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Preventive, screening system for early detection of dementia

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Introduction: The diagnosis of dementia is often delayed, which significantly worsens the prognosis. In Hungary, there is no available artificial intelligence algorithm that could help detect early signs of dementia based on the client`s digital behavioral patterns.

Method: We used the PreDEM system for the early-stage assessment of dementia. In the two pilot periods, we gathered and analyzed over 8000 test data in 3 months in 2021 and over 9200 test data in 5 months in 2023. Participants completed the following tests: short international cognitive tests and games, Stroop tests, memory games, and other cognitive games. We created a standardized evaluation system for cognitive games to compare individual game results.

Result: Our results support the effectiveness of PreDEM. There was a significant difference between the results of individuals diagnosed with dementia and those from the healthy population. These differences will be well illustrated by the density functions of the results from various groups that we present. One of the highly significant observations during the study period is that cognitive game engagement notably improves individuals with memory issues.

Conclusion: It can be stated that the PreDEM detected the first, otherwise imperceptible signs of dementia through artificial intelligence-based risk analysis. Early detection is vital as there`s no cure; we must focus on improving conditions and monitoring through trend analysis. There is a need for preventive screening, as there is a clear correlation between preserved cognitive skills in later life stages and a reduced risk of Alzheimer`s disease and dementia.

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The Influence of Apolipoprotein E ε4 and Lipid Profile on Cognitive Function in Mild Cognitive Impairment

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Objective; The aim of this study is to examine the relationship between lipid profiles including total cholesterol (TC), triglyseride (TG), high-density lipoprotein cholesterol (HDL-cholesterol), and low-density lipoprotein cholesterol (LDL-cholesterol) and cognitive function by the occurrence of the apolipoprotein E (APOE) ε4 in the community-dwelling elderly individuals with mild cognitive impairment (MCI).

Methods; The total number of subjects was 203 (77 men and 126 women) who were diagnosed with MCI from a Korean project of "Early Detection of Dementia". Aged 65-85 years were included in this analysis. The eight neuropsychological domain from the Korean version of Consortium to Establish a Registry of Alzheimer's Disease neuropsychological test battery (CERAD-K, NP) were conducted to test subjects. The lipid profiles of all subjects were measured including TC, TG, HDL-cholesterol, and LDL-cholesterol levels and the correlation between the lipid levels and the neuropsychological test scores was analyzed by the occurrence of the APOE ε4.

Result; There was significant correlation between HDL-C and Word List Recall Test (WLRT) of the neuropsychological test score in CERAD-K (NP) in the presence of APOE ε4 (WLRT/HDL-C: r=0.163, p0.05).

Conclusion; The HDL-C level might be correlated with verbal episodic memory domain in CERAD-K (NP) test in the presence of APOE ε4 in community-dwelling elders diagnosed with MCI.

Key Words; Mild cognitive impairment · Apolipoprotein E · high-density lipoprotein cholesterol · Korean version of Consortium to Establish a Registry of Alzheimer's Disease · Cognitive function

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Frontal versus temporal type memory deficit in amnestic mild cognitive impairment; predictive value in the diagnosis of Alzheimer disease using amyloid PET

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Background: Retention-deficit in verbal learning test is attributed to the medial temporal lobe dysfunction and retrieval-deficit to the frontal. We tried to determine whether memory deficit patterns (the retention-deficit amnestic mild cognitive impairment (rtn-aMCI) vs. retrieval-deficit aMCI (rtv-aMCI)) can discriminate amyloid positive Alzheimer disease (AD) from amyloid negative non-AD neurodegenerative diseases. Method: One hundred and seventy-four MCI patients were enrolled who underwent a set of neuropsychological assessments, brain MRI and flutemetamol amyloid PET. All MCI patients were diagnosed using the Petersen criteria. They were divided into the rtn-aMCI (below -1.0SD on both delayed recall and recognition test) and rtv-aMCI (below -1.0SD on delayed recall, above -1.0SD on recognition test) based on Seoul Verbal Learning Test (SVLT). Result: Of 174 patients, 106 were classified as rtn-aMCI group and 68 were as rtv-aMCI. There was no significant difference in the number of patients with positive β–amyloid PET scan between two groups (50.0% in rtn-aMCI vs. 47.1% in rtv-aMCI; $\chi 2 = 0.143$, $p = 0.705$). Forward digit span (6.06 ± 1.4 vs. 5.25 ± 1.6, p 0.001) & backward digit span (3.68 ± 1.2 vs. 3.29 ± 1.4, p 0.05) were lower in the rtv-aMCI group. Word fluency and Stroop tests were not different between them. Conclusion: This study revealed that the temporal type memory deficit pattern in rtn-aMCI patients is not predictive of amyloid positive AD. We should be aware that temporal type memory deficit can also be observed in non-AD neurodegenerative disorders.

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Rapidly progressive dementia: defining “rapid”

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The definition of RPD is widely disputed in published cohorts. A standardized definition is needed to support multi-center studies required to inform the causes of RPD and optimize recognition and management of treatment-responsive causes. We applied the Clinical Dementia Rating® (CDR®)—a standardized, validated dementia staging tool—to diagnose RPD in patients who develop dementia (CDR ≥1) within 1 year or incapacitation (CDR ≥2) within 2 years of symptom onset. Criteria performance was evaluated in patients with suspected RPD enrolled at Mayo Clinic in Florida (MCF: Jacksonville, FL) and Washington University in St. Louis (WU: Saint Louis, MO), and compared with individuals with dementia included within the National Alzheimer’s Coordination Center (NACC) dataset. 155/226 (68.6%) MCF-WU patients and 836/20418 (0.04%) NACC patients met the proposed RPD criteria, with etiologies including Alzheimer disease and related dementias, Creutzfeldt Jacob disease, autoimmune encephalitis, toxic/metabolic disruption, and primary psychiatric disorders. RPD was diagnosed slightly earlier in patients in the MCF-WU (mean±SD: MCF-WU, 0.81±0.81 years) vs NACC cohort (1.18±0.55 years; p0.001), owing to the prospective collection of patient data in a clinical setting. Rates of progression (ΔCDR sum-of-boxes/year) clearly distinguished patients with RPD from non-RPD in both cohorts (MCF-WU, 13.6±5.8 vs 4.7±5.9, p0.001; NACC, 6.7±3.1 vs. 1.7±1.4, p0.001). The proposed definition of RPD rapidly identified patients with distinct rates of dementia progression and diverse causes of RPD across multiple cohorts. Broad application of this definition may support the implementation of multi-center studies in RPD.

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Overdiagnosis of AD by using ALZAS biomarkers in absence of genetic family tree

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Nowadays; It seems to overlook the crucial role of genetic counseling within family trees by emphasizing the sole reliance on simple blood tests for ALZAS biomarkers in diagnosing Alzheimer`s Disease (AD). While blood tests for biomarkers like ALZAS show promise in aiding early diagnosis, they represent just one part of a complex picture, especially within familial contexts.

Genetic counseling serves as a fundamental component in understanding hereditary patterns and potential genetic predispositions within family trees. It delves into intricate details beyond what a blood test can reveal. By examining family medical histories, genetic counselors can identify patterns of inheritance and potential risk factors for AD. They elucidate the nuances of genetic information, providing invaluable insights into the interplay between genetics and disease manifestation.

Relying solely on blood tests overlooks the intricate genetic landscape that shapes an individual`s risk of developing AD. It neglects the significance of familial inheritance patterns and the diverse genetic influences that can contribute to the disease. Genetic counseling doesn`t just focus on biomarkers; it offers a holistic view, encompassing environmental factors, lifestyle choices, and familial genetic nuances.

Genetic counselors offer tailored guidance, empowering individuals with information on risk mitigation strategies, informed decision-making regarding genetic testing, and psychological support through the complexities of genetic information.

In essence, while blood tests for biomarkers like ALZAS hold promise, they are just a piece of the puzzle. Genetic counseling plays an indispensable role in providing comprehensive understanding and personalized insights into AD risk within familial contexts, offering a more nuanced and holistic approach to diagnosis and management.

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Downstream Implications of Targeting Amyloid Protofibrils and Tau as a Predictive Biomarker: Results of a Clarity Subanalysis

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Background: Lecanemab is a monoclonal antibody selectively targeting soluble amyloid beta aggregated species in the brain of patients with Alzheimer's disease (AD). Tau aggregates are also involved in the pathogenesis of AD and correlate with neurodegeneration and severity of symptoms.

Objective: To present biomarker results from Clarity AD, focussing on subgroups stratified by patients' tau levels.

Methods: Clarity AD was an 18-month, double-blind study in patients with early AD or mild cognitive impairment (MCI) due to AD. Participants were randomly assigned (1:1) to lecanemab 10 mg/kg biweekly or placebo. Primary endpoint was change from baseline at 18 months in the Clinical Dementia Rating-Sum-of-Boxes (CDR-SB). Subgroup analysis was conducted in patients stratified by baseline tau levels.

Results: Patients included in the optional tau positron emission tomography substudy (n=342) were grouped by low (SUVr 1.06, n=141), intermediate (SUVr 1.06–2.91, n=191) and high (SUVr 29.21, n=10) tau levels. In the low tau subgroup, lecanemab reduced decline on CDR-SB at 18 months by -0.59 versus placebo (p=0.022); 60% of patients on lecanemab demonstrated improvement and 76% no decline on CDR-SB compared with 28% and 55% on placebo, respectively. In the low tau group, lecanemab showed the highest impact in the medial temporal lobe, a region of early Braak stages, while in the intermediate-high tau group, it impacted progression more broadly.

Conclusions: Lecanemab impacts tau pathology in all patients regardless of tau levels. The low tau subgroup results support earlier treatment with lecanemab.