WHITE MATTER MICROSTRUCTURE AND AMYLOID AGGREGATION IN COGNITIVELY HEALTHY, ELDERLY IDENTICAL TWINS

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stress adaptation. Given the pernicious effects of Alzheimer's disease (AD)-related neurodegeneration on functional capacity of multiple brain networks, AD pathophysiology may have implications for stress adaptation, which relies on multiple networks that coordinate physiological response and recovery from stressors. **Methods:** In the current study, we examined the relationship between self-perceptions of stress adaptation and the neurobiological response to a laboratory model of stress adaptation in amnestic mild cognitive impairment (aMCI), a group at high risk for AD. We assessed self-perceptions of stress adaptation with the Perceived Stress Scale, which provides subscale measures identified in prior work as perceived helplessness, and self-efficacy. At a subsequent laboratory fMRI visit, we indexed neurobiological stress adaptation by assessing and comparing functional network connectivity at baseline and immediately following, and after recovery from, cognitive challenges. **Results:** The aMCI group and cognitively healthy controls did not differ in neurobiological acute stress recovery (indexed by similarity in neural patterns at baseline and after recovery from cognitive challenges). However, compared to controls, the aMCI group had significantly lower scores on perceived self-efficacy with regard to stress. Notably, higher perceived self-efficacy was associated with greater acute stress recovery in controls, but not among older adults with aMCI. **Conclusions:** These findings suggest that the process of stress adaptation may be compromised in the development of AD.

P1-418 WHITE MATTER MICROSTRUCTURE AND AMYLOID AGGREGATION IN COGNITIVELY HEALTHY, ELDERLY IDENTICAL TWINS

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Background: Lack of effective predictive models and/or treatments for Alzheimer's Disease (AD) has led a growing movement towards better characterization of pre-clinical stages. One currently established biomarker is positron emission tomography (PET) measured amyloid β load. Here, in a genetically informative population of cognitively healthy, elderly identical twins, we compared this biomarker to a promising new candidate; white matter (WM) integrity measured by diffusion tensor imaging (DTI). **Methods:** Eighty-eight genetically identical twin-pairs and 14 individual twins (n=190, mean age(SD)= 70 (7.5)) were selected from the EMIF-AD PreclinAD study. Aβ load, as a measure for amyloid aggregation, was quantified from [18F] Flutemetamol PET scans. Regional measurements of fractional anisotropy (FA) and mean diffusivity (MD), obtained with tract-based spatial statistics (TBSS) from FMRIB's Software Library (FSL), were used as measures for WM integrity. Within-subject associations between amyloid aggregation and WM integrity were estimated using generalized estimating equations, correcting for twin dependency. A possible shared etiology between amyloid aggregation and WM integrity was further explored using a cross-twin cross-trait (CTCT) design, testing whether amyloid aggregation in a twin could predict WM integrity in the co-twin. Analyses were adjusted for age, sex and intracranial volume. **Results:** Amyloid aggregation predicted trends in increased FA and decreased MD. Regions of interest (ROIs) that met p$\leq$0.05 (uncorrected) are listed in table 1. After Bonferroni correction for multiple comparisons (0.05/23 tested ROIs=0.002) our finding that amyloid aggregation was negatively associated with MD in the Corpus Callosum body remained significant (β=-0.188, p=0.001). Results from CTCT analysis were not significant. **Conclusions:** Our findings suggest that WM changes are potentially informative of pre-clinical AD stages. A longitudinal study is currently underway to confirm this. Interestingly, the present association with decreased MD suggests enhanced WM microstructure with amyloid aggregation in our unaffected population. This contradicts earlier studies in AD patients that reported increased MD with increased amyloid aggregation. A tentative explanation may be that there is a mechanism of WM compensation active during early amyloid pathology which breaks down at more advanced stages. Our data do not support a possible shared etiology between amyloid aggregation and WM integrity.

Table 1
WM regions showing trends of increased FA and/or decreased MD with increasing amyloid β load

Region	Fractional anisotropy (FA)		Mean diffusivity (MD)	
	β	p	β	p
Whole brain	0.091	0.050		
Corona Radiata (anterior)	0.137	0.009		
Corona Radiata (superior)			-0.096	0.009
Corpus Callosum (body)	0.168	0.006	-0.188	0.001*
Fornix (column & body)	0.113	0.041		
Fornix (cres stria terminalis)	0.163	0.003		

* significant at Bonferroni-corrected p<0.002.

P1-419 USING A BRAIN NETWORK APPROACH TO PREDICT GENETIC MUTATION IN INDIVIDUAL PATIENTS WITH FAMILIAL FRONTOTEMPORAL DEMENTIA

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