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Editorial

Structural equation modeling confirms interaction of Alzheimer's disease and vascular disease in hippocampal injury



Overwhelming evidence supports the important role played by vascular disease in pathological aspects of Alzheimer's disease. This was initially demonstrated in the landmark study of Snowdon and colleagues in a group of non-cloistered sisters who participated in a longitudinal study with neuropsychological testing and brain donation [1]. Subsequent studies confirmed the interaction of AD and vascular disease with the mixed form of dementia now considered the most common form [2]. These early observations are reinforced by Tang and colleague [3] in this issue of the Journal, using the extensive clinical, imaging and pathological data in the long running NACC database by performing structural equation modeling with multiple mediation analyses. This computer-intensive descriptive study adds further evidence to the link between Alzheimer's disease and vascular disease. The main new finding in the study is the important role played by hippocampal atrophy in the cognitive decline.

They developed three computer models by increasing the number of factors included in the structural equation algorithms. When all the variables were included the mediating role of hippocampal and brain atrophy was revealed. There are limitations of this type of computer modeling which the authors point out. Primarily the lack of longitudinal data and the lack of understanding of the pathophysiology leading to these prominent changes. The next step is to combine this elegant computer modeling with biomarkers that indicate the pathological processes. The data for this future analysis has been collected by Biomarkers in Vascular Cognitive Impairment (MarkVCID) consortium [4]. The consortium measured biomarkers for multiple important molecular pathways including proteases, angiogenic factors and cytokines. This valuable dataset is currently available for the first year and will shortly have data for two years. There is considerable overlap between the NACC and MarkVCID variables collected that will make it possible to identify potential treatment targets at the molecular level. Studies utilizing data collected by the MarkVCID consortium have shown the importance of inflammation in blood-brain barrier disruption, which most likely is important in hippocampal and brain atrophy [5]. The growing information

available in these and other databases will ultimately provide clues to the next steps in therapy.

Declaration of interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

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