

Supplementary Material

Microstructural Neurodegeneration of the Entorhinal-Hippocampus Pathway along the Alzheimer's Disease Continuum

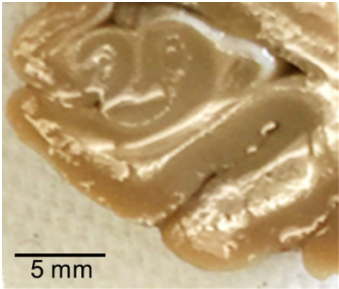
Supplementary Table 1. Summary of demographics and pathological findings in the brain specimens

	Non-AD	Preclinical AD	AD dementia
Demographics			
Age	22	68	93
Sex	Man	Woman	Man
Race	White	White	White
Height	6'	5' 4"	5' 8"
Body weight	174 lbs	112 lbs	158 lbs
Clinical Dementia Rating	0	0	3
Pathology			
Postmortem interval to fixation	20 h	8.5 h	28.5 h
Postmortem interval to image scan	280 days	352 days	233 days
Brain weight	1,520 g	1,210 g	1,290 g
Gross findings	Normal	Normal	Global atrophy
CERAD neuritic plaque score	N.A.	B	C
Thal phase of amyloid- β	N.A.	3	5
Braak stage of neurofibrillary tangles	N.A.	IV	VI
Pathological diagnosis*	Not AD pathology	Intermediate AD pathology	High AD pathology

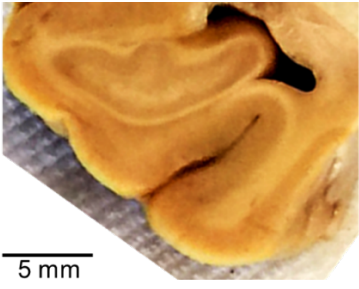
AD, Alzheimer's disease; CERAD, Consortium to Establish a Registry for Alzheimer's Disease.

*National Institute on Aging-Alzheimer's Association guidelines for the neuropathologic assessment of Alzheimer's disease (Montine et al. (2012) *Acta Neuropathol* **123**, 1-11.)

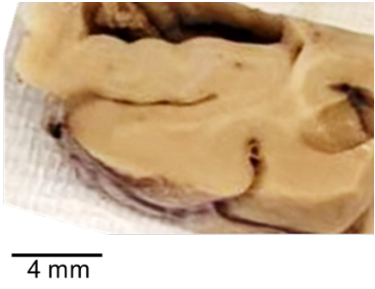
Supplementary Figure 1. Gross finding of the brain specimens



Non-AD

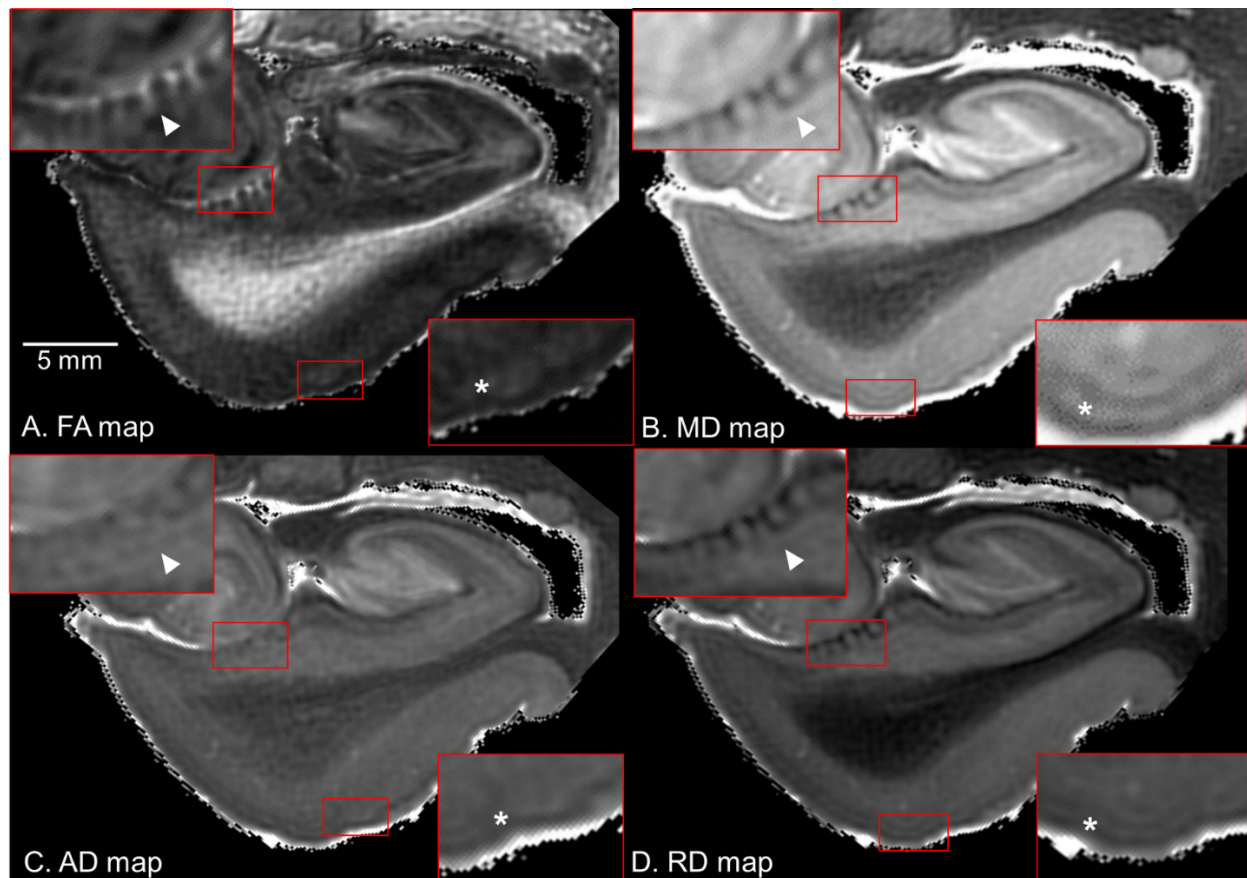


Preclinical AD



AD dementia

Supplementary Figure 2. Coronal panels of the left entorhinal cortex in non-Alzheimer's disease brain tissue. A) Fractional anisotropy (FA) map. B) Mean diffusivity (MD) map. C) Axial diffusivity (AD) map. D) Radial diffusivity (RD) map. The red bounding boxes are 5 \times magnified to visualize the perforant pathway on the presubiculum (left-upper panel) and the entorhinal layer II islands (right-lower panel). Arrowheads point to myelinated fibers in the presubiculum and asterisks denote the entorhinal layer II cortices (A–D). Note that these cortical substructures are clearly discernible in the FA and MD maps.



Supplementary Figure 3. Entorhinal layer II in fractional anisotropy (FA) and mean diffusivity (MD) maps. A, B) The red bounding areas are high FA values of >0.2 . The yellow bounding areas are high MD values of $>1.25 \text{ mm}^2/\text{s} \times 10^{-3}$. Note that neuron-sparse inter-islands, which surround neuronal cells and are filled with myelinated fibers, appear bright on the FA map. Meanwhile, areas occupied by neuronal cells and intercellular matrices appear bright on the MD map.

