

The association between amyloid and tau protein burden and representational similarity in the amygdala's reactivity to negative and neutral stimuli in individuals at risk for Alzheimer's disease



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Background

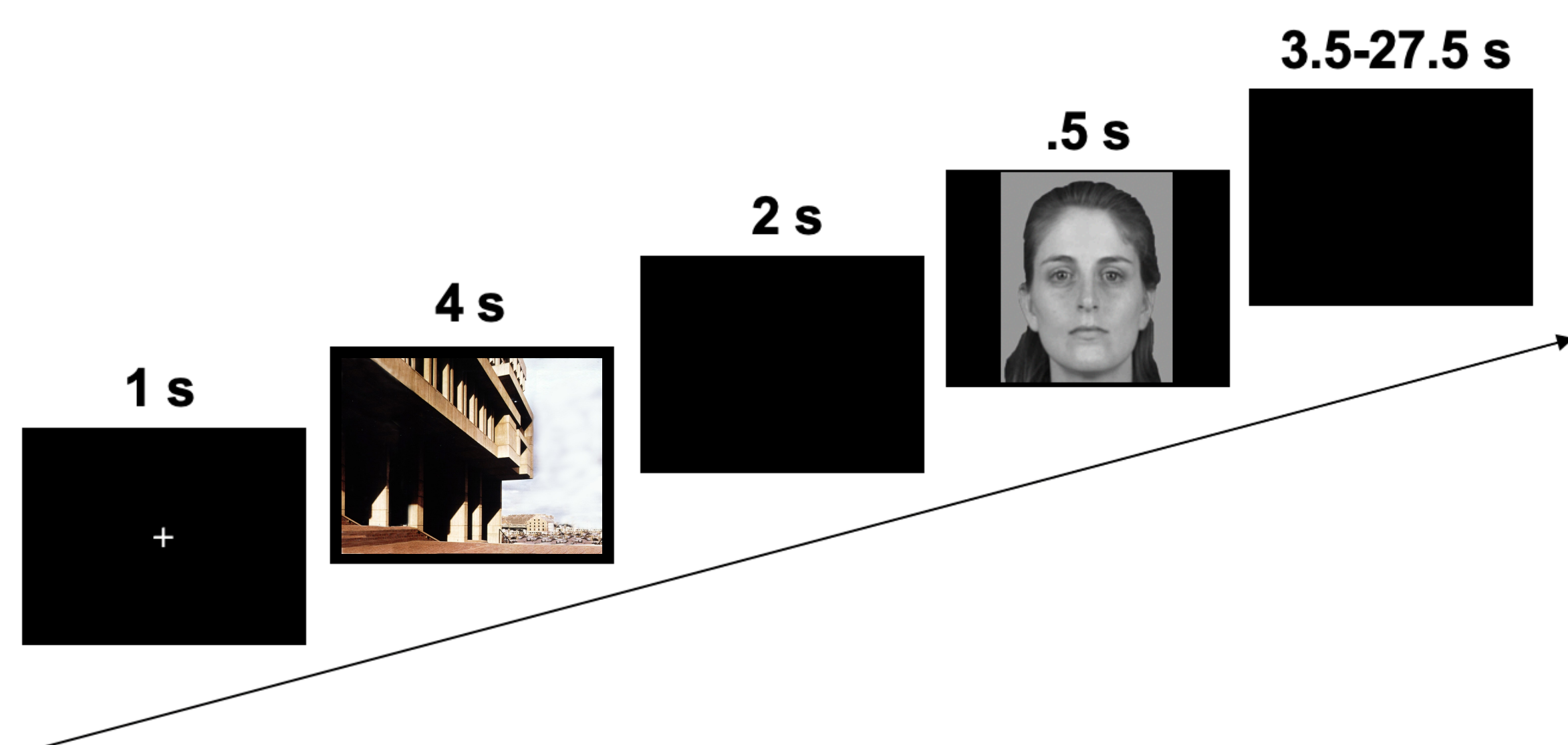
- Older adults at risk for Alzheimer's disease may show emotional differences before they exhibit cognitive decline (Fredericks et al., 2018). A greater degree of neuroticism, which suggests greater sensitivity to negative emotion, has been associated with a higher risk of Alzheimer's dementia (Johansson et al., 2014).
- Amyloid and tau work together to drive healthy neurons into the diseased state.
- Existing studies suggest a relationship between self-reported emotional reactivity and amyloid burden, which is a crucial biomarker in predicting the development of Alzheimer's disease. For example, emotional reactivity, as measured by the revised NEO Personality Inventory, increases with age in adults who are later found to be amyloid-positive (Fredericks et al., 2018).
- It is unclear whether amyloid and tau burden are related to brain reactivity to emotional stimuli in individuals at risk for Alzheimer's disease.

Methods

- Participants: People at risk for Alzheimer's disease from the Wisconsin Registry for Alzheimer Prevention.

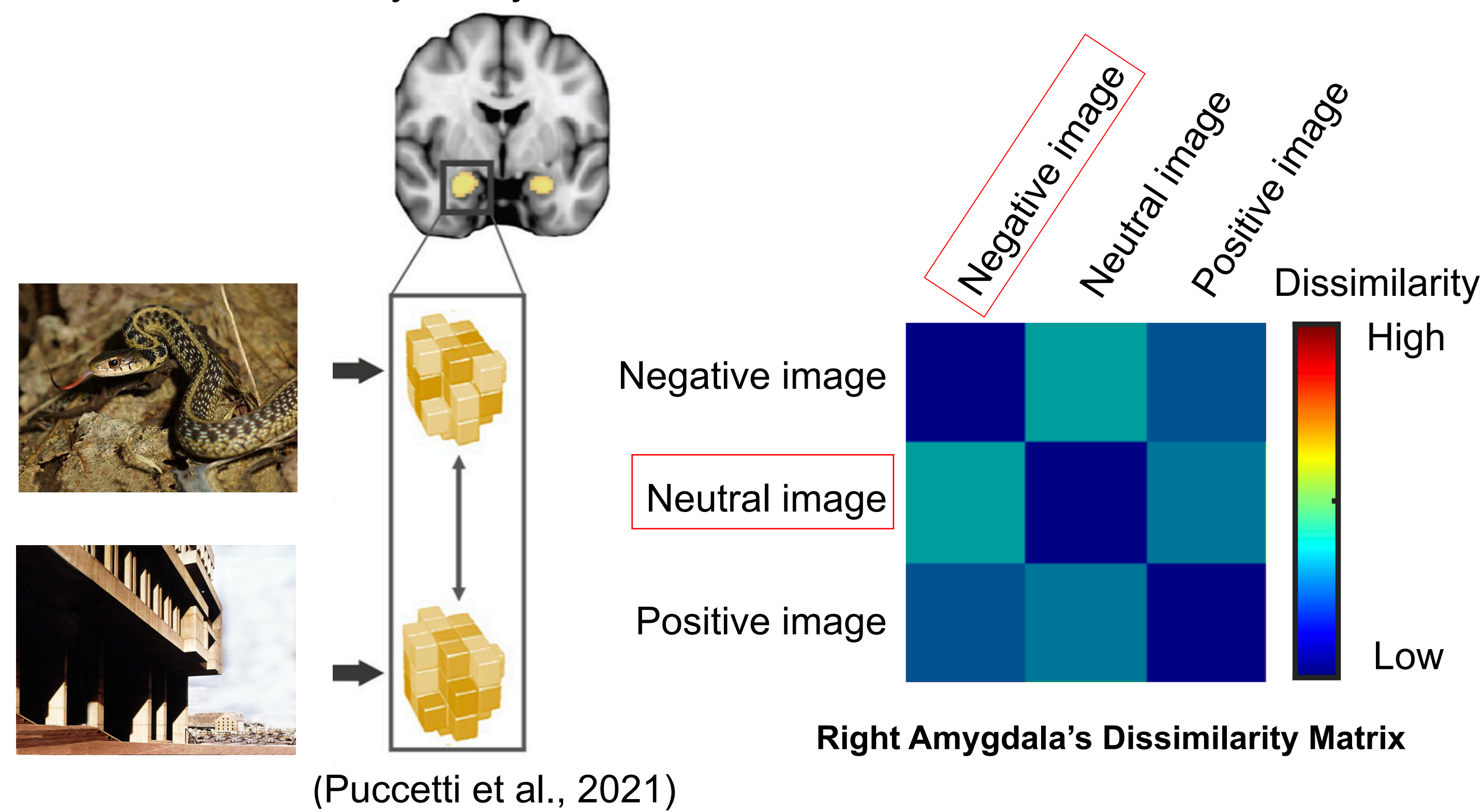
Participant Characteristic	All	Amyloid Negative (A-)	Amyloid Positive (A+)	Tau Negative (T-)	Tau Positive (T+)	Amyloid and Tau Positive (A+T+)
Sample Size	81	70	11	73	8	4
Mean Age	66.56	66.53	68.57	66.33	71.07	69.25
%Female	69%	69%	73%	67%	88%	100%
%BIPOC	6%	6%	9%	7%	0	0

- Task fMRI



- 90 trials: 30 negative, 30 neutral, 30 positive emotional images presented followed by a neutral face.

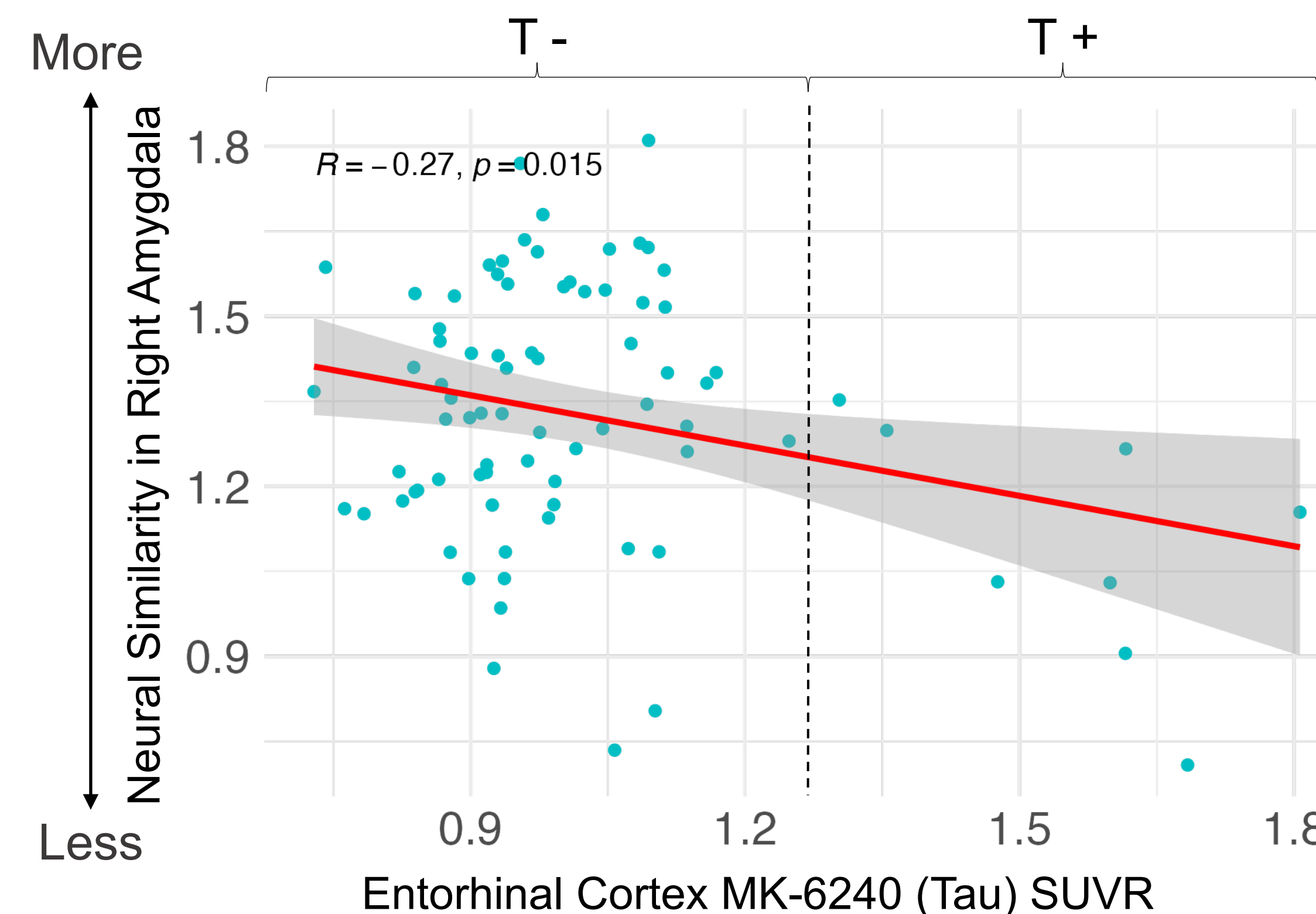
- Representational Similarity Analysis



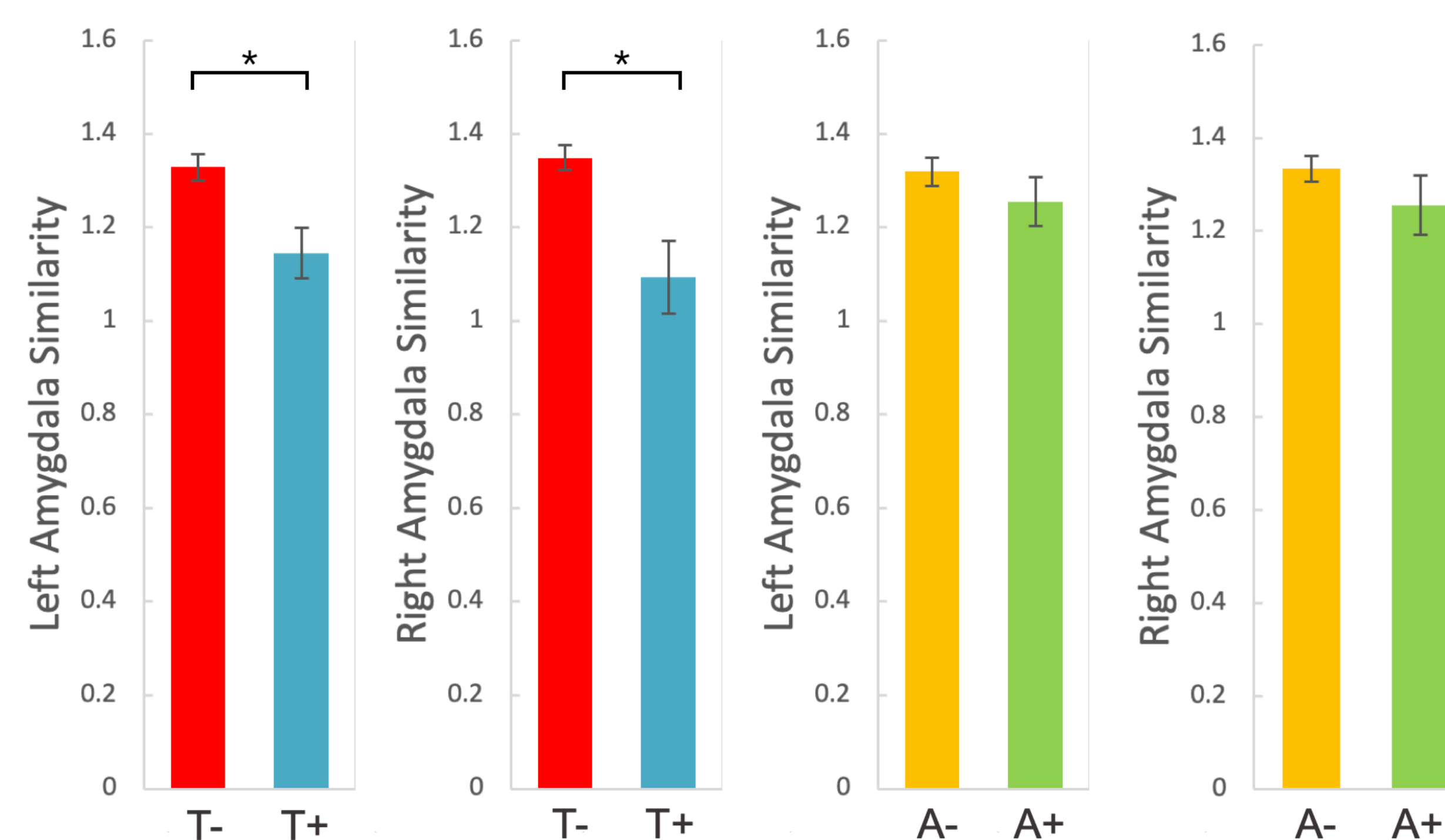
- The representational similarity analysis quantifies how closely the spatial pattern of activation to neutral images resembles the spatial pattern of activation to negative images in the amygdala.

Research Question: Are amyloid and tau burden associated with fMRI indices of emotional reactivity to negative and neutral stimuli in individuals at risk for Alzheimer's disease?

Results



- Tau burden in the entorhinal cortex predicts neural similarity in right amygdala to negative and neutral images when controlling for age, gender and race ($\beta = -0.498$, $SE = 0.246$, $p = 0.046$); but not the neural similarity in left amygdala ($\beta = -0.410$, $SE = 0.259$, $p = 0.118$).



	Neural Similarity in Left Amygdala	Neural Similarity in Right Amygdala
Tau burden in the entorhinal cortex	-0.17	-0.27*
Tau burden in the amygdala	-0.09	-0.18
Global amyloid burden	-0.13	-0.12

- Greater tau burden in the entorhinal cortex is significantly related to less neural similarity in right amygdala to negative and neutral stimuli ($r = -0.27$, $p = 0.015$).

Multiple Linear Regression	β	SE	p value
Neural Similarity in Right Amygdala			
Tau burden in the entorhinal cortex	-0.498*	0.246	0.046
Tau burden in the amygdala	0.300	0.284	0.295
Global amyloid burden	-0.095	0.159	0.552
Gender	0.015	0.055	0.795
Age	-0.002	0.004	0.694
Race	-0.042	0.108	0.697

- The neural similarity in left amygdala ($t = 3.038$, $p = 0.011$) and right amygdala ($t = 3.143$, $p = 0.013$) to negative and neutral stimuli is greater in the T- group, compared with the T+ group.
- The neural similarity in left amygdala ($t = 1.060$, $p = 0.304$) and neural similarity in right amygdala ($t = 1.143$, $p = 0.272$) to negative and neutral stimuli in the A- group is not significantly different from that in the A+ group.

Conclusions

- Greater tau burden in the entorhinal cortex is significantly related to less neural similarity in right amygdala to negative and neutral stimuli, suggesting a greater differentiation of the amygdala's response with higher tau.
- Individual differences of tau burden in the entorhinal cortex but not amyloid burden significantly predict neural similarity in right amygdala to negative and neutral stimuli when controlling for age, gender and race.
- Neural similarity in bilateral amygdala to negative and neutral stimuli is greater in the T- group, compared with the T+ group.
- These findings provide evidence for the association between tau and fMRI indices of emotional reactivity in adults at risk of Alzheimer's disease.
- Future directions: Examine whether the tau burden is associated with the negative affect in daily lives and psychophysiological reactions between negative and neutral stimuli.

References & Funding

- Fredericks, C. A., Sturm, V. E., Brown, J. A., Hua, A. Y., Bilgel, M., Wong, D. F., Resnick, S. M., & Seeley, W. W. (2018). Early affective changes and increased connectivity in preclinical Alzheimer's disease. *Alzheimer's & Dementia: Diagnosis, Assessment & Disease Monitoring*, 10(1), 471-479.
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