

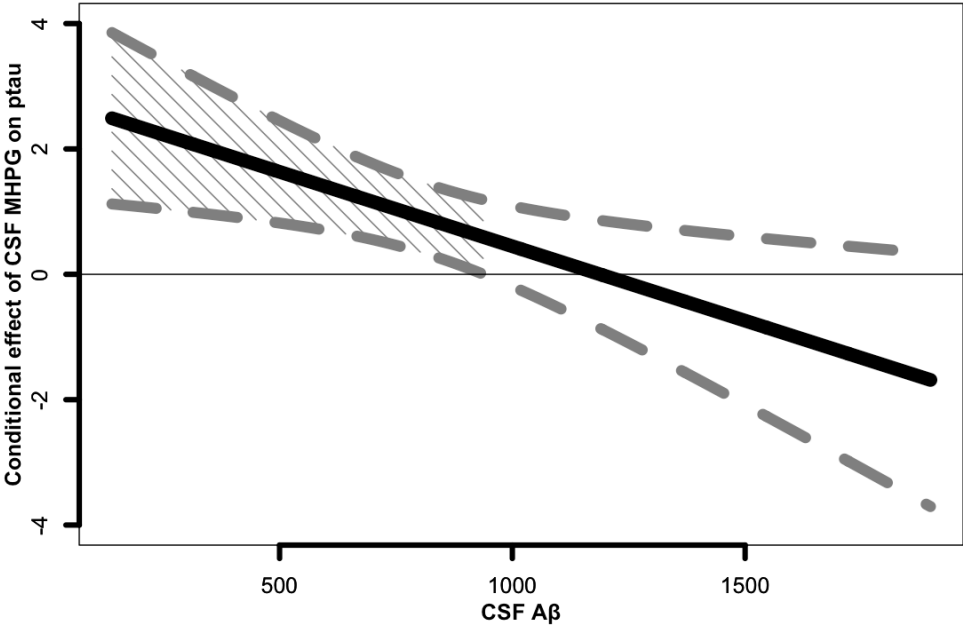
Supplementary Material

Elevated Norepinephrine Metabolism Gauges Alzheimer's Disease-Related Pathology and Memory Decline

Extra Longitudinal Analyses Results

To examine the separate associations between CSF MHPG, CSF A β , or CSF p-tau and decline in learning, we constructed three linear mixed effects models with random intercepts per subject and random slopes for time, with WLT learning as outcome and adjusting for age, sex, education, *APOE*, CDR-score and interactions with time. We observed a negative association between CSF MHPG and learning over time ($t=-3.46$, $p=0.001$) and also between CSF p-tau and learning over time ($t=-2.59$, $p=0.014$). We did not observe a relationship between CSF A β and learning over time ($t=0.70$, $p=0.49$). These patterns are consistent with the literature showing that tau pathology is closer linked to cognition than A β . In addition, the fact that MHPG is associated with longitudinal changes in memory confirms the important role NE metabolism plays in memory function.

Supplementary Figure 1. Floodlight visualization of the interaction between CSF MHPG and A β on p-tau



The Johnson-Neyman plot indicates that a significant positive relationship between MHPG and p-tau occurs at A β values <938 pg/ml. The bold line on the x-axis indicates the range of observed values in the study.