

Methods

A total of 73 participants (70.4±8.4 years, 50.7% female), with cognitive impairment, were randomly assigned into the placebo group (37 participants, nutritious drinks containing balanced carbohydrates, proteins, and fats) or the intervention group (36 participants, nutritional drinks with mature silkworm powder tablets). The primary outcome is the interval change of K-RBANS (Korean version of Repeatable Battery for the Assessment of Neuropsychological Status) after the 12-week intervention. The secondary outcomes are interval changes in nutrient intake, other neuropsychological markers (K-MMSE; Korean version of Mini-Mental Status Examination, CDR; Clinical Dementia Rating, K-IADL; Korean version of instrumental activities of daily living), and blood biomarkers (neurofilament light chain, amyloid-β, total tau, phosphorylated-tau).

Results

After 12 weeks, interval change in the delayed memory domain score of K-RBANS was improved in the intervention group (placebo, 0.0±8.0 vs intervention, 3.8±11.2, p=0.090). Interval changes in other cognitive domain scores and total score of K-RBANS were not statistically significant. The secondary outcomes also showed no significant difference after the 12-week intervention.

Conclusion

This study shows the potential for nutritional supplements to benefit cognitive health. However, it also raised the need for verification on more subjects and further expanded study.

Personalized Hippocampal Network-targeted Stimulation for Alzheimer's Disease: A Randomized Controlled Trial

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Objective

To investigate the effect of a four-week personalized hippocampal network-targeted rTMS on cognitive and functional performance as well as functional connectivity in AD.

Methods

This randomized, sham-controlled, participant- and evaluator-blinded trial was conducted between May 2020 and April 2022. We recruited 44 patients with early AD with evidence of amyloid deposition on positron emission tomography (PET) or CSF testing. Of them, 41 participants who met the inclusion criteria were randomly assigned to receive either hippocampal-network-targeted or sham stimulation. Twenty sessions of personalized rTMS targeting the left parietal area, which is functionally connected to the hippocampus based on individualized fMRI maps, over four weeks. Sham stimulation was defined as the sound of the pulses without actual magnetic stimulation. A personalized 3D-printed frame was used to fix the rTMS coil to the optimal target site. The primary outcome was the change in the Alzheimer's Disease Assessment Scale-Cognitive Subscale test (ADAS-Cog) score eight weeks after baseline. Secondary outcomes included changes in the Clinical Dementia Rating-Sum of Boxes (CDR-SB) and Seoul-Instrumental Activity Daily Living (S-IADL) scales and resting-state fMRI connectivity between the hippocampus and cortical areas.

Results

Among 30 participants (rTMS, n=18; sham, n=12) who completed the 8-week trial, the mean age was 69.8 years; 18 participants (60 %) were female. As the primary outcome, the change in ADAS-Cog score at 8 weeks was significantly different between the rTMS and sham groups (P=0.002). Changes in the CDR-SOB (P=0.007) and S-IADL (P=0.004) scores were significantly different between the groups favoring rTMS. fMRI connectivity analysis revealed that rTMS increased functional connectivity between the hippocampus and precuneus, and these changes were associated with improvements in ADAS-Cog (P=0.005).

Conclusion

The positive effects of rTMS on cognitive and functional performance, combined with the observed plastic changes in the hippocampal-cortical network, support the use of rTMS as a potential non-pharmacological treatment for AD.

PE_164 Pharmacological & Non-pharmacological Treatment

Evaluation of Efficacy and Safety Using Low Dose Radiation Therapy with Alzheimer's Disease: Interim Results of Multicenter Phase II Clinical Trial

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Objective

This study aims to investigate the efficacy and safety of whole-brain low-dose radiation therapy (LDRT) as a potential treatment for patients with mild Alzheimer's Disease (AD).

Methods

This study reports the interim results of a phase II, multicenter, prospective, single-blinded, randomized controlled trial. Patients with mild AD who meet the inclusion criteria were randomly assigned to three groups: experimental I (24 cGy/6 fractions), experimental II (300 cGy/6 fractions), or the control group (0 cGy/6 fractions). The effectiveness of LDRT was assessed through amyloid PET, brain MRI and neurocognitive function tests at baseline, 6 and 12 months post-LDRT. The primary endpoint is the change of the ADAS-K score. The secondary endpoints include the changes in the amyloid PET scans and the score change of K-MMSE-2, CDR, CGA-NPI and K-iADL.

Results

Out of the 28 patients who underwent randomization , 15 patients (5 patients assigned to each 3 groups) who completed assessment tests 6 months post LDRT were analyzed. In the control group, all patients experienced a decline in all cognitive function test scores, while four patients in experimental groups demonstrated improvement in their ADAS-K scores. The baseline ADAS-K, CDR, K-MMSE scores were not statistically different between the groups, however, at 6 months, ADAS-K, CDR and K-MMSE ($p=0.055$, 0.027, and 0.049, respectively) scores were different among the three groups through the Kruskal wallis test. There was also a statistically significant difference between the control group and the experimental group I in ADAS-K (median 42 vs 30, $p=0.047$) and K-MMSE (median 19 vs 23, $p=0.049$) scores through the Wilcoxon rank-sum test. The treatment was well-tolerated in all treatment groups with no grade 1 adverse events.

Conclusion

Whole-brain LDRT for AD patients was tolerable and demonstrated a reduction in the deterioration of cognitive function and clinical symptoms when compared with control group in this interim analysis.

Exploring the Benefits of Tai Chi: Cognitive and Physical Outcomes in Adults Aged 65 and Older

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Objective

Some previous studies have shown that long-term aerobic exercise could increase hippocampal volume. Tai Chi, a traditional Chinese exercise of moderate intensity, may be an effective intervention method for improving the cognitive ability and physical fitness of the elderly. This study sought to determine the direct effects of Tai Chi on cognitive functioning and physical fitness in elderly aged 65 years and older.

Methods

Twenty-five healthy elderly adults aged 65 years and older (mean age 71.48 [SD ± 5.24] years) underwent a 12-week Tai Chi intervention. Outcomes were measured using the Mini Mental State Examination (MMSE), flexibility (back scratch, sit-and-reach [cm]), muscle strength (grip [kg]), cardiopulmonary endurance (2-min standing walk [rep), dynamic balance (timed up and go (TUG) [s]), figure of 8 walk, and short physical performance battery (SPPB).

Results

Post-intervention, significant improvements were observed in cognitive functioning (MMSE, pre: 23.24 ± 1.54, post: 26.46 ± 1.98, $p < 0.001$), flexibility (back scratch, pre: -2.99 ± 10.04, post: 4.28 ± 7.03, $p < 0.05$; sit-and-reach, pre: 14.8 ± 7.62, post: 21.08 ± 6.84, $p < 0.05$), muscle strength (grip, pre: 6.96 ± 6.65, post: 11.00 ± 7.25, $p < 0.001$), cardiopulmonary endurance (2-min standing walk, pre: 113.92 ± 17.39, post: 158.40 ± 24.36, $p < 0.001$), dynamic balance (TUG, pre: 8.87 ± 1.96, post: 7.06 ± 1.32, $p < 0.001$; figure of 8 walk, pre: 16.52 ± 2.66, post: 14.25 ± 2.36, $p < 0.001$), SPPB (pre: 11.68 ± 0.63, post: 12.00 ± 0.00, $p < 0.01$).

Conclusion

Tai Chi offers notable benefits in cognitive functioning and health-related physical fitness among older adults. These findings support the potential of Tai Chi as an effective intervention for cognitive health maintenance, suggesting its inclusion in public health programs targeting this demographic.

PE_166 Pharmacological & Non-pharmacological Treatment

High-intensity Interval Training (HIIT) as an Intervention for Sleep Quality Enhancement in Middle-aged Women

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Objective

Sleep disorders are increasingly recognized as potential risk factors for Alzheimer's disease. Physical activity, known to have a reciprocal relationship with sleep quality, may offer a preventive strategy. This study investigated the efficacy of High-intensity Interval Training (HIIT) in enhancing sleep quality among middle-aged women.

Methods

A clinical trial was conducted with fifteen middle-aged women aged 45-55 years (mean age 49.68 [SD ± 4.76] years). Inclusion criteria encompassed no hearing, vision, or communication impairments; absence of severe physical diseases, mental illnesses, or neurological conditions affecting cognitive function; and no other sleep-related disorders. The primary outcome was the Pittsburgh Sleep Quality Index (PSQI), with secondary outcomes including subjective sleep quality, sleep latency, sleep disturbances, daytime dysfunction, sleep duration, and habitual sleep efficiency.

Results

Post-intervention, the HIIT group demonstrated significant improvements in global PSQI scores (pre: 6.14 ± 2.57, post: 4 ± 2.22, $p < 0.001$), subjective sleep quality (pre: 0.86 ± 0.36, post: 0.50 ± 0.52, $p < 0.05$), sleep latency (pre: 0.71 ± 0.73, post: 0.43 ± 0.65, $p < 0.05$), sleep disturbances (pre: 1.43 ± 0.65, post: 0.86 ± 0.66, $p < 0.05$), and daytime dysfunction (pre: 1.21 ± 0.80, post: 0.50 ± 0.65, $p < 0.05$) compared to baseline. However, sleep duration (pre: 1.21 ± 0.70, post: 1.14 ± 0.77, $p > 0.05$) and habitual sleep efficiency (pre: 0.71 ± 0.73, post: 0.57 ± 0.76, $p > 0.05$) showed no significant changes.

Conclusion

The results indicate that HIIT can serve as an effective intervention to enhance specific aspects of sleep quality in middle-aged women, which may have implications for reducing the risk of neurodegenerative diseases. Public health strategies focusing on brain health in this age group should consider incorporating HIIT as a potential preventive measure.

The Effects of Agility Training on Sleep Quality in Middle-aged Women

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Objective

Recognizing that sleep disorders can be early signs and risk factors for Alzheimer's disease, it's crucial to find ways to improve sleep quality, especially for those most vulnerable. Since physical activity is known to benefit sleep, this study focused on assessing how agility training affects sleep quality in middle-aged women, a group commonly facing changes in sleep.

Methods

A clinical trial involved fifteen middle-aged women aged 45-55 years (mean age 49.68 [SD ± 4.76] years). Inclusion criteria were absence of hearing, vision, or communication impairments; no serious physical diseases, mental illnesses, or neurological conditions that significantly impair cognitive function; and no other sleep-related disorders. The 12-week agility training's impact was assessed using the Pittsburgh Sleep Quality Index (PSQI) and its sub-components: subjective sleep quality, sleep latency, sleep disturbances, daytime dysfunction, sleep duration, and habitual sleep efficiency.

Results

Agility training led to significant improvements in global PSQI scores (pre: 6.36 ± 2.56, post: 4.93 ± 2.40, $p < 0.001$) and in sleep disturbances (pre: 1.36 ± 1.01, post: 0.64 ± 0.75, $p < 0.05$) compared to baseline. However, there was no significant difference in sleep duration (pre: 0.86 ± 0.66, post: 0.79 ± 0.98, $p > 0.05$), sleep latency (pre: 1.29 ± 0.73, post: 1.07 ± 0.62, $p > 0.05$), daytime dysfunction (pre: 1.36 ± 0.63, post: 1.29 ± 0.73, $p > 0.05$), subjective sleep quality (pre: 0.86 ± 0.54, post: 0.71 ± 0.61, $p > 0.05$) and Habitual sleep efficiency (pre: 0.71 ± 0.91, post: 0.43 ± 0.85, $p > 0.05$).

Conclusion

Agility training significantly improves global PSQI scores and reduces sleep disturbances in middle-aged women. However, its broader effects on other sleep parameters remain undetermined, underscoring the need for further research.

Pilot Study on the Effects of Four-Week Healthy Dance Training on Cognitive Function and Sarcopenia-Related Factors in Elderly Women

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Objective

This study aimed to evaluate the impact of a four-week healthy dance training on cognitive function and sarcopenia-related factors in women aged 60-70.

Methods

Participants engaged in health dance training for four weeks, attending 60-minute sessions five times a week. Cognitive function was assessed using the Stroop Color and Word Test (SCWT) and a spatial memory test. To identify potential factors associated with sarcopenia, several tests were administered, including grip strength, 6-meter walking speed, time up and go, ASMI (appendicular skeletal muscle mass index), and the Berg balance test. The SF-36 index was also employed to evaluate quality of life factors.

Results

Post-intervention assessments revealed a significant improvement in the SCWT reaction time (pre 1.67±0.13 s vs post 1.56±0.47 s, $p<.05$).

Conclusion

A four-week healthy dance training regimen provides significant benefits in cognitive function and can mitigate certain sarcopenia-related factors in elderly women. The pronounced improvements in both cognitive and physical domains highlight the potential efficacy of such interventions in promoting the overall health and well-being of this demographic.

The Effects of High-intensity Interval Training on Cognitive functioning in Middle-aged Women

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Objective

Aging is often accompanied by cognitive decline, which can progress to predementia stages, posing significant health concerns. This study seeks to determine the impact of HIIT on cognitive functioning in this demographic, offering insights into its potential as a preventive strategy against cognitive deterioration.

Methods

Fifteen women aged 45-55 years (mean age 49.68 [SD ± 4.76] years) underwent a 12-week HIIT intervention. Inclusion criteria were no hearing, vision, or communication impairments; mental illnesses, or neurological conditions affecting cognitive function; and no sleep-related disorders. Outcomes were measured using the Mini Mental State Examination (MMSE), assessing orientation, registration, calculation, recall, language, chultetable (please verify this term as it seems unfamiliar), and forward digit-span task.

Results

Post-intervention, significant improvements were observed in MMSE scores (pre: 26.71 ±1.64, post: 28.57 ±1.16, $p < 0.001$), orientation (pre: 8.43 ± 0.65, post: 9.71 ± 0.47, $p < 0.001$), registration (pre: 2.86 ± 0.36, post: 2.93 ± 0.28, $p < 0.05$), recall (pre: 2.57 ± 0.65, post: 2.93 ± 0.27, $p < 0.05$), language (pre: 7.93 ± 0.48, post: 8.21 ± 0.58, $p < 0.001$), same-color chultetable (pre: 253.14 ± 56.08, post: 251.43 ± 53.62, $p < 0.001$), and forward digit-span task (pre: 3.50 ± 0.65, post: 4.36 ± 0.63, $p < 0.001$). However, no significant change was noted in calculation (pre: 4.50 ± 0.94, post: 4.79 ± 0.58, $p > 0.05$).

Conclusion

The results demonstrate that a 12-week HIIT regimen significantly improves specific cognitive parameters, such as orientation, registration, recall, language, and forward digit-span task, in middle-aged women. However, the intervention showed no discernible effect on calculation abilities. The results highlight how HIIT specifically affects certain cognitive areas in middle-aged women. This understanding suggests that HIIT could be selectively effective and may inform public health programs aiming to maintain cognitive health in this group.

The Role of Agility Training in Enhancing Cognitive Domains Among Middle-aged Women

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Objective

As individuals transition into middle age, there is a noticeable stabilization followed by a gradual decline in cognitive functioning. This decline elevates the risk of neurodegenerative diseases like Alzheimer's. While previous observational studies have highlighted the potential benefits of exercise in counteracting cognitive decline, the specific impact of Agility Training (AT) remains underexplored. This study, therefore, sought to determine the direct effects of AT on cognitive performance in middle-aged women.

Methods

Fifteen middle-aged women aged 45-55 years (mean age 50.36 [SD ±3.99] years) underwent a 12-week AT clinical trial. Inclusion criteria encompassed no hearing, vision, or communication impairments; absence of serious physical diseases, mental illnesses, or neurological conditions that significantly impair cognitive function; and no sleep-related disorders. Cognitive outcomes were assessed using the Mini Mental State Examination (MMSE) — with components including orientation, registration, calculation, recall, and language — and additional tests like the same color chultetable and the forward digit-span task (DGS).

Results

AT led to significant improvements in the global MMSE score (pre: 26.57 ±1.45, post: 28.36 ±1.01, $p < 0.001$), orientation (pre: 8.79 ± 0.80, post: 9.93 ± 0.65, $p < 0.001$), registration (pre: 2.79 ± 0.43, post: 3.00 ± 0.00, $p < 0.01$), language (pre: 8.21 ± 0.70, post: 8.86 ± 0.36, $p < 0.01$), same color chultetable (pre: 288.43 ± 72.77, post: 248.71 ± 76.82, $p < 0.01$),forward digit-span task (pre: 3.36 ± 0.50, post: 4.14 ± 0.77, $p < 0.001$). However, no significant differences were observed in calculation (pre: 4.71 ± 0.82, post: 4.86 ± 0.36, $p > 0.05$) and recall (pre: 2.07 ± 0.73, post: 2.21 ± 0.80, $p > 0.05$).

Conclusion

AT effectively enhances cognitive performance in middle-aged women. However, its effects on calculation and recall functions are less pronounced. As such, while AT can be considered a promising intervention for enhancing certain cognitive functions, its comprehensive efficacy in broader cognitive preservation requires further exploration.

Improving Elderly Cognitive Function through a Study of Pharmaceutical Chemistry Aspects involving Centella Asiatica Plants

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Objective

Cognitive impairment is a disorder associated with increasing age resulting in decreased brain function related to the ability of attention, concentration, calculation, decision-making, reasoning, and abstract thinking. This cognitive impairment is the cause of dementia in people with Alzheimer's disease. Centella Asiatica (C. asiatica) is one of the herbal plants that has been widely studied for its neuroprotective effects. The aim of this study is to present all the evidence regarding the benefits of Centella Asiatica on cognitive function in the elderly.

Methods

This research method is a description narrative using data from research results in a more comprehensive and balanced presentation of facts. The literature sources used in this article involve literature from national or international journals. Inclusion criteria are journal articles related to Centella Asiatica, Cognitive Function, and the Elderly.

Results

The main chemical component responsible for its pharmacological activity is the triterpenoid group of asiaticoside, madecassoide, asiatic acid, and madecasic acid, which have antioxidant, anti-inflammatory, and antiapoptotic properties. Clinical trial results of C. asiatica extract have been shown to prevent mitochondrial morphological abnormalities in a rat model of kainic acid-induced seizures, which protects synaptic function and alleviates cognitive deficits. In addition, C.asiatica also inhibits Aβ-induced neuronal apoptosis by restoring and maintaining mitochondrial membrane potential. C.asiatica enhances memory and ameliorates mitochondrial biochemistry and dysfunction in a mouse model of aging. The cognitive effects of C.asiatica extract are associated with changes in synaptic plasticity and excitatory neurotransmission, as well as improved neuronal survival. C.asiatica also provides protection against hippocampal dysfunction, a brain region that plays an important role in learning and memory and is severely affected in Alzheimer's Dementia disease.

Conclusion

Based on evidence from experimental animal studies, C. asiatica can improve cognitive function because it contains triterpenoids and flavonoids that have potential as neuroprotectors, antioxidants, anti-inflammatory, and antiapoptotic.

Telephone-based Cognitive Stimulation Program for People with Mild Dementia

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Objective

Nonpharmacological treatments such as cognitive stimulation therapy or cognitive training programs are important for dementia patients to maintain cognitive function and improve the quality of life. To maintain the function of dementia patients in the situation of social restriction(e.g. COVID-19 pandemic), a new method of cognitive program is needed in a non-face-to-face manner. The objective of this study is to develop a new non-face-to-face cognitive stimulation program using telephone calls for people with mild dementia and to evaluate the effect of the program on cognitive function and emotion.

Methods

A workbook for the program was provided to the subject in advance and a trained counselor made a phone call to operate the cognitive stimulation program. The program operated with contents related to a single topic at each time and consists of reality orientation therapy, reminiscence therapy and other cognitive stimulation therapies using music and pictures. The duration of the program is about 30-50 minutes at each time. In this case-controlled study, a total of 12 programs were applied once a week for 3 months. Korean Dementia Screening Questionnaire-C(KDSQ-C) and Subjective Memory Complaints Questionnaire(SMCQ) and the short form of Geriatric Depression Scale (s-GDS) were evaluated after the 3-month course of the telephone-based cognitive stimulation program.

Results

A total of 54 patients with mild dementia were randomized to the intervention group and 50 patients to the control group. At the follow-up the intervention group had significantly improved related to the control group on the KDSQ-C ($p=0.001$), SMCQ ($p<0.001$) and s-GDS ($p<0.001$).

Conclusion

The telephone-based cognitive stimulation program was found to be effective in improving cognitive function and depressive mood in people with mild dementia. This non-face-to-face cognitive stimulation program could be an alternative treatment for dementia patients with limited social contact due to the pandemic or other various conditions.

PE_173 Pharmacological & Non-pharmacological Treatment

Deciphering the Dual Inhibitory Mechanisms of Sesame Bioactive Compounds against Cholinesterases for the Treatment of Alzheimer's Disease

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Objective

A diminution in cholinergic neurotransmission, acetylcholine (ACh), by the hydrolysis of acetylcholinesterase (AChE) and butyrylcholinesterase (BChE), is the molecular hallmark of Alzheimer's disease (AD). As the cortical neurons are lost in the AD progressions, AChE level was decreases, yet, BChE can take over the metabolism of acetylcholine. Presently, galantamine, an AChE inhibitor, and rivastigmine, a dual inhibitor of AChE and BChE, are approved drugs by the FDA. However, certain adverse effects have been documented. The discovery of nature-derived compounds as AChE or BChE inhibitors is considered less toxic than synthetic pharmaceuticals. Employing molecular docking, the bioactive compounds found in sesame (Sesamum indicum L.) were analyzed in this study as potential AChE or BChE inhibitors.

Methods

Molecular docking of 5 major compounds in sesame seeds, sesamol, sesamin, sesaminol, sesamolin, and sesamolinol to the AChE and BChE protein's active site was performed using AutoDock Tools. The standard drugs as a comparison were galantamine and rivastigmine. The drug-likeness, absorption, distribution, metabolism, excretion, and toxicity (ADMET) characteristics of the potential compound was predicted using pkCSM-free online server.

Results

Among sesame compounds, sesaminol has higher inhibitory activity against AChE and BChE than galantamine and rivastigmine based on the binding energy to the enzyme's active sites. The molecular interaction was by hydrogen bonding and pi-hydrophobic binding. While sesamin and sesamolinol only had higher inhibitory activity towards BChE compared to rivastigmine. The estimated inhibition constant of sesaminol towards BChE was 7.49 micromolar. In addition, sesaminol has drug-likeness properties based on Lipinski's rules and is predicted to have less potential toxicity.

Conclusion

In conclusion, the major bioactive compound in sesame, especially sesaminol had a dual inhibitory activities against both AChE and BChE, while sesamin and sesamolinol were good BChE inhibitor. Considering that sesame is a dietary food, this finding provides additional nutritional facts regarding sesame's health benefits for Alzheimer's disease medication.

PE_174 Pharmacological & Non-pharmacological Treatment

Low-intensity Ultrasound Improves Cognitive Function in Patients with Alzheimer's Disease

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Objective

To investigate that the utilization of low-intensity ultrasound for Alzheimer's continuum with mild cognitive impairment or early-stage dementia will result in positive cognitive effects through ultrasound neuromodulation.

Methods

All participants had positive findings on the 18F-florbetaben amyloid PET image prior to ultrasound treatment. To ensure the safety of ultrasound treatment, Brain MRI was conducted before and after treatment. We used low intensity ultrasound device consisting of 4 individual transducers with fundamental frequency of 250kHz. The sonication was administered three times a week for a total duration of four weeks. Each session consisted of a 30-minute sonication duration.

Results

Quantitative analysis showed that the time of Trail Making Test-Black and White (TMT-BW) after four weeks of ultrasound treatment were less than baseline (TMT-BW A, 115.6±70.1 vs. 87.3±56.2, P=0.017; TMT-BW B, 316.2±160.6 vs. 231.3±64.3, P=0.044). We compared nodal degree values through functional connectivity analysis between the pre and post-treatment. We observed moderately higher degrees in the parietal (P=0.070) and temporal lobes (P=0.089), as well as the whole brain (P=0.085) after the treatment, suggesting an integration of functional brain organization. We found larger changes in the early-onset group, indicating that the treatment may be more efficient for groups more vulnerable to the disease. Comparing FDG PET results between pre and post-treatment, we observed a greater increase in FDG PET uptake in the frontal and parietal regions in the early-onset group compared to the late-onset group. Post-ultrasound treatment Brain MRI did not reveal any evidence of cerebral microbleeds or edema.

Conclusion

Our study confirms the safety of low-intensity ultrasound therapy in patients with early-stage AD. Furthermore, it demonstrates that ultrasound therapy can lead to clinical improvements in the AD continuum.

Enhanced Dynamic Glymphatic Activity Using Low-intensity Ultrasound in Alzheimer's Disease

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Objective

To investigate the efficacy and safety of low-intensity ultrasound (LIUS) using serial intravenous contrast-enhanced T1 mapping for the quantitative evaluation of glymphatic activity change and dynamic contrast-enhanced magnetic resonance imaging (DCE MRI) for the evaluation of blood-brain barrier(BBB) integrity in various brain regions in patient with Alzheimer's dementia (AD).

Methods

In this prospective study, 10 patients with prodromal AD and early AD (mean age, 69 years ± 9.2 [standard deviation]; 8 women) underwent LIUS sessions for 4 weeks in the outpatient department and two cycles of MRI (pre-LIUS and post-LIUS cycles). For each cycle, T1 maps were acquired at baseline and 30 minutes, 43.5 minutes, and 10 hours after intravenous contrast material injection in regular daytime. The time (min-T) to reach the minimum T1 value (T1min), the absolute difference between baseline T1 and T1min (peak delta T1), and the slope between two measurements at 30 minutes and 10 hours (slope[30minutes-10h]) were determined from T1 value-time curves in cerebral gray matter (GM), cerebral white matter (WM), cerebellar GM, cerebellar WM, and putamen.

Results

The slope(30minutes-10h) increased from the pre-LIUS to post-LIUS series in only cerebral GM (mean ratio [post-LIUS/pre-LIUS] = 1.3395 [2.0125/1.5179], ; P = 0.034). The slope (30minutes-10h) of other brain regions (cerebellar GM, cerebral WM, cerebellar WM, putamen) were not significantly different in between sonication. The Ktrans and Vp of DCE MRI in all brain regions (including frontal, temporal cortex, choroid plexus, and hippocampus) showed no significant difference in between LIUS treatments. There was no newly appeared focal abnormal lesion in brain parenchyma including edema, and microbleeds on T2WI and SWI, respectively after LIUS sessions.

Conclusion

In this study, we conjectured that LIUS significantly enhances the glymphatic activity function in the patient with AD.

South Korean Study to Prevent Cognitive Impairment and Protect Brain Health through Multidomain Interventions via Face-to-face and Video Communication Platforms in Mild Cognitive Impairment (SUPERBRAIN-MEET): A Randomized Controlled Trial

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Objective

Multidomain interventions that comprehensively manage modifiable risk factors of dementia should be adjusted to specific geographical and cultural contexts and their efficacy tested. We aimed to investigate the effects of a multidomain intervention on cognition in mild cognitive impairment (MCI).

Methods

In a multicenter, outcome assessor-blind, randomized controlled trial, participants with mild cognitive impairment (MCI) and with one or more modifiable dementia risk factors, aged 60-85 years, were randomly assigned in a 1:1 ratio to the multidomain intervention (MI) group or the control group receiving general health advice. The 24-week intervention comprised vascular risk management, cognitive training, social activity, physical exercise, nutrition guidance, and motivational enhancement using Tablet PC app. Face-to-face intervention was conducted at a facility once every 1-2 weeks, and intervention via Zoom was conducted 2-3 times a week. The primary end point was the change from baseline at 24 weeks in total scale index score of Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).

Results

Between September 2021 and August 2022, 300 participants were randomly assigned to the MI (n=148) and control (n=152) groups. In the MI and control group, the retention rates were 87.8% and 80.9%, respectively. The total adherence to the intervention was 87.5% and the adherence in each intervention domain was greater than 85%. The adjusted least-squares mean change from baseline at 24 weeks was 8.50 in the MI group and 4.18 in the control group (difference, 4.17; 95% confidence interval [CI], 1.92 to 6.42; P<0.001). Compared to the control group, depression, quality of Life, dietary habits evaluated by Nutrition Quotient for the Elderly, physical performance, and motivation evaluated by the Self Determination Index were significantly improved in the MI group.

Conclusion

Multidomain interventions with high adherence to dementia modifiable risk factors could improve cognitive function in MCI.

Enhancement of cognitive restoration by glia-like human mesenchymal stem cells in an animal model of vascular dementia

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Objective

Vascular dementia (VaD), the second most common form of dementia after Alzheimer's disease, results from two primary mechanisms: hemorrhagic vascular disease and ischemic vascular disease. Ischemic dementia, in particular, occurs when the arteries supplying blood to the brain become obstructed, leading to chronic reduced blood flow and subsequent brain tissue damage and neuron loss in the hippocampus, manifesting as cognitive dysfunction. In this study, We aimed to investigate the effect of glia-like cells derived from human mesenchymal stem cells (ghMSCs) in improving cognitive function caused by ischemic vascular disease.

Methods

We induced chronic cerebral hypoperfusion in mice, mimicking the lesions characteristic of VaD, through bilateral common carotid artery stenosis (BCAS) surgery. The Morris Water Maze (MWM) test, which records the time taken to find a submerged platform within 60 seconds, was employed to identify dementia-induced mice. Following this pre-MWM test, hMSCs, ghMSCs (Low: $2x10^4$ cells, Medium: $6x10^4$ cells, High: $2x10^5$ cells), or neurobasal medium were administered via intracerebroventricular injection in the second week. Additionally, the CXCR2 antagonist (SB225002) was injected daily for five days, and a post-MWM test was conducted through the fourth week.

Results

In the MWM test, mice treated with $2x10^5$ cells of ghMSCs exhibited a significant improvement in cognitive function compared to both the control group and the hMSCs group, an effect that was inhibited by SB225002. Molecular analysis revealed that ghMSCs enhance neuronal and synaptic plasticity and induce neovascularization.

Conclusion

These mechanisms suggest that ghMSCs may ameliorate cognitive deficits by regenerating neural cells. Furthermore, we discovered that CXCR2 plays a crucial role in the modulatory actions of ghMSCs.

The Effects of Immunosuppressants on the Characteristics of Wharton's Jelly-Derived Mesenchymal Stem Cells

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Objective

Mesenchymal stem cells (MSCs) hold significant promise as potential therapeutic agents for nervous system disorders due to their regenerative capabilities and their ability to secrete paracrine factors beneficial in diseased microenvironments. However, when transplanted into the central nervous system, MSCs can trigger inflammation and fever, necessitating the use of immunosuppressants. Yet, the impact of these immunosuppressants on the inherent characteristics of MSCs remains poorly understood. This study seeks to explore how immunosuppressants affect the morphology, viability, and stem cell characteristics of MSCs.

Methods

To evaluate the characteristics of the cells, we conducted the following assays: the Cell Counting Kit-8 assay to measure cell viability, Oil Red O staining to assess adipogenic differentiation, Alizarin Red S staining to examine osteogenic differentiation, and Safranin O staining to investigate chondrogenic differentiation. In addition, we conducted flow cytometry to analyze the expression of surface antigens on MSCs.

Results

The administration of immunosuppressants, specifically dexamethasone, tacrolimus, or their combination, did not yield any observable alterations in cell morphology or viability. In addition, our results revealed that MSCs retained their ability to differentiate into osteoblasts, adipocytes, and chondrocytes under all three immunosuppressive conditions. Furthermore, MSCs continued to express positive markers (CD44, CD73, CD105, and CD166) and did not express negative markers (CD34, HLA-DR, CD14, and CD19) confirming the preservation of MSC characteristics.

Conclusion

In summary, the use of immunosuppressants (dexamethasone only, tacrolimus only, or dexamethasone and tacrolimus in combination) did not change the characteristics of MSCs. Our results provide supportive evidence for the use of immunosuppressants in MSC clinical trials.

Updates in Treatment of Parkinson's Disease: The Analysis of Nicotine as an Alternative Therapy for Parkinson's Treatment

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Objective

Parkinson's is one of the second diseases in the neurodegenerative realm whose development is quite significant in middle to old-age humans. Although the leading cause of this disease has not been found, research shows that this disease can occur due to DNA factors and ageing, which reduce the functioning of the human nervous system. Considering that this type of disease is widely experienced, several treatment therapies have emerged that can be tried to improve the quality of life of Parkinson's patients. One way is to use Nicotine, which is often found in cigarettes. So, the study aims to examine how nicotine can be an alternative therapy for Parkinson's treatment.

Methods

The research was conducted by summarizing several related scientific journals. We collected articles from 2010-2022 from an electronic database. We were using the keywords Parkinson's therapy and Indonesia.

Results

In efforts to treat Parkinson's, health experts divide the therapy concept into three groups: Symptomatic, Protective and Restorative. The three are a unified therapeutic concept that seeks to reduce symptoms and repair damaged nerve cells. Based on the presentation (Miller & Salil, 2007), the Nicotine in cigarettes can reduce the incidence of Alzheimer's and Parkinson's disease. Even in Indonesia, research has been carried out by Albert (2011) and related research by Emi (2010). Their findings explain that Nicotine can prevent Parkinson's disease. Nicotine works on brain nerve cells through nicotinic acetylcholine receptors (nAChRs), which produce higher brain dopamine levels. Nicotine also works as a protector of degenerating nerve cells and inhibits neuron cell death in people living with Parkinson's disease.

Conclusion

Nicotine is a substance that is often found in cigarettes. Even though cigarettes are known as products that are dangerous to human health, research has provided an overview of the other benefits of Nicotine.

Therapeutic Potential of Porcine Brain-Derived Peptide Mixture (PBDP) in Alzheimer's Disease: An Exploratory Study on Quantitative Electroencephalography (qEEG) Changes

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Objective

This study investigates the potential therapeutic effects of Porcine Brain-Derived Peptide Mixture (PBDP) on patients with Alzheimer's Disease (AD), a neurodegenerative disorder characterized by cognitive decline and neuronal death. The research focuses on changes in quantitative electroencephalography (qEEG) parameters after PBDP injection therapy, as qEEG has been shown to be sensitive to changes in brain function induced by pharmacological interventions.

Methods

The study was conducted retrospectively on 27 AD patients from the CAU dementia registry who received PBDP and a control group of 20 individuals. Both groups had previously been administered donepezil for over three months. EEGs were performed at two-month intervals to monitor these patients.

Results

The results showed significant improvements in qEEG patterns reflecting brain function after just two weeks of PBDP treatment, indicating the potential efficacy of PBDP as a therapeutic approach for managing AD progression. However, no changes were observed in the oligomerization tendency of amyloid beta in the blood using Multimer Detection System-Oligomeric Amyloid-β (MDS-OAβ), suggesting that while PBDP may improve functional aspects, it might not modify beta-amyloid pathology associated with AD.

Conclusion

In conclusion, this exploratory research suggests that strategies aimed at boosting neurogenesis could potentially serve as effective therapeutic approaches for managing some aspects of AD progression.

Did Puzzle Therapy Effect on Cognitive Functions Among Elderly with Dementia In Indonesia?

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Objective

Decreased cognitive function in elderly people with dementia affects their behavior and mood, and can disrupt their quality of life and well-being. One therapy that can be used is puzzle therapy. Like a game, elderly people with dementia will play by arranging the pieces of the picture so that they form a correct whole. This therapy can hone thinking power, train patience, eye and hand coordination and train reasoning. The aim of this study was to find out whether puzzle therapy affects cognitive function in elderly people with dementia.

Methods

This research is a literature review using data from research published from 2019 to 2023. The keywords used are puzzle therapy, dementia, elderly. There were 8 studies that were suitable and carried out in Indonesia.

Results

Most of litteratur (7 of 8) used A quasi-experimental approach and pre-post with control group design. All studies used the Mini Mental Status Examination (MMSE), 2 studies added the Hopkins Verbal Learning Test (HVLT) and Short Portable Mental Status Questionnaire (SPMSQ) instruments. With a total of 149 elderly people with dementia, aged >60 years. After treatment, an average decrease in the level of dementia and the effect of puzzle therapy on the level of dementia in the elderly was found.

Conclusion

There is an influence of puzzle therapy on the level of dementia in the elderly, therefore this therapy can be used by health workers or care givers to improve memory data in elderly people with dementia.

Predicting Depression in Cognitively Impaired Older Adults after the COVID-19 Pandemic Using ICF Model

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Objective

The aim of this study was to test a predictive model of depression in community-dwelling older adults after the COVID-19 pandemic and to identify influencing factors using the International Classification of Functioning, Disability and Health (ICF).

Methods

This study analysed data from 9,920 people, after excluding older adults living alone whose social support could not be measured because they had no surviving children or grandchildren, among 10,097 older adults (≥65 years). Depression was the outcome variable, defined by the Geriatric Depression Scale Short Form-Korea version (GDS-SF-K). The model was tested by path analysis and the goodness of fit criteria of the model were CMIN/DF<3, GFI≥.90, AGFI≥.85, CFI≥.95, TLI≥.95, RMSEA≤.06 and SRMR≤.08. Path significance was assessed using path coefficient estimates and critical ratios (C.R.). Parameter estimates were decomposed into direct and indirect effects, and the statistical significance of the total and indirect effects was tested using bootstrapping analysis.

Results

The results of the path analysis and bootstrapping analysis indicated that subjective health status, instrumental activities of daily living (IADL), number of chronic diseases, satisfaction with social support, household economic level, informal support and participation in social groups were factors directly influencing depression, while formal support, age, gender, education level, employment status and participation in social groups were factors indirectly influencing depression.

Conclusion

It will be necessary to prepare measures to prevent depression in older adults during an infectious disease pandemic, such as the COVID-19 pandemic, based on the results of this study.

Exploring Factors Influencing Suicidal Ideation among Community-dwelling Older Adults with Cognitive Impairment in South Korea Using an ICF Model

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Objective

In this study, we used the International Classification of Functioning, Disability and Health (ICF) model to identify variables that influence suicidal ideation in older adults. The aim of the study was to understand causal relationships in order to systematise complex factors.

Methods

The study used data from 9,920 community-dwelling older adults who completed a national survey in 2020 to classify factors predictive of suicidal ideation (including depression, subjective health status, sociodemographic factors, health factors, social support, instrumental activities of daily living (IADLs), and social participation) using the ICF model. The study examined the significance of critical ratio (C.R.) and squared multiple correlation (SMC) indices to identify causal relationships between variables using path models.

Results

Suicidal ideation was not significantly affected by age, employment status, participation in social groups, formal and informal support, satisfaction with friend/neighbour relationships, education level, income level, IADLs, satisfaction with relationship with children, depression, or number of chronic diseases. Furthermore, the effect of each of these factors on suicidal ideation was mediated by depression.

Conclusion

Among the multiple factors influencing suicidal ideation in community-dwelling older adults, depression was found to be the most direct and mediating factor in suicidal ideation. Further research is needed to develop community-level strategies based on these factors and to understand causal relationships.

Distinct Effects of Blood Pressure Parameters on Alzheimer's and Vascular Markers in 1,952 Asian Populations without Dementia

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Objective

The objective of this study was to investigate the association of repeated blood pressure measurements with Alzheimer's and vascular disease markers.

Methods

We recruited 1,952 participants without dementia between August 2015 and February 2022. Blood pressure variability was quantified with repeated measurements at serial visits.

Results

Increased Aβ uptake was associated with greater mean systolic blood pressure (β = 1.049, 95% confidence interval 1.016-1.083). Increased tau uptake was related to greater systolic blood pressure variability (0.094, 0.001-0.187) and diastolic blood pressure variability (0.096, 0.007-0.184). Increased vascular burden was positively associated with mean systolic blood pressure (odds ratio = 1.293, 95% CI 1.015-1.647) and mean diastolic blood pressure (1.390, 1.098-1.757). Increased Aβ uptake partially mediates the relationship between mean systolic blood pressure and the Mini-Mental State Examination scores. Reduction in hippocampal volumes completely mediates the relationship between diastolic blood pressure variability and Mini-Mental State Examination scores.

Conclusion

Each blood pressure parameter affects Alzheimer's and vascular disease markers differently, which in turn leads to cognitive impairments. Our findings highlight the importance of targeting modifiable blood pressure parameters to prevent the development of dementia. In addition to focusing on blood pressure management, blood pressure variability should also be considered. A better understanding of the pathways from specific blood pressure parameters to cognitive impairment might enable us to select the specific medications targeting the specific blood pressure parameters to prevent dementia effectively.

Changes in Dementia Treatment Patterns Associated with National Policy in Korea among Patients with Newly Diagnosed Alzheimer's Disease between 2011 and 2017: Multicenter, Retrospective CAPTAIN Study

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Objective

South Korea has actively addressed combating dementia since 2008, expanding mandatory long-term care insurance (LTCI) for dementia patients in 2014. This study aimed to investigate changes in treatment patterns for Alzheimer's disease (AD) between July 2011 and June 2017 which spanned the 2014 revision.

Methods

This multicenter, retrospective, observational study of patients with newly diagnosed AD analyzed electronic medical records from 17 general hospitals across Korea. Based on their time of AD diagnosis, subjects were categorized into Cohort 1 (1 July 2011 to 30 June 2014) and Cohort 2 (1 July 2014 to 30 June 2017).

Results

Subjects (N=3,997) divided into Cohorts 1 (n=1,998) and 2 (n=1,999), were mostly female (66.4%) with a mean age of 84.4 years. Cohort 1 subjects were significantly older (P<0.0001) and had a lower number of comorbidities (P=0.002) compared with Cohort 2. Mean Mini-Mental State Examination (MMSE) scores in Cohorts 1 and 2 at the time of AD diagnosis or start of initial treatment were 16.87 and 17.09, respectively (P=0.2790). At 1 year, mean MMSE scores in Cohorts 1 and 2 increased to 17.89 and 17.43, respectively (P=0.1524). Donepezil was the most frequently administered medication overall (75.01%), with comparable rates between cohorts. Discontinuation and switch treatment rates were significantly lower (49.72% vs. 58.01%; P<0.0001), and mean duration of initial treatment significantly longer, in Cohort 2 vs. 1 (349.28 vs. 300.21 days; P<0.0001).

Conclusion

Comparison of cohorts before and after revision of the national LTCI system for dementia patients found no significant difference in mean MMSE scores (time of AD diagnosis or start of initial treatment). The reduction in the proportion of patients who discontinued or changed their initial treatment, and the significant increase in mean duration of treatment, are attributed to revision of the LTCI policy which enabled increased patient access to long-term care.

Sex-specific Effects of MIND Diet on Dementia Risk: Insights from UK Biobank Data with Usual Intake Estimation

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Objective

The relationship between the Mediterranean-Dietary Approach to Systolic Hypertension (DASH) diet Intervention for Neurodegenerative Delay Diet (MIND diet) with cognitive function and dementia has been inconclusive. In previous studies, there often was a failure to consider the shortcomings of the 24-hour recall method, particularly in regard to non-consumption days and day-to-day variability. This study aimed to investigate the relationship between the MIND diet and dementia using usual intake estimations and a sex-specific analysis within the UK Biobank Study.

Methods

We excluded wine, olive oil, and butter/margarine-ingredients that are subjects of going health debates or ambiguously defined in the UK Biobank-from the evaluation of the remaining 12 MIND diet components. Usual food group intakes were estimated by Multiple Source Method (MSM program). Each diet component received 0, 0.5 or 1 based on the original MIND criteria. Dementia diagnosis was ascertained from hospital and death register data recorded by ICD coding system, and self-reported data. We used Cox proportional-hazards regressions adjusted for age, sex, socioeconomic status, education, smoking status, sleep duration, physical activity, and MIND*sex interaction, to explore the associations between the MIND diet and dementia.

Results

Among 68,963 participants aged 60 or older, 1,620 individuals (2.35%) developed dementia during an average follow-up of 10.7 years. Overall, MIND diet was not significantly associated with reduced dementia risk (HR=0.9507, 95% CI: 0.9032-1.0006). However, lower risk was observed in females (HR=0.9475, 95% CI: 0.8997-0.9978), but not in males (HR=0.9998, 95% CI: 0.9564-1.045).

Conclusion

Our study suggests that the effectiveness of MIND diet in reducing dementia risk differs by sex. This finding was made possible through a refined analytical approach that factored in usual dietary intakes and sex differences. Further investigation with advanced modeling could elaborate on these associations.

Insulin Resistance and Survival in Dementia Patients: Uncovering a Significant Association

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Objective

Diabetes, characterized by insulin resistance, has been linked not only to heart-related factors like strokes but also to episodes of hypoglycemia, which can damage the brain's memory center. Moreover, the "type 3 diabetes" hypothesis suggests a direct connection between diabetes and Alzheimer's disease, highlighting shared molecular features. This study explores the association between survival in dementia patients and insulin resistance calculated by TyG index in UK biobank database.

Methods

Following the application of rigorous inclusion and exclusion criteria, data from UK biobank consists of 657 individuals diagnosed with dementia, for whom mortality data was available, were analyzed. The primary objective of this analysis is to discern the association between the duration of survival after the diagnosis of dementia and their corresponding TyG index values.

Results

The results of our correlation analysis revealed a statistically significant negative association between the TyG index and survival in dementia patients, with a Pearson's correlation coefficient of $r = -0.10$ ($p = 0.006$). This finding was further substantiated by a linear regression analysis, which demonstrated a significant association, with a regression coefficient of -475.04, a standard error of 173, and a p-value of 0.006. These results indicate that as the TyG index increases, the duration of survival in dementia patients tends to decrease.

Conclusion

In conclusion, our study provides compelling evidence that dementia patients with higher levels of insulin resistance, as indicated by the TyG index, experience significantly shorter survival. This finding underscores the importance of considering insulin resistance as a potential prognostic factor in dementia patient care and highlights the need for further research to elucidate the underlying mechanisms of this association and explore potential interventions to improve outcomes for this vulnerable population.

The Correlation between Physical Fitness and Cognition Function in Korean Elderly People

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Objective

Physical performance as well as cognitive function decline as people are getting older. We aimed to evaluate usefulness of physical fitness measures for screening cognitive impairment in Korean elders.

Methods

The study included total 88 people male 16 man, 72 woman. The average age was 70.6±5.1 years old. Physical fitness tests were assessed by Grip Strength, Sit-and-Reach, 30 Second Chair Stand, 2-Minute Step in Place, 3m timed-up-and-go (TUG), 8 walk, and T-wall. Cognitive function tests were evaluated by Repeatable Battery for the Assessment of Neuropsychological Status (RBANS). Pearson'scorrelation analysis was used to find out the correlation between physical fitness factors and cognitive function.

Results

Most Physical fitness factors were not significantly correlated with the RBANS total score in man. However, only TUG was significantly correlated with attention in man($r= -.655$, $p< 0.01$). Physical fitness factors of Grip Strength, TUG, 8 walk, and t-wall time were significantly correlated with RBANS total score in woman ($r=.379, p<0.05$; $r=-.344, p<0.05$; $r=-.366, p<0.01$; $r=-.541, p<0.05$ respectively). Physical fitness factors(grip strength, TUG, 8 walk and T-wall time) were significantly correlated with RBANS indexes (visuospatial construction, language, attention, delayed recall) in woman ($p<0.05, p<0.01$, respectively). However, Physical fitness factors (sit-and reach, 30 second, 2-minute step inplace, TUG, 8 walk, and T-wall time) were not significantly correlated with any RBANS indexes.

Conclusion

Our findings suggest that Physical fitness factors of strength, agility, coordination may contribute to thecognitive functions in woman. In males, the number of subjects is insufficient, so further research on needed.

A Systematic Review of Sedentary Behavior and Its Impact on Cognitive Function, Dementia Onset, and Subjective Cognitive Complaints in Older Adults: Passive vs. Active Sedentary Behavior

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Objective

Sedentary behavior (SB) refers to activities with low energy expenditure while sitting or lying. Recent studies have shown that mentally passive SB (e.g., watching TV) might negatively affect cognitive function, while mentally active SB (e.g., using a computer or reading) could potentially be beneficial for maintaining cognitive function in older adults. This review summarizes the evidence on the associations between passive or active SB and cognitive function, dementia onset, or subjective cognitive complaints in older adults aged 60 years and older.

Methods

We systematically searched publications in PubMed and Web of Science using the following terms: ("screen time" OR TV OR television OR computer OR internet OR reading) AND (sitting OR sedentary) AND (older* OR elder* OR aged OR aging) AND (cogniti* OR "executive function" OR memory OR dementia OR "Alzheimer's disease" OR subjective cognitive OR subjective memory).

Results

Out of 540 relevant articles, 9 articles (6 cross-sectional and 3 longitudinal studies) were included. Among the five cross-sectional studies on cognitive function, passive SB was negatively related in 2/5, while active SB was positively related in 1/1. In a cross-sectional article on subjective cognitive complaints, active SB was strongly related, while passive SB was not. In two longitudinal articles on cognitive function, passive SB was negatively related in 2/2, and active SB was positively related in 1/2. In two longitudinal articles on dementia onset, passive SB was positively related in 1/2, and active SB was negatively related in 2/2.

Conclusion

This review suggests that passive SB may be associated with poorer cognitive function, higher risk of dementia, and more subjective cognitive complaints, while active SB may be related to better cognitive function, lower risk of dementia, and fewer subjective cognitive complaints. The presence of confounding bias (physical activity and sleep) along with recall bias, may potentially impact the findings of the selected articles.

Association of Physical Fitness and Cognitive Function in Community-based Older Adults

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Objective

Cognitive function declines with the aging process. Although the association of physical fitness with cognitive function has been proved, how many and how well the physical fitness components are linked to cognitive function is not clear. This study aimed to evaluate the relationship between distinct physical fitness components and cognitive function.

Methods

The present study included 84 older people in the community with a mean age of 70.7± 5.25 years. The physical fitness items including hand grip strength test, 30s sit-to-stand test, 3m sit–walk-and-return test, sit-and-reach test, 2min step in place test were measured to reflect strength, flexibility, coordination, balance and cardiopulmonary endurance respectively. The cognitive function of the participants was measured by Repeatable Battery for the Assessment of Neuropsychological Status(K-RBANS).

Results

Following age adjustment, the K-RBANS total scale demonstrated positive correlations with grip test, 2m stationary march ($r = .265$, $p < 0.05$; $r = .263$, $p < 0.05$), but a negative correlation with t-wall response time ($r = -.417$; $p < 0.01$). Utilizing K-RBANS scores as the dependent variable and incorporating physical fitness items and age as independent variables, t-wall response time emerged as a predictive factor for cognitive function in older adults residing in the community ($t = -5.78$, $p < 0.001$), accounting for 28% of the variance in K-RBANS Total scores.

Conclusion

The findings suggest that there is an association between physical fitness and cognitive function, and the grip test, 2m step in place and t-wall response time can help explain the cognitive function in older adults. Especially, T-wall response time emerged as a predictive factor for cognitive function in older adults. More attention needs to be paid to the increase in physical fitness for improving the cognitive dysfunction of older persons, and further longitudinal study is needed.

Overestimated Prediction of Alzheimer's Disease Using Polygenic Risk Score Derived from Summary Statistics

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Objective

Polygenic risk score (PRS) is often derived from summary statistics, from which the independence between discovery and replication sets cannot be monitored. Prior studies, in which the independence is strictly observed, report a relatively low gain from PRS in predictive models of binary traits. We hypothesize that the independence assumption may be compromised when using the summary statistics, and suspect an overestimation bias in the predictive accuracy.

Methods

We consider the task of Alzheimer's disease (AD) prediction across genetics datasets, including the International Genomics of Alzheimer's Project (IGAP), AD Sequencing Project (ADSP), and Accelerating Medicine Partnership - Alzheimer's Disease (AMP-AD). PRS is computed from either sequencing studies for ADSP and AMP-AD (denoted as rPRS) or the summary statistics for IGAP (sPRS). Two variables with the high heritability in UK Biobank, hypertension, and height, are used to derive an exemplary scale effect of PRS. Based on the scale effect, the expected performance of sPRS is computed for AD prediction.

Results

sPRS without APOE is derived from International Genomics of Alzheimer's Project (IGAP), which records ΔAUC and ΔR2 of 0.051±0.013 and 0.063±0.015 for Alzheimer's Disease Sequencing Project (ADSP) and 0.060 and 0.086 for Accelerating Medicine Partnership - Alzheimer's Disease (AMP-AD). On UK Biobank, rPRS performances for hypertension assuming a similar size of discovery and replication sets are 0.0036±0.0027 (ΔAUC) and 0.0032±0.0028 (ΔR2). For height, ΔR2 is 0.029±0.0037.

Conclusion

Considering the high heritability of hypertension and height of UK Biobank and sample size of UK Biobank, sPRS results from AD databases are inflated. Independency between discovery and replication sets is well-known basic requirements for PRS studies. However, a lot of PRS studies cannot follow such requirements because of impossible direct comparisons when using summary statistics. Thus, for sPRS, potential duplications should be carefully considered within the same ethnic group.

The Impact of Metabolic Health on the Relationship of Obesity with and Alzheimer's and Vascular Markers

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Objective

We aimed to investigate the effect of metabolic health on the association between obesity and Aβ positivity or severe white matter hyperintensities (WMH).

Methods

We recruited 1,736 non-demented participants aged ≥55 years who underwent Aβ PET scan. They were categorized by BMI: <18.5kg/m^2 (underweight); between 18.5kg/m^2 and 25kg/m^2 (normal weight); ≥25kg/m^2 (obese). Each group was divided into metabolically healthy and unhealthy groups based on ATP-III criteria. Aβ positivity was defined as Aβ PET centiloid>20. Severe WMH was defined as ≥10mm periventricular and ≥25mm deep WMH. Data on plasma glial fibrillary acidic protein (GFAP) levels, hippocampal volume (HV), and clinical dementia rating scale sum of boxes (CDR-SOB) were collected. Logistic and linear regression analyses were performed using BMI status groups as predictors for Aβ positivity, severe WMH, and plasma GFAP, controlling for potential confounders. To examine the interaction between BMI status and metabolic healthiness, regression analyses were performed with an interaction term of BMI status*metabolic healthiness.
Mediation analyses were performed to investigate the complex relationships among aforementioned factors.

Results

Being underweight increased Aβ positivity risk (OR=2.37), whereas obesity decreased it (OR=0.63). The interaction was significant for obesity and metabolic healthiness on Aβ positivity (p for interaction<0.001), but not for underweight versus normal weight. For severe WMH, being underweight had no effect, but obesity increased odds (OR=1.69) without significant interaction between obesity and metabolic healthiness. Being underweight predicted higher plasma GFAP (β=0.190, p=0.048), whereas obesity was associated with lower levels (β=-0.115, p=0.001) with no significant interaction between obesity and metabolic healthiness. Mediated analyses of Aβ-positivity mediated pathways found that being underweight was associated with lower HV and higher CDR-SOB, while obesity showed the opposite effect.

Conclusion

The protective effects of obesity on Aβ positivity are different according to metabolic healthiness and being underweight is a risk factor for Aβ positivity regardless of metabolic healthiness.

Age- and sex-specific Mediating Effects of Depression in the Relationship between Frailty and Cognitive Function in Korean Middle Aged and Older Adults: Results from the Korean Genome and Epidemiology Study (KoGES)-Cardiovascular Disease Association Study (CAVAS)

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Objective

The purpose of this study was to examine whether the effects of depression, which previous research has identified as mediating the effects of frailty on cognitive function, differ by age and sex.

Methods

This study included a total of 2,241 KoGES-CAVAS participants aged 55 to 80 years (mean age 67.21±6.36 years; 816 men, 1,425 women; mean education 9.87±4.09 years). All participants were administered the Korean version of the FRAIL (K-FRAIL) scale, the Seoul Neuropsychological Screening Battery-Core (SNSB-C), and the Center for Epidemiologic Studies Depression Scale (CES-D). Mediation analyses were performed using SPSS PROCESS macro to estimate the direct and indirect effects of frailty on various cognitive functions (overall cognition, memory, and executive function) by assessing the role of depression as a mediator.

Results

In the 65+ age group, frailty had a direct effect on overall cognition and executive function, as well as an indirect effect through depression, but only an indirect effect through depression on memory. In contrast, in the < 65 age group, frailty had only an indirect effect through depression on overall cognition, executive function, and memory, with a very weak indirect effect on memory. In both men and women, frailty directly and indirectly affected overall cognition and executive function through depression, but only indirectly affected on memory through depression, and this indirect effect was very weak in men.

Conclusion

These results showed that the mediating effect of depression on the relationship between frailty and cognitive functioning varies by age and sex, but also by type of cognitive function. Unlike overall cognition and executive function, where partial mediating effects were found, full mediating effects of depression on the relationship between frailty and cognitive functioning was found for memory, with these effects being stronger in the 65+ age group and in women.

Physical Frailty and Cognitive Functions in Older Adults Living in Rural Korea: Results from the Korean Genome and Epidemiology Study (KoGES)-Cardiovascular Disease Association Study (CAVAS)

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Objective

The aim of this study was to compare differences in cognitive functions according to physical frailty status among older adults living in rural Korea.

Methods

A total of 1,493 KoGES-CAVAS participants aged 65 years or older (mean age 71.31 ± 4.09 years; 915 women, 578 men; mean education 8.60 ± 4.38 years) participated in the study. The Korean version of the FRAIL scale (K-FRAIL), the Center for Epidemiologic Studies Depression Scale (CES-D), and the Seoul Neuropsychological Screening Battery-Core (SNSB-C) were administered to all participants. Participants were stratified by frailty status: 902 (60.4%) in the not-frail group, 510 (34.2%) in the pre-frail group, and 81 (5.4%) in the frail group.

Results

The not-frail, pre-frail, and frail groups were characterized by being progressively older, more women, less educated, and more depressed, in that order. The pre-frail group had worse attention than the not-frail group, but did not differ from the frail group. The not-frail group did not differ from the pre-frail group in language and visuospatial functions, but did show significant differences from the frail group. Memory, on the other hand, did not differ between groups by frailty status. Significant differences were observed between these three groups in frontal/executive function and SNSB-C total scores, with the highest in the not-frail group and the lowest in the frail group.

Conclusion

These findings of differences in cognitive function across physical frailty status suggest that the impact of frailty on cognition depends on the type of cognitive function. It is suggested that attention is affected from the pre-frail stage, while language and visuospatial functions are not affected until the frail stage. Frontal/executive function and overall cognition are suggested to be strongly associated with frailty, whereas memory is suggested to be unaffected by frailty.

Estimate of Gait Speed by Physical Fitness Test in older adults

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Objective

Physical fitness is a crucial health indicator among the elderly, with the Korean National Fitness 100 being a representative elderly fitness assessment tool(muscular strength, muscular endurance, flexibility, cardiovascular endurance, dynamic balance, and coordination). Gait speed is also recognized as a critical health-related determinant in the elderly; however, limitations are associated with the use of expensive equipment and the need for a spacious area. This study aims to correlate physical fitness factors with walking speed, ultimately estimating walking speed through fitness assessments.

Methods

For this cross-sectional validation study, 28 healthy community-dwelling older persons (age range 70-79; mean age 72.6±4.13 years; 75% women) walked at normal speed over an instrumented walkway (Optogait, MicroGate). Additionally, the National Fitness 100 elderly fitness assessment includes the following components: grip test for upper body muscle strength (force of grip), chair stand test for lower body muscle endurance (number within 30 seconds), sit and reach test for body flexibility (distance between fingers and toe), timed-up-and-go(TUG) test for agility and dynamic balance (time to rise, walk 3m and return to the chair), Step in Place Test(2 minute) to measure cardiovascular endurance (number of steps completed in 2 min), fast walking on an "8"-shaped trajectory (The Figure-of-8 walk Test; F8WT) for coordination (time it takes to walk back to the figure of 8).

Results

The correlation analysis between gait speed and physical fitness factors revealed that F8WT exhibited the highest correlation (r = -.673), followed by the chair stand test (r =.625). Regression analysis was employed to estimate gait speed for each factor, resulting in root mean square estimation (RMSE) values of 0.095 for F8WT and 0.101 for the chair stand test.

Conclusion

The F8WT or chair stand test could be effectively utilized in the field for a simple estimation of walking speed.

Quantifying Dementia Risk Factors: A Machine Learning Analysis of Genetic Markers in Alzheimer's Disease Progression

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Objective

Alzheimer's disease (AD) is the most common form of dementia, with a complex etiology involving both genetic and environmental factors. Understanding the genetic contributions to AD progression is crucial for early diagnosis and targeted interventions. In this study, our aim was to develop a highly specific predictive model that quantifies the impact of genetic markers on the risk of AD progression, utilizing advanced machine learning techniques.

Methods

We conducted a genome-wide association study (GWAS) on a cohort of 1,500 AD patients and 1,500 age-matched controls, carefully selected to ensure demographic parity. The GWAS identified a set of genetic markers associated with AD progression. Leveraging these markers, we developed a machine-learning model based on an ensemble of gradient-boosting trees, specifically XGBoost. This model incorporated genetic data from single nucleotide polymorphisms (SNPs) and utilized feature engineering to capture gene-gene interactions. Cross-validation and external validation were performed to assess model robustness and generalizability.

Results

Our predictive model achieved a striking level of specificity, with an accuracy of 92.3% in identifying individuals at high risk of AD progression within a 5-year time frame. The precision of our model was exceptional, with a positive predictive value of 94.7%, significantly reducing false positives. Additionally, the model demonstrated an area under the precision-recall curve (AUC-PR) of 0.91, indicating excellent performance in identifying at-risk individuals. Further, the model provided odds ratios and 95% confidence intervals for each genetic marker, offering precise quantification of risk.

Conclusion

Our study utilized advanced machine learning and genetic markers to develop a highly specific model using XGBoost. This model excelled in predicting Alzheimer's disease progression, surpassing current methods. This precision enables targeted screening and interventions, reducing the strain on healthcare resources. Our findings emphasize the potential for personalized medicine in Alzheimer's care, offering tailored risk identification and more effective early interventions.

The Association between Glucose Variability and Parkinson's Disease: Using the PPMI Datasets

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Objective

The association between glucose control and the risk of Lewy body disease (LBD) has not been elucidated. In this study, we evaluated the association between glucose variability and the risk of Parkinson's disease (PD) based on Parkinson's Progression Markers Initiative (PPMI) dataset. The effects of glucose variability on longitudinal changes in cognition and motor function were also evaluated among PD patients.

Methods

413 PD patients and 195 control subjects underwent baseline evaluation including glucose variability and calculation for genetic risk score for PD (GRS-PD). Clinical, neuropsychological, and motor evaluation in addition to dopamine transporter (DAT) imaging were performed at baseline and follow-up (mean duration of 4.4 years for controls and PD patients). The effects of glucose variability and GRS-PD for the presence of PD and baseline striatal DAT uptake were evaluated in overall subjects using logistic regression analyses and general linear models (GLMs), respectively. The effects of glucose variability on cross-sectional and longitudinal cognition, motor function, and striatal DAT uptake were evaluated among PD patients using GLMs and linear mixed models, respectively. Covariates included age, sex, and education.

Results

Higher glucose variability and GRS-PD were independently associated with an increased risk of PD. Among overall subjects, higher glucose variability was associated with lower baseline putamen DAT uptake. Among PD patients, higher glucose variability was associated with faster increase in tremor score, but slower decline in caudate DAT uptake and slower increase in levodopa equivalent daily dose.

Conclusion

Glucose variability could be a risk factor for the development of PD, but it was related with slower deterioration in striatal DAT uptake and motor function among PD patients. These results suggest that glucose variability is an important risk factor for PD.

Partivulate Matter Exposure Accelerates Tau Pathophysiology, Inflammation and Cognitive Deficits in Tau-BiFC Mice

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Objective

Particulate matter (PM) exposure has been shown to influence neurodegenerative disease and studies have shown an increase in amyloid plaques and inflammation. However, the effect of PM on tau pathology remains largely unknown. Here we investigated the effect of PM on tau pathology in a Tau-BiFC mouse model.

Methods

We made use of a soot-generating whole-body inhalant exposure system to expose PM1. PM1 is able to penetrate deep into the body and cause inflammation and pathology. To replicate the natural way of whole-body inhalation of PM1, we adapted a soot generating exposure system to expose 6- and 12-month old Tau-BiFC mice for a three-week, 8-hour daily exposure period with an average daily concentration of 137ug/m3 of PM1. To evaluate the effect of PM1 on tau pathophysiology we made use of a fluorescent sensor mouse model that expressed tau aggregation and pathophysiology in an age-dependent way by showing increased fluorescence signal. We performed behavioral tests to define cognitive functioning and extracted the brain to quantify tau pathophysiology and inflammation as well as differentiate affected RNA markers.

Results

Based on behavioral assessment, we found an increase in anxiety and impaired recognition function, speculating that PM1 exposure may lead to cognitive deficits. Brain analysis showed an increased intensity in BiFC, AT8 and GFAP in hippocampal and cortical regions, indicating an increase in tau hyperphosphorylation and astrocytic inflammation upon PM1 exposure. RNA sequencing indicates epithelial cell and astrocytes as the most affected cell type, with the potential of PM1 to penetrate the brain via blood vessels, activating astrocytes and in turn leading to tau pathology and disease exacerbation.

Conclusion

PM1 exposure causes a rapid progression of AD-related tau-pathophysiology and inflammation indicated by increase of Tau-BiFC intensity and inflammatory markers, as well as anxiety and impaired recognition function.

PE_200 Risk Factors, Public Health and Epidemiology

Clinicopathological Correlation of Neurodegenerative Diseases in National Brain Biobank of Korea (NBBK)

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Objective

In Korea, systematic brain banking began was recently initiated in 2015, with the National Brain BioBank of Korea (NBBK) linking 4 regional brain banks encompassing the neuropathological diagnosis and clinical correlation. In the current study, we examined clinicopathological correlation from the summary data gathered from NBBK.

Methods

The NBBK, a consortium of brain banks funded by the Korean Centers for Disease Control and Prevention (KCDC) and Korea National Institute of Health (KNIH) started the dementia brain bank project in August 2016 and set up four brain banks in four hospitals; Samsung Medical Center, Seoul National University Hospital, Pusan National University Hospital, and Myoungji hospital.

Results

By September 2023, a total of 164 brain specimens have been acquired and pathologically assessed across the four institutions (SNU 111 cases, PNU 26 cases, SMC 21 cases, MJH 6 cases). The average age at the time of consent was 70.8±12.1 years, and at the time of autopsy, it was 71.5±12.0 years. There were 65.4% (n=104/159) males and 34.6 % (n=55/159) females. The patient diagnosed with dementia during their lifetime was 81.1% (n=133), while cognitively unimpaired (CU) was 18.3% (n=30). Clinical diagnoses were most frequently AD dementia (n=29, 17.7%), followed by IPD (n=27, 16.5%), CU (n=22, 13.4%), and unspecified dementia (n=19, 11.6%), while pathological diagnoses were most commonly AD (n=40, 24.4%), cerebral vasculopathy (n=24, 14.6%), and PD (n=21, 12.8%) in order.

Conclusion

This is the first Korean report about clinical-pathological correlation of neurodegenerative diseases based on the data from four hospital based cohorts, KBBN. Combined data from clinic- and community-based cohorts are needed to gain insights into the exact data on the prevalence of AD or other neurodegenerative diseases in Korea.

Indonesian's Health Service Apps for Caregivers of Dementia Patients: Future Challenges

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Objective

The lack of professional caregivers for dementia in Indonesia is one of the continuously unsolved problems. Meanwhile, the Satusehat app, a newly implemented app that integrated society's data health has far more than to solve this problem. This study seeks the answer of optimization of Satusehat apps and alternative ways to help dementia caregivers.

Methods

This study employs quantitative research by collecting online survey data from 109 dementia caregivers in different areas of Indonesia. Then, this study adopts the partial least squares approach to structural equation modeling (PLS-SEM) to examine data.

Results

The path coefficient of this study shows that Perceived confirmation did not have a correlation to satisfaction with t-statistics and p-values 0.107 (0.905). With the perceived confirmation, dementia caregivers have not found satisfaction because Satusehat has not implemented an integrated guideline to take care of dementia patients. Meanwhile, expectations have a positive association with perceived performance and satisfaction. The regression analysis showed the path supported with t-statistics and p-values 3.707 (0.000), and 3.587 (0.001) respectively. Dementia caregivers found that using other sources rather than Satusehat apps, such as professional practitioners dementia caregivers, helps them to treat dementia patients.

Conclusion

Satusehat has a long way to go and requires major improvement to cover the caregivers' work, especially in dementia patients. This study suggests the Indonesian government create health regulations to collaborate with professional practitioners in order to serve the guideline contents to non-professional dementia caregivers.

Quality of Life Memory-Related Disease Patients in Indonesia Using Indonesia Family Life Survey

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Objective

Memory-Related disease is one of the most common diseases in Indonesia. This study analyzes the quality of life of patients with memory-related disease in Indonesia.

Methods

The study uses IFLS-5 (Indonesia Family Life Survey-5) data. Descriptive tabulations are used in this study. The number of respondents was 71 respondents with memory-related disease. The analysis carried out was the quality of life of memory-related diseases of patients in terms of Physical Functioning, Activities of Daily Living (ADL) and Instrumental Activities of Daily Living

Results

The results show that from a physical functioning perspective, out of 71 respondents, 18 patients had difficulty carrying a heavy load (like a pail of water) for 20 meters, 17 patients had difficulty sweeping the house floor yard, 33 patients had difficulty walk for 5 kilometers, 18 patients had difficulty drawing a pail of water from a while, 12 patients had difficulty bowing, squats, knees. If seen from the Activities of Daily Living (ADL), 8 sufferers find it difficult to eat , 9 patients have to control urination or defecation. When viewed from the quality of life based on Instrumental Activities of Daily Living, 28 patients found it difficult to prepare hot meals (preparing ingredients, cooking and serving food), and 16 patients had difficulty taking medicine (taking the right portion right on time).

Conclusion

So it can be seen that the quality of life for memory disease of sufferers in Indonesia is quite good as can be seen from the negative impact which is only around 10%. From a physical point of view, the most influential indicator is difficulty walking 5 kilometers. When viewed from daily activities, the most influential indicator is difficulty controlling urination or defecation. As well as the Instrumental Activities of Daily Living, the biggest cause is the difficulty in preparing hot meals .

A Study on the Relationship Between Physical Activity Levels in the Elderly and the Experience of Cognitive Impairment

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Objective

This study aims to investigate the correlation between physical activity and the experience of cognitive impairment in the elderly, utilizing raw data from the Community Health Survey conducted by the Korea Disease Control and Prevention Agency. Through quantitative research, we seek to establish clinically objective evidence for the prevention of cognitive dysfunction and provide foundational data for intervention development.

Methods

The study focused on individuals aged 65 and above, ultimately analyzing data from 74,345 participants. The research investigated the correlation between types of physical activity (high-intensity physical activity per week, moderate-intensity physical activity per week), the frequency of weekly walking, and the experience of cognitive impairment.

Results

The mean frequency of high-intensity physical activity per week was 0.34±1.27 days, moderate-intensity physical activity was 0.97±2.04 days, and walking practice was 3.81±2.85 days. Regarding physical activity, moderate-intensity physical activity showed a slightly negative correlation with the experience of cognitive impairment (r=-.043), and the number of days of walking practice exhibited a slightly higher negative correlation compared to moderate-intensity physical activity (r=-.055).

Conclusion

The findings of this study reveal the association between the prevalence of moderate-intensity physical activity and the frequency of walking practice in the elderly and cognitive function.

Does Socio-Economic and Education Matters the Patient's Quality of Life

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Objective

Quality of Life (QoL) is closely linked to well-being (World Health Organization, 2005). The United Nations Development Program (UNDP) introduced the human development index (HDI) in 1990 as a key gauge of progress in promoting well-being. It is widely acknowledged that development should not only focus on increasing quantity (physical structures) but also quality (life, human), and as such, various sectors play a critical role.

Methods

This study uses a literature review that follows the PRISMA method and a literature search on PubMed and Google Scholar using the keywords "Socio-Economic," "Quality of Life" and "Education". Several articles that fit the criteria were found in the search results for the years 2013–2023.

Results

According to Madakam, (2020) said that a good quality of life is reflected in the condition of good health then followed by healthy socio-economic conditions. Socio-economic is recognized as a major determinant of health among people of all ages, presenting a major challenge to health worldwide. Some previous researchers suggest that parent/caregiver socio-economic status (SES) may be a determinant of HRQoL in children and adolescents with chronic illness. The most frequently reported SES indicators that predict this are household income and mother's level of educational desire. These findings are consistent with studies involving children without chronic disease, with most of these studies demonstrating a causal and additive relationship between financial resources and children's health outcomes.

Conclusion

In conclusion, it is expected that all ages will start paying attention to their health to improve their quality of life which is also assisted with support from the government. Evenly distributed development in various sectors (socio-economic and education) is the key to improving the quality of life. It turns out that there are no sectors that do not play a role. From there, results will emerge that strengthen the quality of life indicators

Frequency of Limbic-predominant age-related TDP-43 encephalopathy neuropathological change (LATE-NC) in a Dementia Clinic-based Cohort: A Preliminary Study

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Objective

LATE-NC is an underlying pathology of LATE, which is a newly defined clinical syndrome characterized by amnestic cognitive deficits affecting limbic areas in advanced-age people. In this study, we investigated the prevalence of LATE-NC in a dementia clinic-based cohort in Korea and reported preliminary results.

Methods

Fifty two participants who consented and underwent brain autopsies at the Pusan National University Hospital Brain Bank from 2011 to 2023 were initially included in this study. The assessment of LATE-NC followed the 2019 LATE-NC guidelines, and ADNC followed the 2012 NIA-AA guidelines.

Results

Of the 42 participants, 14 with diverse primary pathological diagnoses exhibited coexisting LATE-NC (33%). The mean age at death and the onset age of LATE-NC (+) group was 79.9 years and 70.8 years which were significantly different from those of the LATE-NC (-) group. Of those with LATE-NC (+), 11 demonstrated ADNC. LATE-NC was more frequently observed in patients with intermediate ADNC than those with low or high ADNC. Participants with LATE-NC were distributed at 50.0%, 28.6%, and 21.4% at stages I, II, and III, respectively. The LATE-NC stage was correlated with increased age at death and increased age of onset. LATE-NC stage was not associated with Braak stage scores, MMSE score and CDR score but higher LATE-NC stages tended to be associated with lower Thal-phase.

Conclusion

A recent study conducted on community-based or population-based autopsy cohorts indicated that the frequency of LATE-NC was 40% which is higher than that of our preliminary study and LATE-NC was relatively common in severe ADNC which was not consistent with our results. These discrepancies between the previous study and ours might be attributed to the differences in study participants (community versus hospital-based), as well as differences in the scale of the study. Therefore, further studies with a larger number of participants are warranted.

Early Detection of Dementia Disease: How Community-based Health Centers (puskesmas) Take the Important Role among 17k Islands in Indonesia?

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Objective

More than 4 million of Indonesia's population are having dementia. The burden of government social insurance financing for dementia until September 2023 reached USD 3.3 million excluding chronic drug costs, or increased by 94% compared to 2022. Preventive program conducted by the government through Community-Based Health Centers (Puskesmas) reaches remote areas. However, little is known about the effectiveness of Puskesmas in the framework of controlling dementia disease.

Methods

We utilize the 2014 Indonesia Family Life Survey (IFLS) to evaluate the effectiveness of the Puskesmas in improving the function of early detection and treatment for dementia.

Results

The prevalence of the elderly with dementia is 1.4% and increases in senior citizens by two times (60%: men). The elderly with dementia, whether they have government social insurance or not, tend to access treatment at the Puskesmas. Meanwhile, 56% of those who do not have insurance prefer traditional practitioners. Given that Indonesia uses the Gate-Keeper system, the first-level health facilities are at the sub-district or community level. Posyandu Lansia as an extension of Puskesmas, is a monthly village-based activity that is accessed by 16.35% of the elderly for routine health checks, obtaining food/supplements, and various meetings and counseling. The elderly with dementia are one of the highest accessors to the Posyandu Lansia (42.3%). Various integrated services can be accessed by the elderly from 80,353 Posyandu Lansia spread across 81,616 villages in Indonesia. Puskesmas is highly effective in improving the senior QoL in various aspects of life.

Conclusion

Puskesmas outreach program is carried out by trained cadres and medical staff. Posyandu Lansia carries out early detection of dementia disease and is very accessible in preventive programs and improving the elderly QoL through various services. It also needs to address the covered social insurance for treatment and caregivers.

Effect of Dietary Habits on Alzheimer's Disease Progression

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Objective

Research on the relationship between diet and dementia among Koreans are lacking. This study investigated the association between dietary habits and dementia progression over 3 years in patients with Alzheimer's disease dementia (ADD).

Methods

This study included 705 patients with mild-to-moderate ADD. Dietary habits were assessed using the Mini Dietary Assessment Index, comprising 10 questions. Outcome measures included the Clinical Dementia Rating scale-Sum of Boxes (CDR-SB), Seoul-Instrumental Activities of Daily Living, Caregiver-Administered Neuropsychiatric Inventory (CGA-NPI), and neuropsychological test battery (NTB) z-scores, which were evaluated annually over 3 years.

Results

In Q10 (eat all food evenly without being picky), the 3-year mean differences in CDR-SB (increases in scores represent worsening) compared to the "rarely" group were −1.86 (95% confidence interval [CI] = −3.64 ~ −0.09, P = 0.039) for the "usually" group and −2.23 (95% CI = −4.40 ~ −0.06, P = 0.044) for the "always" group. In Q7 (add salt or soy sauce to food, when eating), the 3-year mean differences in CDR-SB compared to the "always" group were −2.47 (95% CI = −4.70 ~ −0.24, P = 0.030) for the "usually" group and −3.16 (95% CI = −5.36 ~ −0.96, P = 0.005) for the "rarely" group. The "rarely" and "usually" groups in Q7 showed significantly less decline in NTB z-score and CGA-NPI compared to the "always" group.

Conclusion

Eating a balanced diet and reducing salt intake were associated with a slower decline in dementia severity, cognition, and behavioral alterations in patients with ADD.

Prediction Model for Mild Cognitive Impairment in Patients with Type 2 Diabetes Using an Autonomic Function Test

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Objective

Type 2 diabetes mellitus (T2DM) is a risk factor for cognitive impairment, and heart rate variability (HRV) has been correlated with cognitive function in elderly individuals. This study investigated risk factors and validated a predictive model for mild cognitive impairment (MCI) in patients with T2DM using an autonomic function test.

Methods

Patients with T2DM, 50–85 years of age, who attended the diabetes clinic at Gyeongsang National University Hospital between March 2018 and December 2019, were included. Cognitive function was assessed using the Montreal Cognitive Assessment-Korean version (MOCA-K); MCI was defined as a total MOCA-K score ≤ 23. Risk factors for MCI in patients with T2DM, including demographic- and diabetes-related factors and autonomic function test results, were analyzed. Based on multivariate logistic regression, a nomogram was developed as a prediction model for MCI.

Results

In total, 124 (31.45%) patients were diagnosed with MCI. Age, education, and cardiovagal function were associated with high risk for MCI, with cardiovagal function exerting the greatest influence. The nomogram demonstrated excellent discrimination (area under the curve, 0.832) and was well-calibrated.

Conclusion

Approximately one-third of patients had MCI; as such, carefully evaluating cognitive function in elderly patients with T2DM and reduced HRV is important to prevent progression to dementia.

Health Literacy Status of Caregivers of People with Dementia in South Korea

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Objective

The dementia prevalence rate of the elderly in South Korea is estimated to be 10.33% in 2023, and is predicted to reach 16.56% by 2050. The increasing prevalence of dementia among the people is likely to increase the burden of caregivers. Health literacy of caregivers of people with dementia may influence patients' healthcare outcomes; however, research in this area is insufficient. Therefore, this study examined the current status and related factors of health literacy of caregivers of people with dementia in South Korea.

Methods

An online survey, including the Korean translation of the European Health Literacy Survey Questionnaire (HLS-EU-Q47) and questions related to dementia care experience, was taken by 677 caregivers with experience in caring for people with dementia, between August&September 2023. The HLS-EU-Q47 comprises 47 questions on a 4-point Likert scale. The Korean translation was verified by experts for the content validity and socio-cultural translation. Statistical analyses are conducted using SPSSver.28.0.

Results

The average general health literacy of caregivers of people with dementia in South Korea was 36.1±9.1 out of maximum 50 points. Women caregivers, those with comparatively lower household income and education level, and those who identified themselves as the primary caregivers showed lower health literacy scores in general. Lack of knowledge for healthcare ranked the third among care hardships, followed by stress from the responsibility and problematic behaviors of patients.

Conclusion

Although health literacy of Korean caregivers of people with dementia was statistically higher than that of European adults (33.8±8.0), women with lower education and income, who proffer majority of the dementia care tend to have lower health literacy. The Dementia National Responsibility System was implemented six years ago, yet caregivers of people with dementia still face difficulties such as lack of expertise and knowledge. Policy alternatives, such as health literacy competency education and support programs for caregivers may help.

Baseline Demographic and Clinical Characteristics of Longitudinal Study of Early Onset Dementia And Family Members (LEAF)

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Objective

Patients with early-onset dementia (EOD) tend to be different from patients with late-onset dementia in their rarities, atypical presentations, higher genetic predisposition and diverse etiologies. Although EOD has devastating impacts on patients and

families, and their societies, there are few longitudinal observational studies providing sophisticated clinical, biomarkers and genetic information of EOD. Here, we introduce a Longitudinal study of Early onset dementia And Family members (LEAF) which was launched in April 2021.

Methods

LEAF was originally designed to enroll at least 400 patients with EOD consisting of patients with Aβ-positive EOAD (LEAF-AD), FTD (LEAF-FTD), and other EOD (LEAF-Others) with annual follow-up. Family members with a clear family history have also been enrolled in family cohort. Participants undergo a standardized clinical assessment and brain MRI and amyloid PET. We collect plasma, serum, and DNA for biomarkers and genetic studies. Clinical evaluations and blood collections are annually performed, and brain MRIs are followed up every two years.

Results

We have currently recruited a total of 290 participants with EOD. Aβ-positive AD spectrum (n = 195) , FTD (n = 60), and Other EOD (n = 35). The mean age was 60.4 for EOAD, 64.3 for FTD, and 57.9 for other EOD. The prevalence of women was higher in the EOAD (69.7%) and FTD (63.3%), while the prevalence of men (60.0%) was higher in other EOD. The prevalence of APOE 4 was significantly higher in EOAD than in FTD and other EOD. Family histories of dementia were reported 35% in EOAD, 33% in FTD, and 43% in other EOD. We have, so far, identified 8 pathogenic variants and enrolled five families as family cohort.

Conclusion

LEAF is the first nationwide multicenter, hospital-based longitudinal study for EOD in Korea, and this will ultimately shed light on prevention and management of EOD and EOD-related social issues.

Dementia Prevention: The Challenges and the Future from Literature Review

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Objective

Dementia is a brain disorder in the elderly. The main causes of dementia are Alzheimer's disease (AD) and cerebrovascular disease. Until now there is no curative treatment available, but several epidemiological studies are now able to find and modify protective factors that can be addressed to prevent or delay the onset of AD and dementia.

Methods

This article uses a literature review method from various journals such as The Journals of Gerontology, Journal of Clinical Nursing, etc., using the keywords dementia, prevention and epidemiology

Results

First, decline in cognitive function (including dementia) can be reduced by actively involving older people in social, physical and mental stimulation activities. In Europe, there are studies of media and lifestyle interventions aimed at increasing cognitive reserve. Second, priority observations by establishing second-generation memory clinics (brain health services) have shown efficacy of reducing the prevalence of dementia. Third, the importance of screening for dementia. Participants who were lost to follow-up after screening tended to have higher rates of incident dementia than those who completed follow-up. Finally, the prevalence of dementia has been reduced in high-income countries. This is related to improving education, economic conditions and strengthening disease prevention rather than treatment for Alzheimer's disease.

Conclusion

International collaborative research for the improvement of dementia prevention strategies appears to be a priority for expertise around the world.

Updated Treatment for Tremor: Cutting-Edge Brain Surgery with No Cutting and Pharmacotherapy

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Objective

Tremors are shaking movements that occur involuntarily and repeatedly. This condition often occurs in the hands but can also attack other body parts, such as the head or feet. Tremor treatment procedures can be based on the severity, and the symptoms that appear can use medication, therapy and surgery. So, this study aims to examine the updated treatment of tremors.

Methods

This research uses a bibliometric systematic review method. We collected articles from 2010-2022 from an electronic database (pubmed.gov, springer, science direct, Gleneagles). Then, as many as three selected papers were reviewed to answer the aim of this study.

Results

Based on Shah et al. (2022), current pharmacologic and non-pharmacologic therapies are focused only on the symptomatic treatment of upper limb tremors. After decades of research, propranolol and primidone remain the most effective agents, with high doses of topiramate also showing clinical efficacy. Also, Robinson (2022) found that a new treatment for tremors is Cutting-edge brain surgery with no cutting. The procedure involves using high-frequency sound waves directed with pinpoint precision by magnetic resonance imaging to ablate or burn the focal point deep within the brain that is causing tremors. Current treatment options include pharmacotherapy, neurostimulation (with deep brain stimulation), and ablative therapies (with radiofrequency, stereotactic radiosurgery, or focused ultrasound), but each has its limitations (Kalia, 2022).

Conclusion

Treatment for tremors has been done. Several updates include pharmacologic and non-pharmacologic therapies, Cutting-edge brain surgery with no cutting, and pharmacotherapy, neurostimulation, and ablative therapies.

Clinical Research Platform for Multisource Brain disease (CLIMB) Registry: An National-wide Platform for Recruitment, Assessment, and Longitudinal Monitoring of Participants for Neuroscience Studies

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Objective

Dementia, Alzheimer's disease, and other neurodegenerative conditions pose significant societal and economic challenges. To accelerate clinical trials and cost-effectively improve neuroscience research, registries are important. Therefore, this study introduces the CLInical research platform for Multisource Brain disease (CLIMB) registry, a comprehensive nationwide platform designed.

Methods

For prospective standardization, we followed 4 steps to ensure standardization and efficiency. First, the standardization of the variables to be collected was prioritized based on a review of existing cohort data and discussions. Second, we searched for appropriate instruments to measure these common domains and items. Third, we planned standardized procedure to collect data, and documented. Fourth, we set up the standardized input system using electronic case report forms (eCRFs) established on the platform. Participants register after providing basic personal information and electronic consent. The registry collects various data, including clinical information, questionnaires, genetic testing, and neuroimaging, and is seamlessly integrated with the Korean National Health Insurance Service (K-NHIS) database.

Results

From 2021 to 2023, we were obtained 363, 585, 729 and 1764 in early-onset dementia, hospital-based dementia, Parkinson's and aging cohort, respectively. Cross-sectional analysis from the time of cohort entry shows that individuals on average 70 years old, and 61% were female. More than 0.2% were have severe cognitive impairment at entry. The missing rate was 8%.

Conclusion

The nationwide CLIMB registry provides a robust, secure, and well-integrated platform with the potential to accelerate the development of new treatments, reduce costs, and expand the reach of clinical studies.

Relationsip between Amyloid Burden and Sleep Characteristics in the Elderly with Subjective Cognitive Decline

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Objective

Alzheimer's disease (AD) is a neurodegenerative disease characterized by progressive cognitive decline and worsening of daily activities. Recent studies display efforts to establish relationships between AD and sleep, a phenomenon so mundane but not yet fully understood. It is believed that patients with AD pathology show alterations in sleep characteristics years before clinical symptoms become apparent. This study was conducted to explore whether sleep characteristics differ between cognitively asymptomatic patients with and without amyloid burden.

Methods

Sleep characteristics of 76 subjects aged 60 years or older diagnosed with subjective cognitive decline (SCD) but not with mild cognitive impairment (MCI) or AD were analyzed using Fitbit(R) Alta HR, a wristwatch-shaped wearable device. Amyloid burden was evaluated using brain amyloid plaque load (BAPL) and standardized uptake value ratio (SUVR) from fluorine-18 Florbetaben positron emission tomography (PET) in all subjects. Each component of measured sleep characteristics was analyzed for statistically significant difference between amyloid-positive and amyloid-negative groups.

Results

Of the 76 subjects included in this study, 49 (64.5%) were female. The average age of subjects was 70.72±6.09 years at the beginning of the study. 15 subjects were classified as amyloid-positive by BAPL. Average SUVR was 1.598±0.263 in amyloid-positive group and 1.187±0.100 in amyloid-negative group. Time spent in slow wave sleep was significantly lower in amyloid-positive group (39.4±13.1 minutes) than in amyloid-negative group (49.5±13.1 minutes) (p-value: 0.009).

Conclusion

This study's results indicate that slow wave sleep is a key difference between the elderly population with and without amyloid burden. How slow wave sleep affects AD pathology remains to be determined.

Physical Fitness, Depression, and Their Influence on Cognitive Frailty Among Community-Dwelling Elderly

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Objective

To quantitatively assess the interplay between objective measures of physical fitness, depression, and their cumulative impact on the susceptibility to cognitive frailty in older adults.

Methods

This cross-sectional study included 186 participants aged > 64 years. Based on frailty status and cognitive decline (CD), participants were categorized into four groups: i) robust (n=48); ii) frailty without CD (n=31); iii) CD without frailty (n=54); and iv) cognitive frailty (combined frailty and CD) (n=52). Frailty status was assessed using Fried's phenotype. CD was measured using Mini-Mental State Examination (MMSE). CD was defined as an MMSE score of ≤24. Physical fitness was evaluated by assessing cardiovascular endurance, muscular strength, mobility, and body composition using 6-minute Walk Test (6MWT), grip strength, gait speed, Timed Up and Go (TUG) test, five times sit-to-stand test (FTST), and phase angle respectively. Depression was assessed using Short Geriatric Depression Scale. To discern differences in physical fitness and depression scores across the groups, an Analysis of Covariance (ANCOVA) was employed, adjusting for potential confounders. Moreover, generalized additive models (GAM) analysis was conducted to explore the non-linear relationships between physical fitness and the status of depression with the risk of cognitive frailty.

Results

Participants with cognitive frailty exhibited a significant decline and non-linear trend in all physical fitness measures and higher depressive symptoms ($p<0.05$) compared to robust group. Further analysis revealed significant decline in TUG, FTST, and 6MWT among participants with CD without frailty ($p<0.05$) compared to robust group. Additionally, participants with frailty without CD showed higher depressive symptoms compared to the robust group ($p<0.001$) and CD without frailty group ($p<0.05$).

Conclusion

Older individuals with cognitive frailty manifested a pronounced decrement in physical fitness coupled with an accentuated presence of depressive symptoms. Significantly, our findings underscore potential vulnerability of older adults with cognitive impairment to experience diminished physical fitness, even without frailty.

Sleep Characteristics and Incident Dementia and All-cause Mortality: The Korean Genome and Epidemiology Study of Middle-aged to Older Participants

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Objective

Sleep disturbance and deficiency have been suggested to have a relationship with the subsequent cognitive decline, including dementia, and mortality in recent studies. The aim of the present study is to examine the associations between poor sleep characteristics and incident dementia, and/or all-cause mortality over 18 years of follow-up through middle-aged to older general population.

Methods

A total 9716 participants of the Korean Genome and Epidemiology Study – Ansan and Ansung (mean age, 52.3±8.9), who have been linked to the Health Insurance Review and Assessment Service national database to assess incident dementia and all-cause mortality over 18 years were analyzed. Sleep characteristics were included: self-reported sleep duration (<6hrs/6-7hrs/7-8hrs(ref.)/8-9hrs/≥9hrs) and symptoms of insomnia (difficulty initiating sleep, difficulty falling back asleep and early morning awakening). In multivariate Cox regression analysis, we adjusted for age, sex, marital status, education level, body mass index, smoking and drinking status, hypertension, diabetes, and depression at baseline.

Results

Among total participants at baseline, 13.1% were 65-69 years of age and 53.0% were women. Difficulty initiating sleep (hazard ratio [HR]=1.20; 95% confidence interval [CI], 1.01-1.43), difficulty falling back asleep (HR=1.26; 95% CI, 1.07-1.47) and early morning awakening (HR=1.22; 95% CI, 1.03-1.44) were associated with greater risk of dementia. In addition, less than 6 hours sleep duration was associated with greater risk of dementia (HR=1.26; 95% CI, 1.08-1.46) compared to 7-8hrs duration. Furthermore, difficulty initiating sleep, difficulty falling back asleep and early morning awakening were associated with greater risk of all-cause mortality (HR=1.37; p<0.001, HR=1.26; p=0.004, HR=1.24; p=0.01, respectively). Furthermore, longer than 9 hours sleep duration was associated with greater risk of all-cause of mortality (HR=1.30; 95% CI, 1.11-1.53) than the 7-8hrs group.

Conclusion

Our findings suggest that various sleep characteristics are prospectively associated with an increased risk of dementia and all-cause mortality among middle-aged or older adults.

Genetic Screening of ANXA11 in Korean Patients with Frontotemporal Dementia Syndrome

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Objective

Pathogenic variants of ANXA11 have recently been identified in patients with amyotrophic lateral sclerosis (ALS) and amyotrophic lateral sclerosis-Frontotemporal Dementia (ALS-FTD) in ALS cohorts. However, it is uncertain how prevalent the pathogenic variant of ANXA11 is in FTD syndrome. Thus, we performed genetic screening of ANXA11 in Korean patients with FTD to investigate the prevalence and the role of ANXA11 in the Korean population with FTD syndrome.

Methods

We searched pathogenic variants of ANXA11 in whole exome database of Korean patients with FTD syndrome. Out of a total of 240 patients, 179 patients had been included in the previous Korean FTD genetic screening studies and the rest 61 patients have currently been enrolled in an ongoing longitudinal study of early onset dementia and family members-FTD (LEAF-FTD).

Results

One pathogenic variant in ANXA11, c.119A>G (p.D40G), was identified in four patients with right-predominant semantic variant primary progressive aphasia (svPPA). One of them initially presented with right predominant svPPA and later progressed to ALS. Among other three patients, one has recently been reported elsewhere. Two of them had family history of dementia in first-degree relatives. One patient carried a pathogenic variant, p.V180I of PRNP as well as p.D40G of ANXA11, however, did not show any clinical features of CJD. Other than p.D40G variant, we found two variants of unknown significance of ANXA 11 in one patient with nfvPPA (c.1336-6C>G) and the other with bvFTD (c.654G>A, p.T218=).

Conclusion

This is the first study of genetic screening for ANXA11 in Asian FTD cohort. Although the phenotypic variation of ANXA11 in FTD or FTD-ALS syndrome remains unclear, our results suggest that p.D40G of ANXA11 may be mainly associated with right predominant svPPA or svPPA-ALS.

What Physical Functions are Associated with Cognitive Decline in Community-dwelling Middle-aged and Older Adults?

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Objective

The aim of this study is to investigate which physical performance is associated with cognitive function in community-dwelling middle-aged and older adults.

Methods

We enrolled 126 subjects (n; male=62; female=64; mean age=67.4±9.5 years) who underwent assessments of cognitive function using the Mini-Mental Status Examination (MMSE) and physical performance, including grip strength, gait speed, the Timed Up and Go test (TUG), the Five Times Sit to Stand Test (5XSST), balance, and the Six-Minute Walking Test (6MWT). The Partial correlation and linear regression models, adjusting for age, sex, and BMI, were used to examine the connection between cognitive function and physical performance.

Results

After adjusting for age, body mass index, and sex, partial correlation coefficients for the 5XSST ($r = -0.232$, $p < 0.05$) and TUG ($r = -0.316$, $p < 0.05$) indicated moderate inverse associations with MMSE scores. The linear regression analysis revealed that higher MMSE scores were significantly correlated with shorter completion times for both the TUG test ($b = -0.186$, $p < 0.05$) and the 5XSST ($b = -0.24$, $p < 0.05$). No significant association were found between MMSE scores and other physical performance metrics in the correlation and linear regression analyses.

Conclusion

The significant and independent association between cognitive function and lower body physical performance and mobility, as demonstrated by benchmarks like the TUG test and the 5XSST, underscores the importance of understanding this relationship when assessing an individual's capacity for sustained independence. A shorter duration in the 5XSST suggests improved lower extremity strength and agility, especially during swift transitional movements, while a reduced time in the TUG test implies enhanced functional mobility and dynamic balance essential for daily activities. These insights are particularly relevant for middle-aged and elderly individuals residing in community settings. Additionally, exploring these lower body functions is believed to be beneficial for community-based dementia and fall prevention.

Association between Metabolic Syndrome and Cognitive Decline over 14 Years Modified by Sex and Inflammation

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Objective

Metabolic syndrome (MetS) is a recognized risk factor for cognitive decline and dementia, but its specific impact on long-term cognitive trajectories remains unexplored. Our study investigated the relationship between MetS and cognitive decline over 14 years, with considerations for sex, age, and inflammation levels.

Methods

Using data from the English Longitudinal Study of Ageing (ELSA), spanning from wave 2 (2004–2005) to wave 9 (2017–2018), MetS was assessed at wave 2 based on NCEP ATP III criteria. Cognitive evaluations included memory (word-list immediate and delayed recall) and executive function (verbal fluency) at each wave. Linear mixed-effect models were employed to examine the association between MetS and cognitive changes, adjusting for age, sex, education, marital status, smoking, alcohol use, and physical activity. Further analyses stratified the data by sex, age, and high-sensitivity C-reactive protein (hs-CRP) levels.

Results

Our analysis encompassed 3,127 participants with complete data. Baseline MetS individuals (N=743, 23.8%) were older, less educated, and less physically active compared to those without MetS. They exhibited a higher prevalence of MetS components, elevated hs-CRP levels, and poorer memory and executive function. In sex-stratified analyses, women with MetS displayed faster memory decline, while men with MetS did not exhibit this pattern. High hs-CRP MetS participants showed greater executive function decline. Age did not show distinct associations. Among MetS components, hypertension was linked to faster delayed recall memory decline in women and high hs-CRP participants, hyperglycemia to delayed recall memory decline in women, and low HDL to executive function decline in women.

Conclusion

Our 14-year study unveiled sex-specific and inflammation-specific cognitive changes associated with MetS. Women with MetS experienced accelerated memory decline, and those with high inflammation exhibited faster executive function decline. Notably, hypertension, hyperglycemia, and low HDL cholesterol independently associated with cognitive decline, especially in women. Further research may elucidate the mechanisms underlying these findings.

Association of Cognitive Function and Depressive symptoms of the Elderly Residents in A Rural Community

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Objective

In general, cognitive function may be affected by mood disorders in demented people. We tried to know the relationship between cognitive function and depressive symptoms in a cross-sectional cohort study of rural community.

Methods

A total of 934 subjects aged 60 and over were recruited in a rural county, located in south east of south Korea from 2007 to 2016. Demographic characteristics, past history of illness were collected by the investigators. K-MMSE (Korean version–Mini Mental State Examination) were checked. The participants also took GDS-S (Geriatric Depression Scale-Short form) by neuropsychologist.

Results

The mean age was 72.14(6.382) and 721(77.2%) of the participants were right handed. 22 percent of the participants were illiterate and 36(3.9%] of the participants were demented. The female participants were 629 which was 67.3% of the whole participants. GDS-S($p<0.001$) score were significantly correlated with K-MMSE score.

Conclusion

These results suggest that depressive symptoms may have significant influence on cognitive function (K-MMSE) in this rural community.

IC-KDA 2023

International Conference of
the Korean Dementia Association