

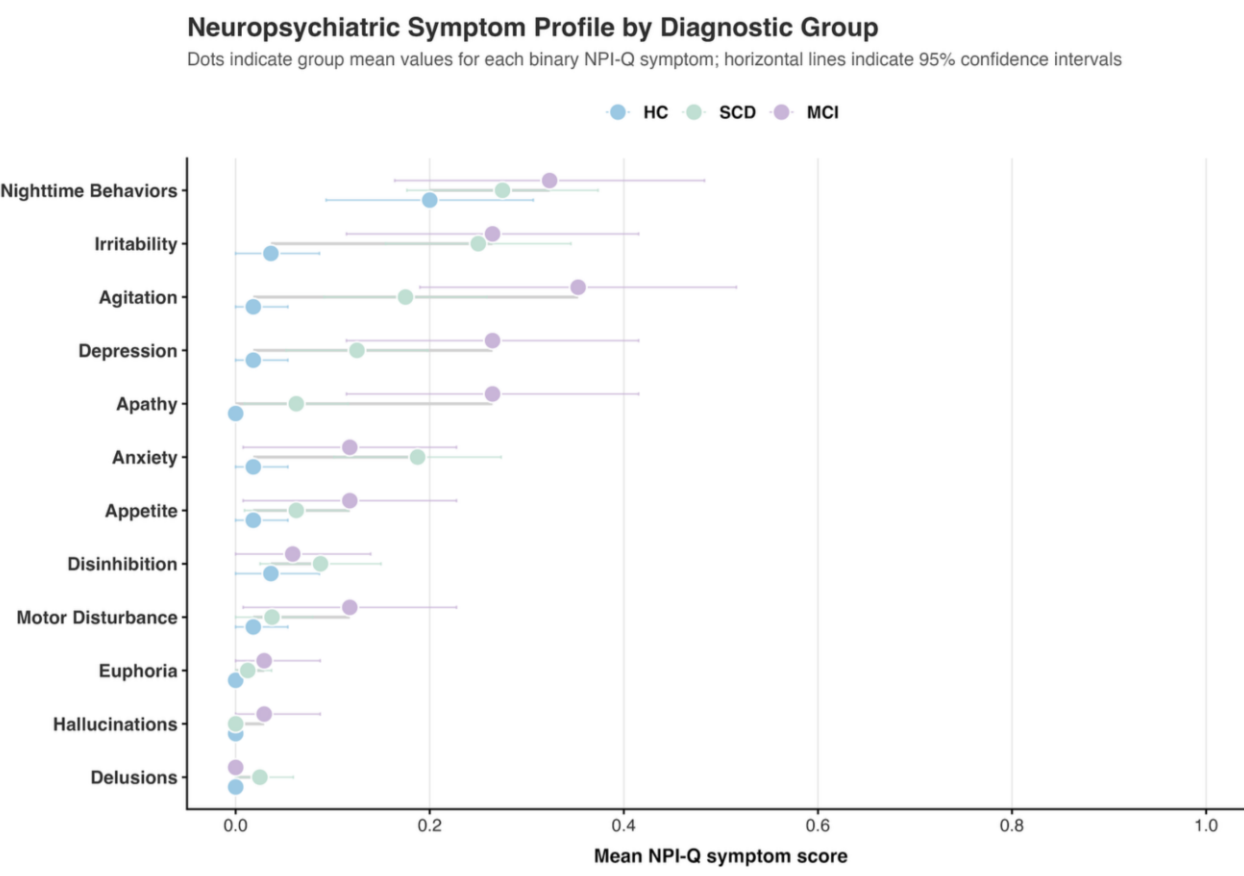
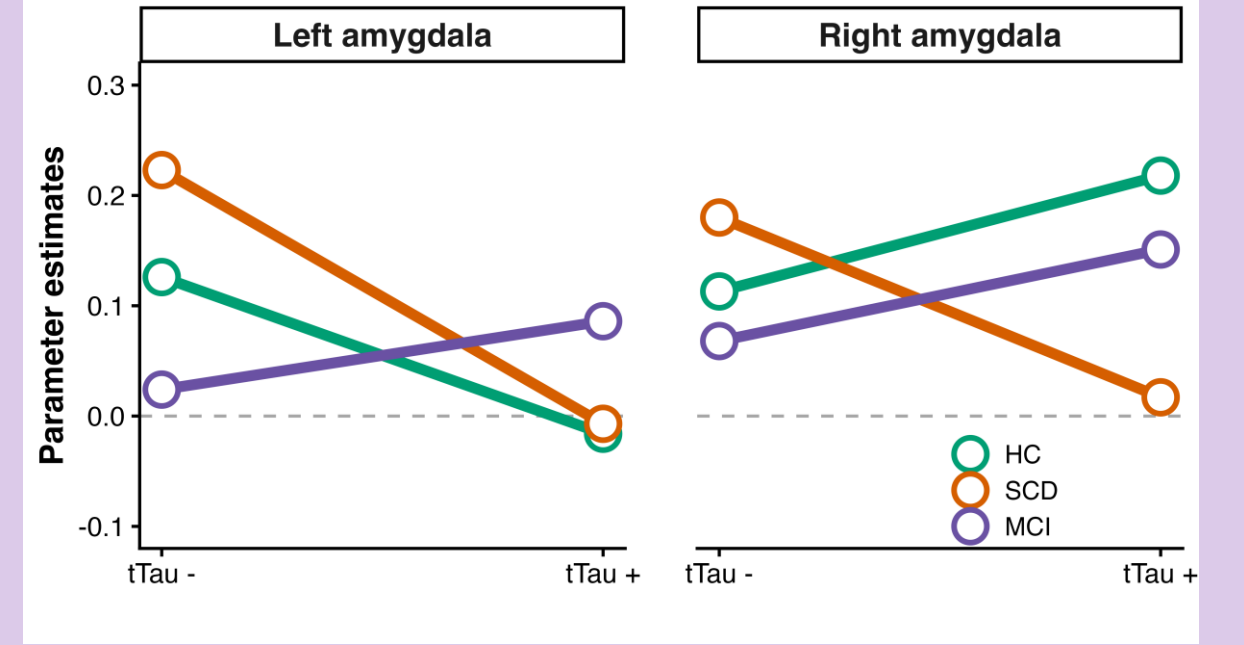
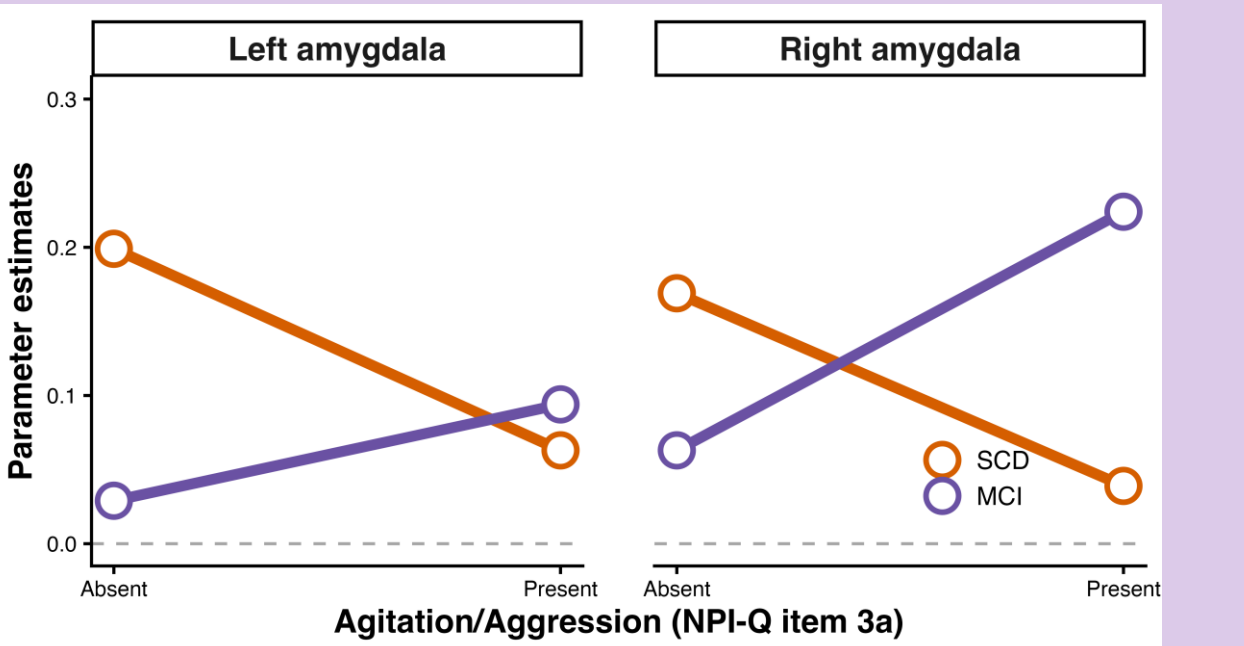
Amygdala Novelty Response Varies With Tau And Agitation/Aggression In Alzheimer Risk Groups

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1. Tau-negative SCD maintains greater left amygdala novelty reactivity than tau-negative MCI, suggesting tau pathology progressively suppresses amygdala function in preclinical AD
2. Absent agitation/aggression in SCD is associated with higher left amygdala novelty responses than MCI, suggesting better-preserved novelty encoding and learning capacity at this stage

INTRODUCTION	METHODS	RESULTS	TABLES & GRAPHS	CONCLUSIONS
AD pathology begins decades before clinical symptoms. The preclinical phase is a critical window for early detection. The amygdala is among the earliest sites of tau accumulation (Braak stage III), before objective memory impairment. In preclinical Alzheimer’s disease (AD), tau pathology and neuropsychiatric symptoms (NPS) distinctly modulate amygdala responses to novel stimuli before the onset of measurable cognitive decline. This study aims to investigate how neuropsychiatric symptoms assessed by the Neuropsychiatric Inventory (NPI) and cerebrospinal fluid (CSF) tau levels influence amygdala responses to novelty in individuals at risk for AD, using functional MRI.	DELCODE study participants (N=169): 55 Healthy Controls (HC), 80 with Subjective Cognitive Decline (SCD), 34 with Mild Cognitive Impairment (MCI). Measured NPS via NPI total scores, cognition via PACC5, CSF biomarkers (pTau181, tTau181, Aβ42), and amygdala activity during 3T fMRI novelty task. Applied ANOVA with post-hoc t-tests, covarying for age, education, and site.	The interaction between diagnosis and total tau was found to be significant ($F(2, 159)= 3.124, p= 0.047$). Post hoc analyses revealed that total tau-negative individuals with SCD exhibited higher left amygdala novelty-related activation compared to total tau-negative individuals with MCI ($p= 0.006$). Additionally, the interaction effect between diagnosis and agitation/aggression (NPI subdomain) scores was also significant ($F(1, 106)= 4.201, p= 0.043$). Post hoc analyses indicated that SCD patients without agitation/aggression showed higher left amygdala activation than MCI patients without agitation/aggression ($p = 0.017$). No significant results with Aβ42 levels	Neuropsychiatric Symptom Profile by Diagnostic Group Dots indicate group mean values for each binary NPI-Q symptom; horizontal lines indicate 95% confidence intervals   	Tau-negative SCD maintains amygdala reactivity relative to MCI, consistent with less advanced neurodegenerative processes at this earlier stage. The absence of agitation/aggression symptoms in SCD further preserves this neural response, suggesting specific NPS subdomains may protect compensatory mechanisms. The findings hint at a possible relationship between tau pathology, behavioral changes and preclinical AD trejectories..