SYMPOSIUM PRESENTATION 3: PHYSICAL AND MENTAL HEALTH

Early prediction and diagnosis of Alzheimer's disease based on Gwangju Alzheimer's and related dementia (GARD) cohort

K. H. Lee (Convener)

Participants: Kun Ho Lee, Jae Gwan Kim, Jungsoo Gim, Sunjae Lee **ISSUE** Alzheimer's Disease (AD) is one of the well-known chronic diseases among older adults. A type of AD that onset over 65 years of age is currently uncurable. As the aging of the population proceeds, the number of people with AD diagnoses and the socio-economic burden on AD both increase. To discover the scientific mechanism underlying AD, we have established the cohort dedicated to AD research named Gwangju Alzheimer's and Related Dementia (GARD) cohort. We collect magnetic resonance imaging (MRI), positron emission tomography (PET), fluid biomarker data, and cognitive test results of local elderly participants. Since 2014, we have gathered over 15,136 population data that could yield valuable results on Alzheimer's Disease in older adults. **CONTENT** The current symposium introduces Alzheimer's bioinformatics research based on our elder population cohort data. Each research focused on 1) AI-based scoring on Visuospatial task, 2) Near-infrared spectroscopy, 3) Genome-wide association study, and 4) Personal microbiome to generate population statistics, which results converge into a single goal, the prediction of AD. **STRUCTURE** In our first talk, Prof. Kun Ho Lee will explain how we implemented artificial intelligence (AI) to predict biomarker pathology and grading complex visuospatial cognitive tasks. The second speaker, Prof. Jae Gwan Kim will demonstrate machine-learning-based AD stage prediction based on prefrontal near-infrared signals of participants. Next, Prof. Jungsoo Gim presents a prediction tool for amyloid PET positivity conversion based on personal genomic information. Finally, Prof. Sunjae Lee will demonstrate a microbiome project that aims to develop a probiotic solution for AD prevention and an oral-microbiome screening kit for detecting AD-risk microbes. **CONCLUSION** The presented talks demonstrate the current stage of AD prevention research based on our dementia cohort data. We believe the implementation of innovative gerontechnology on elderly population data will contribute to the healthy and happy lives of elders by unraveling the hidden causes of chronic diseases like AD.

Keywords: alzheimer's disease, AI, population cohort, near-infrared spectroscopy, genome-wide association study, microbiome

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Prediction of Amyloid β and Tau Pathology using deep learning based artificial intelligence system

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Purpose The pathological cascade of Alzheimer's disease (AD) begins decades before the development of clinical symptoms (Jack et al, 2010). Thus, predicting Alzheimer's before disease onset can minimize the socioeconomic burden and delay the cognitive impairments of patients. The Rey-complex figure task (RCFT) was revisited as the sensitive neurocognitive evaluator that is associated with cerebrospinal fluid amyloid β, tau levels and neurodegeneration observed by magnetic resonance imaging (MRI) (Seo et al, 2021). But the application of these findings is limited in real life. Assessing brain biomarker content with positron emission tomography (PET) is not readily accessible to ordinary patients, and the scoring system of RCFT is unstable due to the interrater gap in scores. To overcome this problem, we propose AI, deep-learning-based solutions for RCFT scoring, and MRI-based PET prognosis. **Method** We obtained 20,040 scanned RCFT images from Gwangju Alzheimer's and Related Dementia cohort in Korea. The images copy, immediate recall, and delayed recall) rated by experienced psychologists were fed into an input for the DL model. DenseNet (Huang et al, 2017) architecture was used as the backbone. Finally, we conducted an external validation with 150 images scored by five experienced psychologists. The PET prognosis platform, NeuroAI, computes PET positivity rate based on T1, T2 Flair image, Apoe4 type, and demographics of patients. **Results and discussion** Our model obtained mean absolute error (MAE) = 1.24 [points] and R-squared (R^2) = 0.977 for 5-fold cross-validation. For the 150 independent test sets, the MAE and R^2 between our model and average scores by five human experts were 0.64 [points] and 0.994, respectively. Our results suggested no fundamental difference between the rating scores of human experts and those of our AI psychologists. Altogether, our work proves the potential of AI usage as a faster and more cost-effective to contribute to screening the early stages of AD.

References

Jack, C.R., Knopman, D.S., Jagust, W.J., Shaw, L.M., Aisen, P.S., Weiner, M.W., ... & Trojanowski, J.Q. (2010). Hypothetical model of dynamic biomarkers of the Alzheimer's pathological cascade. The Lancet. Neurology, 9(1), 119-28.

Seo, E.H., Lim, H.J., Yoon, H.J., Choi, K.Y., Lee, J.J., Park, J.Y., ... & Lee, K.H. (2021). Visuospatial memory impairment as a potential neurocognitive marker to predict tau pathology in Alzheimer's continuum. Alzheimer's research & therapy, 13(1), 167.

Huang G, Liu Z, Van Der Maaten L, Weinberger KQ (2017) in Proceedings of the IEEE conference on computer vision and pattern recognition, pp. 4700-4708.

Keywords: Alzheimer's disease, rey complex figure test, Artificial Intelligence, deep learning, convolutional neural network

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Classification of Alzheimer's disease stages by analyzing prefrontal near-infrared signals during olfactory stimulation with machine learning

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Purpose Alzheimer's disease (AD) is known as a disease caused by the accumulation of beta-amyloid or tau protein in neurons, blocking signal transmission and causing death. Since there is no cure for this disease, early detection is an important aspect of AD (Rasmussen J et al., 2019). It has been reported that the olfactory function decreases earlier than the cognitive dysfunction in AD patients. (Roberts RO et al., 2015). We have previously reported that the brain hemodynamic signals measured by functional near-infrared spectroscopy during olfactory stimulation could classify the stage of Alzheimer's disease based on a statistical model using 98 patients (55 normal, 26 mild cognitive impairments, 16 dementia) (Kim J et al., 2022). In this study, we recruited additional 34 subjects and applied machine learning to find its potential in AD screening. **Method** The existing data from 97 participants were used for internal verification, and 34 new participants' data were used as external verification data. All patients were recruited from the GARD cohort. We applied a statistical method and machine learning algorithm to both datasets. For a statistical model, a linear regression was employed, and a naive Bayes-based machine learning algorithm was chosen as a machine learning algorithm applied for AD screening. **Results and Discussion** A naive Bayes-based machine learning performed better than the statistical method on both internal and external validation datasets. The statistical model reported a classification accuracy of 87% in patients with mild cognitive impairment and Alzheimer's dementia on 97 internal validations and 63% on 34 external validations. On the other hand, naive Bayes-based machine learning algorithm achieved 95% accuracy on internal validation data and 85% accuracy on external validation data suggesting that machine learning has the potential to screen AD from various patient groups better than a statistical model.

References

Rasmussen, J., & Langerman, H. (2019). Alzheimer's Disease - Why We Need Early Diagnosis. Degenerative neurological and neuromuscular disease, 9, 123-30.

Kim, J., Yon, D.K., Choi, K.Y., Lee, J.J., Kim, N., Lee, K.H., & Kim, J.G. (2022). Novel diagnostic tools for identifying cognitive impairment using olfactory-stimulated functional near-infrared spectroscopy: patient-level, single-group, diagnostic trial. Alzheimer's research & therapy, 14(1), 39.

Roberts, R.O., Christianson, T.J., Kremers, W.K., Mielke, M.M., Machulda, M.M., Vassilaki, M., ... & Petersen, R.C. (2016). Association Between Olfactory Dysfunction and Amnestic Mild Cognitive Impairment and Alzheimer Disease Dementia. JAMA neurology, 73(1), 93-101.

Keywords: cognitive impairment, Alzheimer's disease, fNIRS, mild cognitive impairment, machine learning
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Converging multi-modal evidences for the primary prevention of Alzheimer's dementia

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Purpose Predicting risk of Alzheimer's disease for the primary prevention and early intervention. **Method** We investigated the performance of combining multi-modal biomarkers obtained from GWAS study (n=14,000). We first predict the lifetime risk of AD using the ethnicity adjusted SNVs incorporating the prior genome-wide association (GWA) knowledge and predict the onset year for those with high lifetime risk by learning neuropsychological test scores and life-log (sleep quality and daily activity) information. **Results and discussion** When validated with three independent samples, the lifetime risk of AD using the proposed genomic prediction showed 75.3% of average accuracy (max 79.1%) with 74.8% and 73.7% of average sensitivity (max 80.5%) and specificity (73.7%), respectively. For those with high risk, we predicted onset within two years, our deep learning model showed 77.4% of accuracy. Strict blind test and application of the proposed model on GARD cohort shows its validity in application for screening and prevention of AD patients, especially in preclinical stage.

Keywords: genome-wide association study, AD risk prediction
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Systems biology of human microbiome for the prediction of Alzheimer's disease prognosis

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Purpose There are numerous microorganisms dwelling on various parts of our body. The community of those microorganisms has been called microbiome, regarded as our “second genome”. Since birth, microbiome composition changes through lifespan and influences host human physiology. In older adults, an imbalance of the gut microbiome has been reported to initiate harmful inflammation (Ragonnaud and Biragyn, 2021). There have been increasing amounts of evidence that dysbiotic microbiome could lead to neurodegenerative diseases. In Alzheimer’s disease cases, treatment with prebiotic supplements improved AD-like symptoms and shifted the levels of associated biomarkers (Arora et al, 2020). In this presented study, we initiated the in-depth shotgun metagenome study with GARD elderly cohort data. We aim to specify causal microbiome strain associated with AD onset, subsequent screening kit development, and to invent AD-preventing probiotics. **Method** We gather oral, gingival, and fecal samples from 300 participants from the GARD cohort. Obtained samples go through shotgun metagenome sequencing, a way to identify microbiome composition in each sample environment. From those metagenome sequence data, we pinpoint AD-risk oral microbe and test the effectiveness of probiotic supplements. **Results and discussion** Based on in-depth microbiome profiling of shotgun metagenomic data, we identified drastic changes in oral, gingival, and fecal microbiome in patients with Alzheimer’s diseases. In addition, these changes are initiated from the asymptomatic stages of AD patients, thereby observing the possibility of diagnosis of AD early on-set, just using fecal and saliva sampling. We also applied machine learning model to develop a prediction model of AD progression, which would help the early diagnosis of AD patients without invasive measurement of brain functions.

References

Ragonnaud, E., & Biragyn, A. (2021). Gut microbiota as the key controllers of "healthy" aging of elderly people. Immunity & ageing : I & A, 18(1), 2.

Arora, K., Green, M., & Prakash, S. (2020). The Microbiome and Alzheimer's Disease: Potential and Limitations of Prebiotic, Synbiotic, and Probiotic Formulations. Frontiers in bioengineering and biotechnology, 8, 537847.

Keywords: human microbiome, shotgun metagenome, Alzheimer’s disease

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