

# Plasma clusterin as a potential link between diabetes and Alzheimer's disease

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## Abstract

**BACKGROUND** Plasma clusterin is a promising biomarker of Alzheimer's disease (AD). Interestingly, it has also been associated with several metabolic diseases including diabetes mellitus (DM). However, clusterin has not been investigated considering a relationship with both DM and AD.

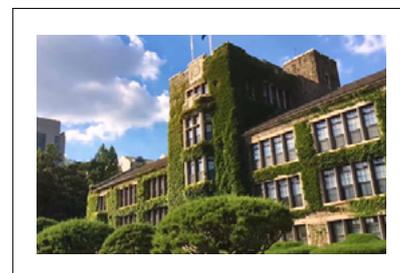
**PARTICIPANTS & METHODS** We aimed to examine the triadic relationship between plasma clusterin, AD, and DM by classifying participants according to the severity of their cognitive (normal cognition (NC), mild cognitive impairment (MCI, AD) and metabolic (healthy control, prediabetes, DM) impairments. We evaluated cognitive and metabolic functions of the participants with neuropsychological assessments, brain MRI, and various blood tests, to explore potential relationships with clusterin.

**RESULTS** Plasma clusterin was significantly higher in participants with AD compared to those with NC and MCI ( $p < 0.001$ ). Participants with metabolic impairments (prediabetes, DM) had increased plasma clusterin levels, compared to healthy controls ( $p = 0.002$ ). A two-way ANCOVA revealed no synergistic, but an additive effect of AD and DM on clusterin levels (interaction;  $p = 0.351$ ). Clusterin was correlated with cognitive scores of the Mini-Mental State Examination (MMSE), delayed word recall, and the Clinical Dementia Rating Sum of Boxes (CDR-SB). Clusterin was also associated with metabolic status indicated by HbA1c, the Homeostatic Model Assessment for Insulin Resistance (HOMA-IR) index, and fasting C-peptide. In addition, we found significant correlations between clusterin and the degree of medial temporal atrophy and periventricular white matter lesions, indicating neurodegeneration and microvascular insufficiency, respectively. Since our multivariate linear regression analysis pointed to metabolic impairment (prediabetes, DM) as the most significant predictor of clusterin, we performed a mediation analysis to further understand the triadic relationship between clusterin, AD, and DM. The result revealed a potential of clusterin as a mediator of the indirect relationship between DM and AD.

**CONCLUSION** These results demonstrate that clusterin is a promising biomarker of DM as well as of AD. Additionally, our data suggest that clusterin may have a role in linking DM with AD as a potential mediator between the two diseases.

## Biography

Dr. Ha has her expertise in evaluation of neurodegenerative disease and passion in improving the health and wellbeing of elderly people. Diabetes mellitus is most common metabolic disease and it is considered a risk factor for Alzheimer disease; however, there is a lack of research on how clusterin levels change in relation to both AD and DM when considered simultaneously. Therefore, we aimed to examine the triadic relationship between plasma clusterin, AD, and DM, expecting to find interactive effects between the two diseases. Hope this study will provide future direction of further research on AD.



## Pubication

1. Ha, J., H. J. Jun, H. Shin, I. J. Chung, E. Park, S. K. Min, and E. Kim. "Predicting Behavior Problems in Korean Preschoolers: Interactions of the Slc6a4 Gene and Maternal Negative Affectivity." [In eng]. *Clin Psychopharmacol Neurosci* 17, no. 2 (May312019):200-10. <https://doi.org/10.9758/cpn.2019.17.2.200>.
2. Jang, Sooah, Eun Woo Kim, Yinhua Zhang, Jimin Lee, So Yeon Cho, Junghee Ha, Hyunjeong Kim, and Eosu Kim. "Particulate Matter Increases Beta-Amyloid and Activated Glial Cells in Hippocampal Tissues of Transgenic Alzheimer's Mouse: Involvement of Parp-1." *Biochemical and Biophysical Research Communications* 500, no. 2 (2018/06/02/2018):333-38.
3. Yun, J. D., J. Ha, S. Kim, H. A. Park, J. Yoo, S. S. Ahn, S. M. Jung, et al. "Predictor of Depressive Disorders in Patients with Antineutrophil Cytoplasmic Antibody-Associated Vasculitis." [In eng]. *ClinRheumatol*(Jul162019). <https://doi.org/10.1007/s10067-019-04657-4>.

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