IC-P-030 CONNECTIVITY OF THE LEFT FRONTAL CORTEX ATTENUATES DETRIMENTAL EFFECTS OF CSF-TAU ON MEMORY IN PRECLINICAL AND CLINICAL ALZHEIMER'S DISEASE

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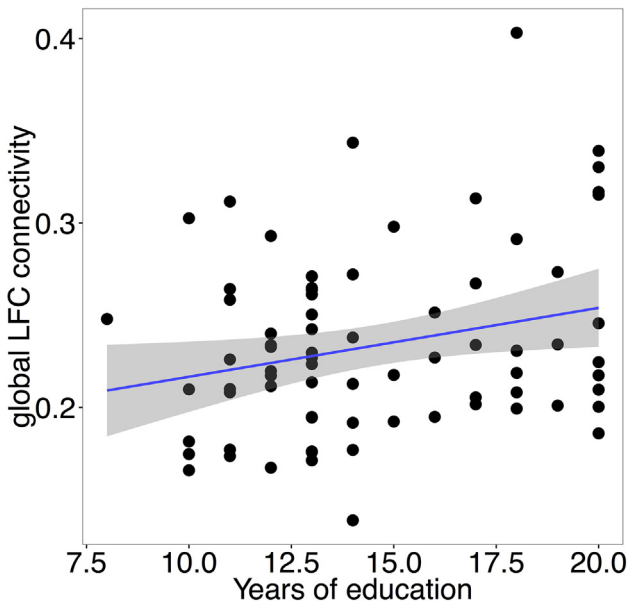
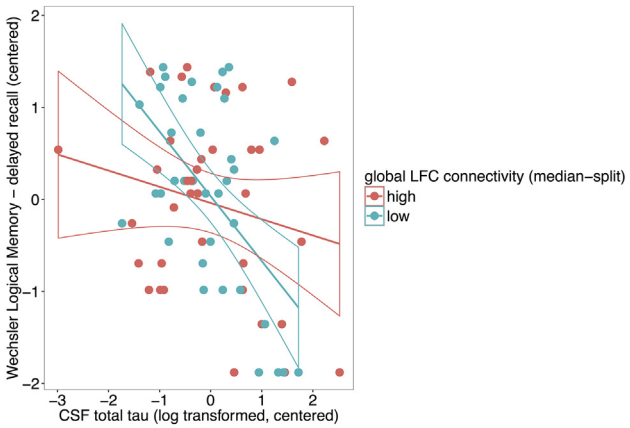
Background: Cognitively normal (CN) subjects with subjective cognitive decline (SCD) and emerging amyloid pathology are at increased risk of Alzheimer's disease (AD). The ability to maintain cognition in the face of beginning neurodegeneration (ie. cognitive reserve) may be critical for the clinical progression in subjects at increased risk of AD. The aim here was was to test functional network characteristics that confer higher reserve across the early clinical spectrum of AD. Specifically, based on our previous findings in prodromal AD showing that global functional connectivity of a left frontal cortex hub (gLFC-connectivity) was associated with higher reserve (Franzmeier, Neurology, in press) we hypothesized that: 1) higher education, a protective factor, is associated with higher gLFC-connectivity 2) higher gLFC-connectivity attenuates detrimental effects of tau pathology on memory performance in preclinical and clinical stages of AD. **Methods:** We included 75





Ab+ individuals in different AD stages (25 CN, 23 SCD, 14 Mild Cognitive Impairment (MCI), 13 AD Dementia), as well as 50 Ab- individuals (24 CN, 17 SCD, 9 MCI) all recruited within the German DELCODE study on biomarker changes in AD. GLFC-connectivity was computed as the average resting-state fMRI-connectivity between an 8mm spherical LFC-ROI (BA6/44) and each grey matter voxel. Using linear regression stratified by Ab-status, we tested whether education predicted higher gLFC-connectivity. Next, we tested whether gLFC-connectivity moderates the association between CSF-tau and the Wechsler Logical Memory delayed recall score. All regression models were controlled for age, gender and diagnosis. **Results:** Greater education predicted higher gLFC-connectivity in Ab+ (p=0.031; Figure 1) but not Ab-. The interaction gLFC-connectivity x CSF-tau was significant (p=0.027) in Ab+, such that at higher gLFC-connectivity the association between higher CSF-tau and memory impairment was attenuated (Figure 2). When tested separately in preclinical (CN-Ab+ & SCD-Ab+) and clinical (MCI-Ab+ & AD dementia) groups, the interaction remained at trend level significance (preclinical: p=0.067; clinical: p=0.059), suggesting compensatory effects of gLFC-connectivity on Tau pathology already in preclinical AD. No interaction was found in Ab- participants. **Conclusions:** Higher connectivity gLFC-connectivity is a neural substrate of CR that allows compensating detrimental effects of tau pathology on memory already in CN and SCD participants.

IC-P-031 INTRINSIC CONNECTIVITY NETWORKS IN POSTERIOR CORTICAL ATROPHY: A ROLE FOR THE PULVINAR?

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Background: Amnestic Alzheimer's disease (AD) is characterized by disrupted default mode network (DMN) connectivity with corresponding increased salience network (SN) connectivity. Posterior