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Microstructural white matter changes in Alzheimer's disease

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Alzheimer's disease is a neurodegenerative disorder characterized by cognitive decline. Current study used diffusion tensor imaging data from the Alzheimer's disease neuroimaging initiative 2 databases to examine microstructural white matter changes in individuals with Alzheimer's disease relative to healthy controls.

Introduction:
Alzheimer's disease (AD) is a gradual progressive neurodegenerative disorder in which memory deficit is typically the most salient cognitive symptom. Patients with amnestic mild cognitive impairment (aMCI) are at higher risk of developing Alzheimer's disease (AD) where aMCI is frequently considered as an early stage of Alzheimer's disease (AD). Converging evidence suggests that both Alzheimer's disease (AD) and aMCI are associated with the large-scale functional network dysconnectivity. Especially in the default mode network (DMN) which consists of the posterior cingulate cortex (PCC), precuneus, medial prefrontal cortex (mPFC), and bilateral angular gyrus4. DMN dysconnectivity is often associated with the worsened memory. In parallel grey matter volume (GMV) loss in the medial temporal lobe (MTL) and DMN regions are typically related to the memory decline in Alzheimer's disease (AD) patients.

Moreover, the diffusion tensor imaging (DTI) studies have revealed that the compromised white matter (WM) microstructures particularly in the corpus callosum, cingulum, and fornix, are associated with the memory deficit in Alzheimer's disease (AD). Recently the free-water (FW) imaging using diffusion MRI data was also proposed to address the partial volume effect problem. As a result FW increases have been associated with the extracellular processes such as inflammation and small vascular damage in neurodegenerative diseases. On the other hand the FW-corrected DTI metrics represent the microstructural tissue changes such as degeneration and myelin sheath alterations. However one critical gap is whether and how these brain structural and functional degenerative processes differ in the temporal sequence of their influence on memory performance in the Alzheimer's disease (AD) continuum.

The spectrum of Alzheimer's disease (AD) spans from clinically asymptomatic to severely impaired. Based on the hypothetical Alzheimer's disease (AD) cascade model the influences of the abnormal brain imaging measures on memory in Alzheimer's disease (AD) would be more appropriately considered as a multi-facet process moving along a seamless continuum rather than as discrete clinical stages. Recent evidence suggests that the pathophysiological abnormalities of

To address these gap we examined the stage-dependent associations between multimodal brain measures and memory decline in Alzheimer's disease (AD) continuum using a novel sparse varying coefficient (SVC) model. SVC model allows us to use the one model to simultaneously compare the trajectories from multiple brain measures. Furthermore the unlike conventional linear models in previous studies, SVC model does not assume as a constant linear association between the brain measures and memory performance across stages. Instead it allows the association to vary non-linearly with dementia severity. Specifically based on the prior evidence that WM microstructural abnormalities and functional network degeneration might occur earlier than the MTL atrophy in Alzheimer's disease (AD). We hypothesized that the influence of WM microstructural abnormalities and DMN functional dysconnectivity on memory impairment would take place in the aMCI stage while the influence of MTL atrophy would be more prominent later.

Methods:
Participant's data were collected from 23 individuals with Alzheimer's disease and 35 similarly aged controls. Diffusion weighted images were corrected for distortions related to eddy currents. Fractional anisotropy radial and mean diffusivity maps were also created using the digit and input into tract-based spatial statistics. Individuals with Alzheimer's disease were compared to controls.

The methods includes the Ethics approval and consent to participate, Participants, Image acquisition, Diffusion MRI data pre-processing, Free-water imaging method, Voxel-based morphometry, Functional image pre-processing, Functional connectivity analyses, Statistical analyses.

Results:
Tract based spatial statistics revealed that individuals with Alzheimer's disease had reduced fractional anisotropy and increased mean and radial diffusivity in left corticospinal tract, right and left anterior thalamic radiation, minor and major forceps relative to controls. In the right corticospinal tract, we only saw reduced fractional anisotropy and increased radial diffusivity relative to controls.