Smaller Social Networks in Preclinical Alzheimer's Disease Relate to Default Mode and Limbic Network Atrophy

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INTRODUCTION

Accumulation of Amyloid-β in the brain is a widely used biomarker in diagnosing Alzheimer's Disease (AD)

- AD is a neurodegenerative disease characterized by deficits in episodic memory as well as changes in language, visuospatial processing, and executive functioning during its early stages.
- AD biomarkers include the Apolopoprotein E4 (*APOE4*) allele, a potent genetic risk factor, and amyloid PET imaging, which can detect abnormal accumulation of amyloid prior to symptom onset.
- Amyloid positivity can predict AD onset up to 30 years.[1]
- A cognitively normal older adult who is amyloid positive has a strong chance of developing AD and is considered in the preclinical stages of AD.[2]
- Structural and functional changes in the default mode network are characteristic of AD in the clinical and preclinical phases and are accompanied by increased connectivity in the salience network, a system that supports emotion.

Emotional Changes May Also Be Present in Preclinical AD

- Cognition is typically studied in preclinical groups, but there is an indication that changes in emotion might be common.[3]
- Previous work has shown certain forms of empathy such as emotional contagion[3] are enhanced in AD, but little is known about emotion and social behavior in the preclinical phase of the disease.

STUDY OBJECTIVE

- We examined whether preclinical AD pathology is related to the size of one's social network and its association with brain structures previously shown to be impacted in early AD and associated with socioemotional functioning.

METHODS

Participants

- Participants were volunteers that underwent assessment of neurological, cognitive, behavioral, and emotional functioning, which confirmed they were free of neurological and psychiatric disorders.

	Amyloid Negative	Amyloid Positive	*p*
N	86	23	
Age	74.4 (5.8)	74.8 (7.2)	.97
Sex (M/F)	39/47	12/11	.73
Education	17.5 (2.1)	17.2 (1.7)	.53
APOE (+/-)	71/15	15/8	.13
Mini Mental State Exam	29.2 (1.0)	29.4 (0.8)	.30

METHODS

Measures

Socioemotional Functioning

- Participants completed the Social Network Index, a questionnaire that measures the size of social networks by quantifying the number of people with whom a participant interacts on a regular basis.

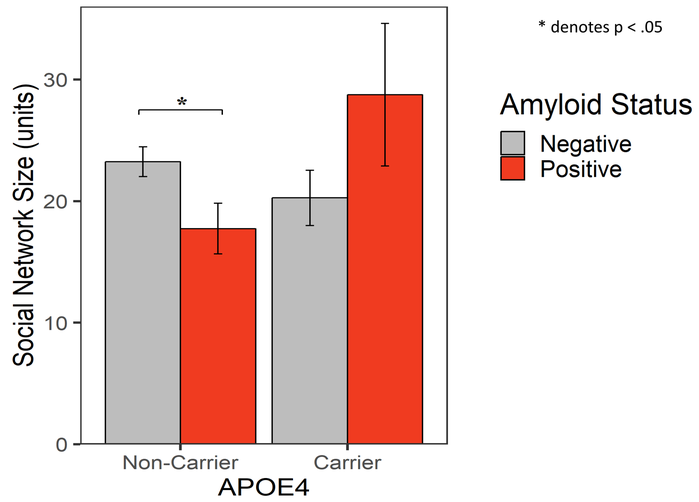
Genotyping

- Genomic DNA was extracted from peripheral blood using standard protocols. *APOE* genotyping was conducted using a TaqMan Allelic Discrimination Assay.

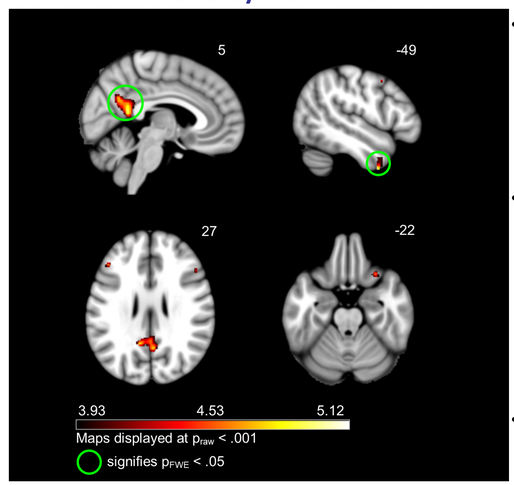
Neuroimaging

- Participants underwent an MRI scan within one year of completing the Social Network Index questionnaire. Participants were scanned with either a 3T scanner at the UCSF Neuroscience Imaging Center or a 4T scanner at the UCSF Veterans Affairs Medical Center.

RESULTS: Social Networks are Smaller in APOE4-Negative Healthy Adults with Preclinical Alzheimer's Disease



RESULTS: Smaller Social Networks in Preclinical Alzheimer's Related to Smaller Gray Matter Volume



- Smaller social network size was associated with smaller volume in the bilateral precuneus/ posterior cingulate cortex and left temporal pole at pFWE < 0.5.
- At a more relaxed threshold of p_uncorrected < 0.001, smaller volume of right orbitofrontal cortex, anterior insula, and bilateral middle and frontal gyri were also associated with smaller social networks in preclinical AD
- All analyses controlled for age, sex, *APOE4* status, and total intracranial volume.

DISCUSSION

Changes in Social Behavior Precede Cognitive Symptoms in Preclinical AD

- Amyloid burden in preclinical AD may contribute to subtle behavioral and emotional shifts that result in a decline in social network size.
- Social network size declining in healthy older adults with amyloid burden cannot be attributed to factors such as cognitive ability, age, or gender (none of which differed between the groups) nor the knowledge of one's amyloid status.

Smaller Social Network Size in Preclinical AD May Reflect Early Atrophy in Memory- and Emotion-Relevant Brain Systems

- Atrophy in brain regions included in the default mode network, as well as regions relevant to emotional regulation, were found to be associated with smaller social network sizes in preclinical AD.
- The findings together suggest that it is possible that the increased sensitivity and vulnerability to negative emotions found in preclinical AD also increases the burden of maintaining larger social networks.

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