familiar objects") was associated with EC tau (r=0.317, p=0.018) and item 13 ("Making decisions about everyday matters") was associated with ITL tau (r=0.296, p=0.028). **Conclusions:** A mixture of language, executive function, and memory informant concerns as well as memory and executive self-concerns were most strongly associated with tau deposition. These findings suggest that concerns across both memory and non-memory domains are important markers of pathology. Given that the CCI-20 is relatively short and easy to administer, this measure may be useful to include in future studies. References: [1] Buckley et al. (2017) JAMA Neurology. [2] Jessen et al. (2010) Arch Gen Psychiatry.

P2-460 A STUDY OF AMPLITUDE OF LOW-FREQUENCY FLUCTUATION OF FUNCTIONAL MRI IN MILD COGNITIVE IMPAIRMENT

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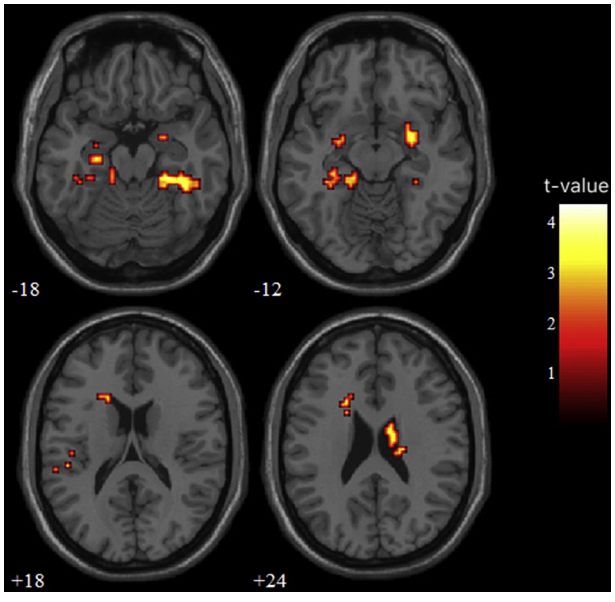
Background: Alzheimer's disease (AD)is the most common cause of dementia in the aging people. The early diagnosis of the AD is very important to slow the progression and improve the prognosis of the disease. At present, most researches focus on the mild cognitive impairment (MCI) which is considered as the preclinical stage of AD. **Methods:** Fifty patients with MCI and 50 normal controls were recruited. All subjects were examined by fMRI to analyze the difference of resting-state brain function between MCI and normal controls based on the ALFF method. **Results:** Compared with the normal controls , ALFF in the bilateral parahippocampal gyrus, bilateral caudate nucleus, left putamen and left insula decreased in MCI group. No increased region is found. **Conclusions:** The activity of bilateral parahippocampal gyrus and some cognitive related subcortical structures decreased in the resting-state fMRI. The findings in left insula reflect some changes in brain activity in MCI.



P2-461 ENTORHINAL TAU PATHOLOGY IS ASSOCIATED WITH WHITE MATTER ABNORMALITIES IN UNCINATE FASCICULUS IN PRECLINICAL AUTOSOMAL DOMINANT ALZHEIMER'S DISEASE

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Background: Amyloid pathology is thought to accelerate tau propagation via neuronal connections in individuals at high risk for Alzheimer's disease (AD). Carriers of AD-causing mutations have elevated levels of amyloid pathology several years before tau accumulation. We hypothesized that the earliest tau pathology will be associated with connectivity abnormalities in the uncinate fasciculus, a tract innervating the entorhinal cortex. Further, we examined the association between white matter abnormalities, age and cognitive performance. **Methods:** 15 non-demented carriers from the Colombian-kindred (age range =28-45 years, Figure 1) underwent PiB-PET, Flortaucipir- FTP PET, diffusion tensor imaging (DTI) and memory testing (CERAD Word List Learning). The DTI-data were processed with TRACULA (FreeSurfer), tract of interest was the uncinate fasciculus (UF) and the control tract was the angular cingulum bundle (CB). Regional FTP was measured in entorhinal (EC) and inferior temporal (IT, control region) cortices. PiB was measured in a neocortical aggregate region. We performed Spearman's rank correlations (also partialling out age) to investigate associations between tau, diffusion metrics and memory. **Results:** Higher levels of left EC tau pathology were associated with higher axial diffusivity (AxD), higher mean diffusivity (MD) and higher radial diffusivity (RD) in the UF in the carriers (Figure 2).

	Carriers (n=15) median (IQR)
Age	35.75 (9.75)
Education	11 (5)
Sex (Females, n (%))	9 (60%)
Amyloid burden (DVR)	1.25 (0.26)
EC Tau (SUVr)	1.46 (0.65)
MMSE score	29 (1.5)
WLL delayed recall	7 (3)

Note: abbreviations: IQR = interquartile range, DVR = distribution volume ratio, EC = entorhinal cortex, SUVr = standardized uptake value ratio, MMSE = Mini-Mental State Examination, WLL = word list learning

Figure 1. Demographics of the carriers.

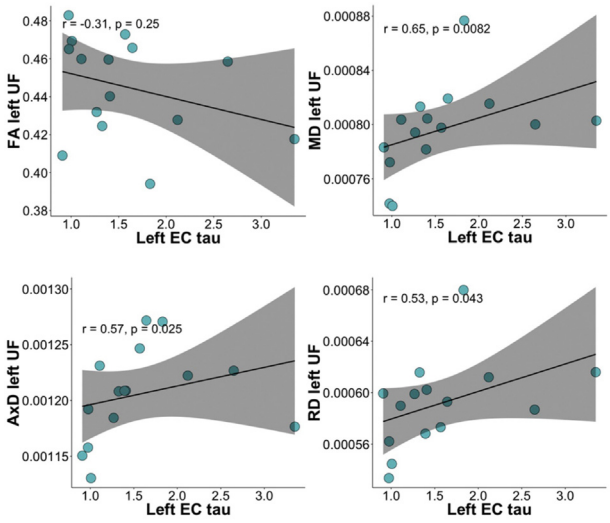

Figure 2. The association between entorhinal tau pathology and diffusion in the uncinate fasciculus in preclinical autosomal dominant Alzheimer's disease

Note: the interaction group by EC tau pathology on tract diffusivity is plotted and statistical significance for the interaction is provided in the panels (corrected for age, robust regressions). Note the limited range in tau pathology in the non- carriers. Abbreviations: FA = Fractional Anisotropy, MD = Mean Diffusivity, AxD = Axial Diffusivity, RD = Radial Diffusivity, EC = Entorhinal cortex, UF = uncinate fasciculus

The associations for MD and RD remained significant after controlling for age (r=0.55,p=0.04; r=0.58, p=0.03 respectively). Spatial analyses showed that group differences in the relationship between EC tau and UF diffusion occurred close to the EC (Figure 3). No associations were found for the right side or the CB tract or IT

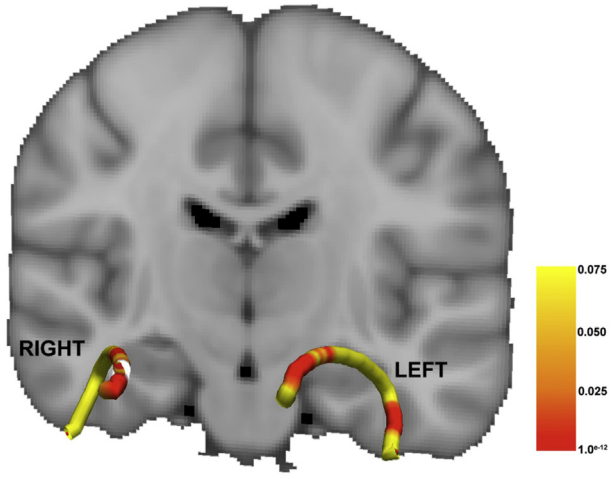

Figure 3. spatial distribution of the group differences of the association between entorhinal tau pathology and uncinate fasciculus diffusivity

Note: for each voxel along the center of the tract, we plotted the p-values (see scale bar) for the Spearman's rank correlations between entorhinal tau and mean diffusivity of the uncinate fasciculus in carriers. Red/orange voxels indicate where the interaction was significant at $p < 0.05$. Consistent with figure 2, we observed mostly left-sided effects. The sagittal plane view was slightly rotated along the z-axis for optimal viewing of the morphology of the tracts.

tau (all $p>0.05$). Left UF diffusivity did not correlate with memory performance or MMSE scores (with or without controlling for age, all $p>0.05$). **Conclusions:** These results suggest that EC tau pathology in PSEN1 E280A mutation carriers is associated with diffusion abnormalities in connected tracts, several years before clinical onset. They also suggest that tau may propagate via neuronal connectivity rather than proximity. Larger samples sizes, including a control group, will be necessary to investigate differences between carriers and non-carriers for the interaction between white matter and tau pathology on memory performance.

P2-462 UNBIASED ASSESSMENT OF GLOBAL AMYLOID LOAD AS DETERMINED BY VOXEL-WISE RECEIVER OPERATING CHARACTERISTIC ANALYSIS

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Background: Recent efforts have focused on characterizing individuals as amyloid positive or negative in order to enrich disease-modifying clinical trials. However, current Aβ dichotomizations ignore the regional distribution of amyloid pathology, which may have important implications for clinical progression. In this study, we investigated the regional patterns of amyloid deposition that can optimally differentiate between AD patients and controls. **Methods:** We assessed cognitively normal (n=302), and AD (n=224) individuals who underwent [^{18}F]Florbetapir PET, cognitively normal (n = 26) and AD (n = 35) individuals scanned with [^{11}C]PiB and cognitively normal (n = 30) and AD (n = 30) scanned with [^{18}F]AZD4694. To identify the brain regions that optimally differentiate controls from AD patients, we conducted a ROC curve in every brain voxel. Then, parametric maps of area under the curve were generated for each amyloid imaging agent (Figure 1). Area under the curve values were highest in clusters in the precuneus, posterior cingulate, lateral temporal, and medial prefrontal cortices, as well as the striatum. Next, to determine if amyloid burden in these structures is related to outcome measures related to disease severity, we conducted linear regressions assessing the relationship between amyloid burden from AD signature regions and the standard neocortical composite mask and brain metabolism as assessed by [^{18}F]FDG uptake in MCI (n = 502). **Results:** In MCI subjects, we observed stronger relationships between [^{18}F]FDG uptake and amyloid in AD signature regions (adj R2=0.27, p=6.74-5) than with global amyloid burden (adj R2=0.25, p=0.005). We furthermore observed a more widespread pattern of metabolic decline (FDR corrected at 0.05) when amyloid was assessed in the AD signature regions (Figure 2). **Conclusions:** Our results suggest that the regional distribution of amyloid pathology plays a role in AD, which is overlooked by global amyloid measurements. Our results further suggest that the optimization of masks as proposed here may increase the sensitivity to detect amyloid-related metabolic or cognitive dysfunction in clinical trials.