ORAL PRESENTATIONS

Incorporating regional diffusion MRI-based VCID biomarkers in aging and dementia studies

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Background

Alzheimer's disease pathologies and cerebrovascular disease (CVD) are two prominent pathological contributors to the cognitive decline seen with aging and in Alzheimer's disease and Alzheimer's related dementias (AD/ADRD). The burden of AD pathologies (amyloid and tau) is now measurable *in vivo*, but the multiplicity of the CVD processes and the heterogeneity in the mechanisms impedes accounting for them in cognitive aging and AD/ADRD studies. Not accounting for these CVD processes prevents us from identifying vascular contributions to cognitive impairment and dementia (VCID).

Methods

In the last few years, we have conducted a series of studies to understand VCID in the population-based sample of Mayo Clinic Study of Aging (n=1500+ participants, with positron emission tomography (PET) and magnetic resonance imaging (MRI) imaging and longitudinal neuropsychological assessments).

Results

We found that regional diffusion MRI markers specifically quantification of the genu (anterior) of the corpus callosum captures early systemic vascular risk-related changes.[1] Using post-mortem data in a subset of participants with antemortem diffusion MRI, we found that diffusion MRI markers are more specific to the extent of CVD neuropathology seen on post-mortem tissue in comparison to visible lesions on MR.[2] These early systemic vascular risk changes observed in the genu of the corpus callosum were predictive of future brain atrophy and cognitive decline.[3]

Given that FLAIR, T2*GRE/SWI, and diffusion MRI are the commonly acquired images in AD/ADRD studies for CVD assessment, we also evaluated which source of information among WMH, microbleeds, and infarctions would be most useful for capturing VCID. We found that a combination of white matter hyperintensities (WMH) and diffusion changes in the genu of the corpus callosum were key predictors of future cognitive decline across all cognitive domains and aided in capturing the dynamic ongoing white matter damage due to VCID.[4] Further, the information provided by this combination biomarker had a similar impact on cognitive health as cortical amyloid deposition (Figure 1). These results highlight the importance of accurately accounting for VCID in AD/ADRD research and clinical studies.

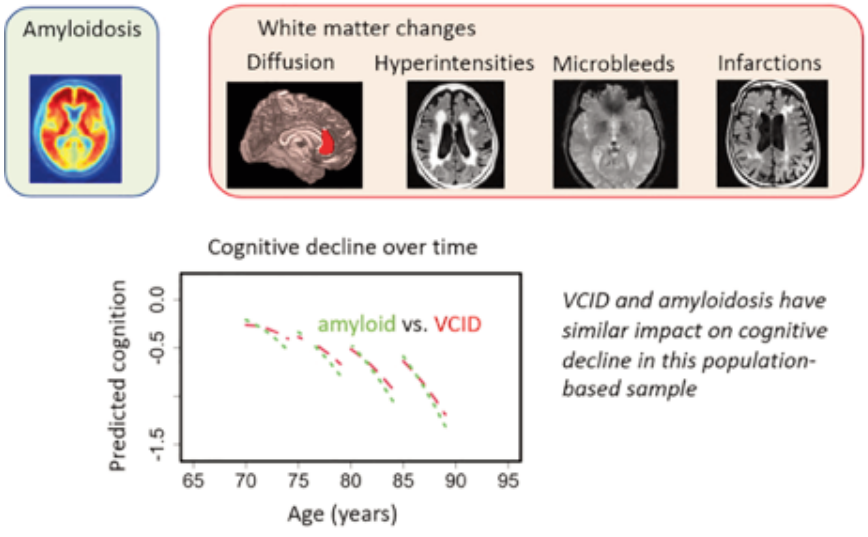

Figure 1. Incorporating and accurately accounting for VCID in AD/ADRD studies is important for identification and prevention of underlying cerebrovascular etiology of cognitive impairment (Figure from Reference 5).

Conclusions

Our current work has been focused on refining the diffusion markers using advanced diffusion MRI models for capturing early changes due to VCID. We have found that advanced models may be additionally useful for distinguishing the underlying substrate of cognitive impairment in older adults.[5] Specifically, VCID can be captured using anterior corpus callosum diffusion changes in comparison to neurodegenerative processes (caused by tau deposition or TDP-43 pathology) can be captured using temporal lobe diffusion changes. The knowledge gained so far coupled with newer quantification and processing methods has brought us closer to VCID biomarkers based on diffusion MRI that can be easily incorporated in AD/ADRD studies. The next step includes validation of these diffusion MRI markers in different populations.

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