National Conference on Women's Health and Sex Differences Research
October 23 – 25, 2024
Poster Abstract

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Hair Cortisol Concentration Associates with Cognitive Performance in Healthy Late Peri- and Early Postmenopausal Women

Background: Perimenopause is associated with decrements in cognition, including attention and verbal learning/memory. Brain regions underlying these functions--the prefrontal cortex and hippocampus--are susceptible to the effects of estrogen and cortisol. Whether long-term markers of hypothalamic-pituitary-adrenal (HPA) axis activity, like hair cortisol concentration (HCC) levels, are associated with these cognitive decrements over perimenopause has not been studied. This project sought to determine the degree to which HCC levels are associated with cognitive performance on tests of (1) verbal memory/learning, and (2) attention and working memory among healthy women in late perimenopause or early postmenopause.

Method: Fifty-nine participants who were healthy, not on hormone therapy, and in the late perimenopause or early postmenopause completed online cognitive tests and provided a hair sample under supervision via Zoom. Verbal learning and verbal memory was assessed using the California Verbal Learning Test – Third Edition (CVLT-3; immediate recall, delayed recall, overall recall). Attention and working memory were assessed using the 3-back trial of the letter n-back task (true positives, false positives). Hair samples were assessed for HCC levels using an enzyme immunoassay. HCC levels were log-transformed due to a right skew. A multiple linear regression with an adjusted and unadjusted model was used to assess the association between HCC levels and verbal learning/memory, while negative binomial regressions were used for the 3-back tests due to their count nature. All adjusted models included race/ethnicity, education, and age as covariates.

Results: Regarding attention and working memory performance, HCC levels had a negative and statistically significant association with true positive responses on the n-back in the unadjusted (RR=.78, 95% CI [.65, .94], p=.011) and adjusted models (RR=.77, 95% CI [64, .94], p=.01). Higher levels of hair cortisol were linked with lower true positive scores. Conversely, HCC levels had a positive and statistically significant association with false positive response scores in the unadjusted (RR=1.97, 95% CI [1.11, 3.49], p=.02) and adjusted models (RR=1.92, 95% CI [1.15, 3.19], p=.01; i.e., higher HCC levels were associated with higher false positive scores). In all models, no statistically significant associations were found among any of the covariates and

true/false positive response scores. Regarding verbal learning/memory performance on the CVLT-3, HCC levels showed no significant associations in either unadjusted or adjusted models with respect to immediate recall index scores (unadjusted model: B=-3.60, 95% CI [-15.65, 8.45], p=0.551; adjusted model: B=-4.10, 95% CI [-17.37, 9.17], p=0.538), delayed recall index scores (unadjusted: B=-4.82, 95% CI [-16.09, 6.45], p=.395; adjusted: B=-3.73, , 95% CI [-16.24, 8.78], p=.552), or overall recall index scores (unadjusted: B=-4.80, 95% CI [-16.78, 7.16], p=.424, adjusted: B=-4.44, 95% CI [-17.58, 8.70], p=.500). No covariates in any of the models showed statistically significant associations.

Conclusions: This work suggests that an HPA-axis activation marker that captures total cortisol secretion over multiple months (i.e., HCC) is associated with cognitive performance on an attention and working memory task in perimenopause. Study designs allowing for causal interpretations are needed to inform whether and how interventions may be helpful to promote HPA-axis health and improve cognition during perimenopause.