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NEUROIMAGING

Circulating stress hormones and multimodal measures of brain and cognition in older adults: Cross-sectional findings from the AGE-WELL cohort

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Abstract

Background: Increased stress, a proposed risk factor for Alzheimer's disease (AD), is associated with increased brain and cognitive vulnerabilities in older populations, which may be different in women and men.

Objective: To examine cross-sectional associations between circulating stress hormones (epinephrine, norepinephrine, cortisol, dehydroepiandrosterone sulfate (DHEAS), and DHEAS/cortisol ratio) and multimodal measures of brain health and cognition sensitive to AD.

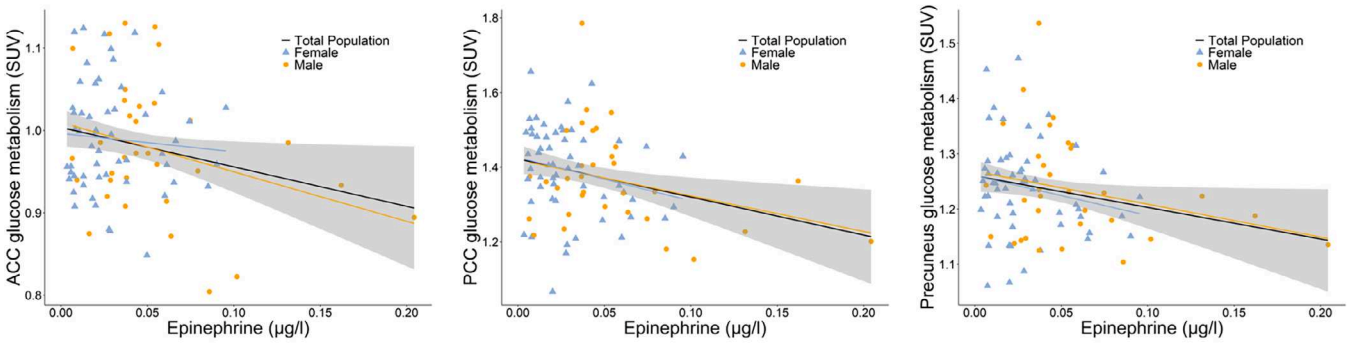
Method: 132 cognitively unimpaired older participants without clinical depression (age = 74.0 ± 4 years, females: n = 80) were included from the Age-Well baseline dataset. Stress hormones were measured in overnight fasting blood serum (cortisol, DHEAS) and plasma (epinephrine, norepinephrine). The association of stress hormone levels with glucose metabolism and perfusion in AD sensitive brain regions, including the anterior and posterior cingulate cortex (ACC, PCC), insula and, precuneus, along with neocortical amyloid deposition and cognitive markers, including memory and Preclinical Alzheimer's Cognitive Composite-5 (PACC5), was assessed. Linear regression models with and without stratification by sex adjusting for covariates of age, sex, education, subclinical anxiety, and depression were conducted.

Result: In the total cohort, higher epinephrine was associated with lower glucose metabolism (Figure 1) in the ACC (adj.-β = -0.26, p = .027), PCC (adj.-β = -0.32, p = .006), and precuneus (adj.-β = -0.27, p = .021) and lower perfusion in the PCC (adj.-β = -0.23, p = .013). Sex-stratified analyses showed interactions (all p's < .1): In males (but not in females), higher cortisol was associated with lower episodic memory (adj.-β = -0.33, p

= .02), short-term memory (adj.-β = -0.32, p = .014) and PACC5 scores (adj.-β = -0.28, p =.04), suggesting a stress-related vulnerability in the cognitive system of men. Stress biomarkers were not associated with neocortical amyloid deposition (all p's ≥ .1).

Conclusion: Our results demonstrate the involvement of stress hormones, particularly epinephrine and cortisol, in increased vulnerability of the brain and cognition in older adults and the manifestation of sex specificities in this context. The role of stress on brain and cognitive health and related sex differences needs to be considered in intervention programs.

Figure 1. Association between plasma epinephrine levels and brain glucose metabolism.



Results are shown for plasma epinephrine levels and brain glucose metabolism. Epinephrine was negatively associated with glucose metabolism in AD sensitive brain regions, namely the anterior cingulate cortex (ACC), posterior cingulate cortex (PCC) and precuneus, in the total cohort (all *p*'s < .05). Black lines indicate regression slope for the total cohort and gray shaded indicate the confidence interval of the total population, coloured dots and coloured lines indicate data points and regression lines for males (blue) and females (orange).