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Sex Hormones Modulate Vascular and Cognitive Function in a Diverse, Middle-Aged Cohort

THE
PREVAIL
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Dementia Prevention Program

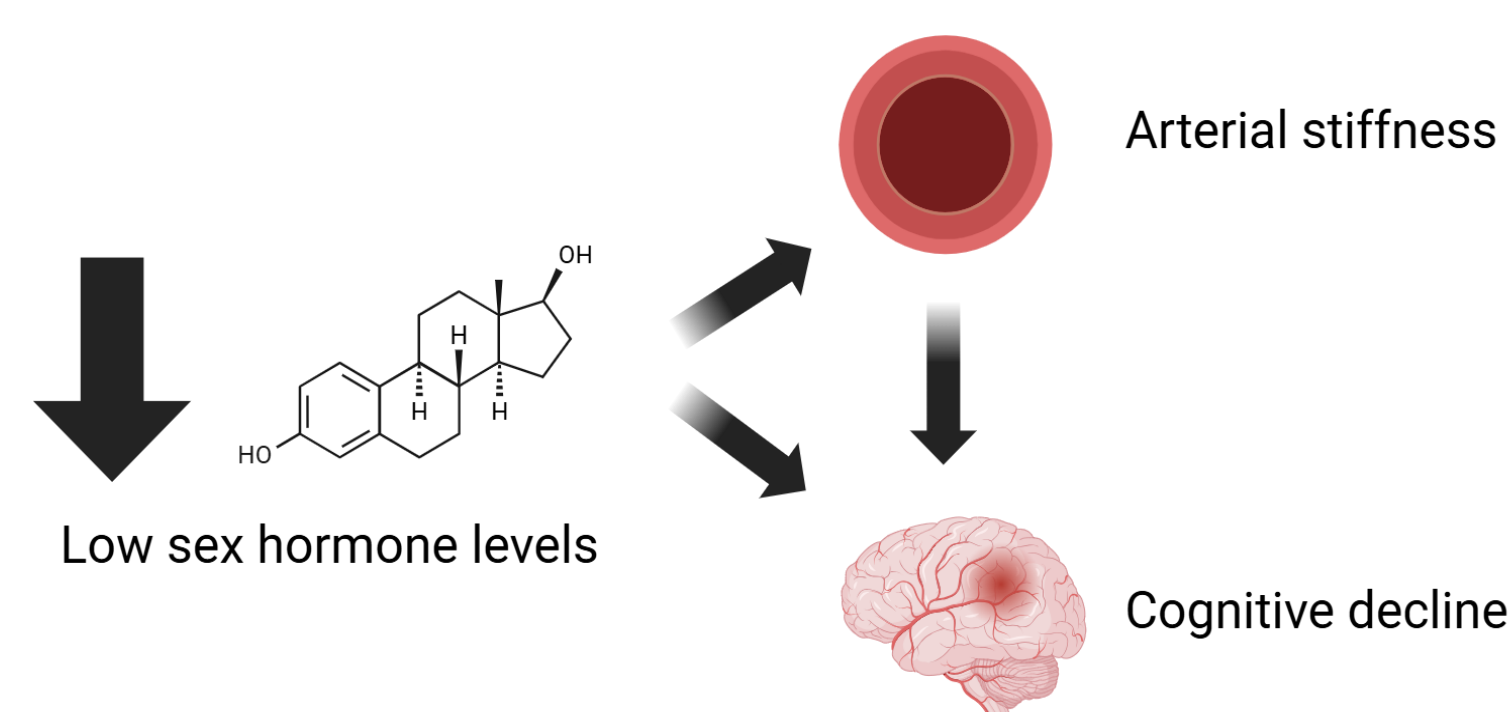
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In a racially diverse, middle-aged cohort, greater sex hormone levels were associated with lower arterial stiffness, lower diastolic blood pressure, and better cognitive performance.

Background

- Alzheimer's Disease (AD) affects more women than men, partially attributed to sex-based differences in APOE genetic risk, lifespan, pregnancy complications, and psychiatric comorbidities.
- Studies also suggest an association between the menopausal transition and AD pathology in mid-life.
- At menopause, there are declines in circulating sex hormones like estrogen, which regulates various physiological mechanisms and supports biological systems, including cognition and cardiovascular health.
- During menopause, women experience increased arterial stiffness, a vascular marker associated with cognitive impairment.
- There are complex interactions among sex hormones, vascular risk, and cognition that remain to be explored.



Purpose

The purpose of this study is to examine how sex hormone levels influence vascular and cognitive function in a cognitively normal sample of middle-aged adults.

- How do E1, E2, and SHBG levels correlate with cognitive test performance, arterial stiffness, and BP?

Methods

SAMPLE:

- Baseline data from Sex Hormones & Alzheimer's Disease Prevention Research Study (E2)
- Racially diverse, middle-aged sample (N=117) of cognitively unimpaired adults

MEASURES:

- Blood draw- analyses of sex hormone levels (E1, E2, and SHBG)
- Vascular ultrasound (PWA/PWV)- blood pressure and arterial stiffness
- Cognitive testing- verbal fluency, processing speed, visuospatial ability, working memory, attention

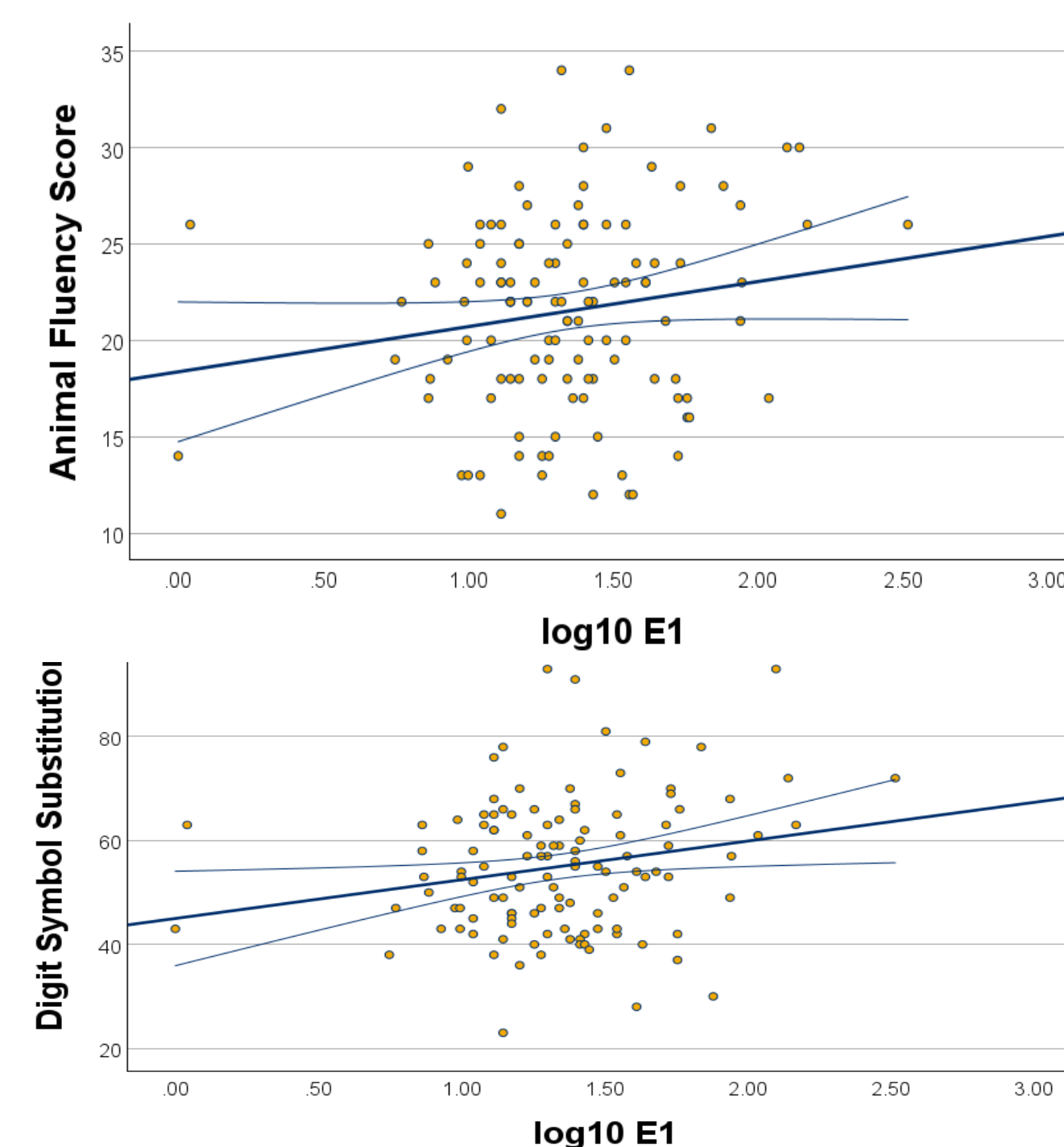
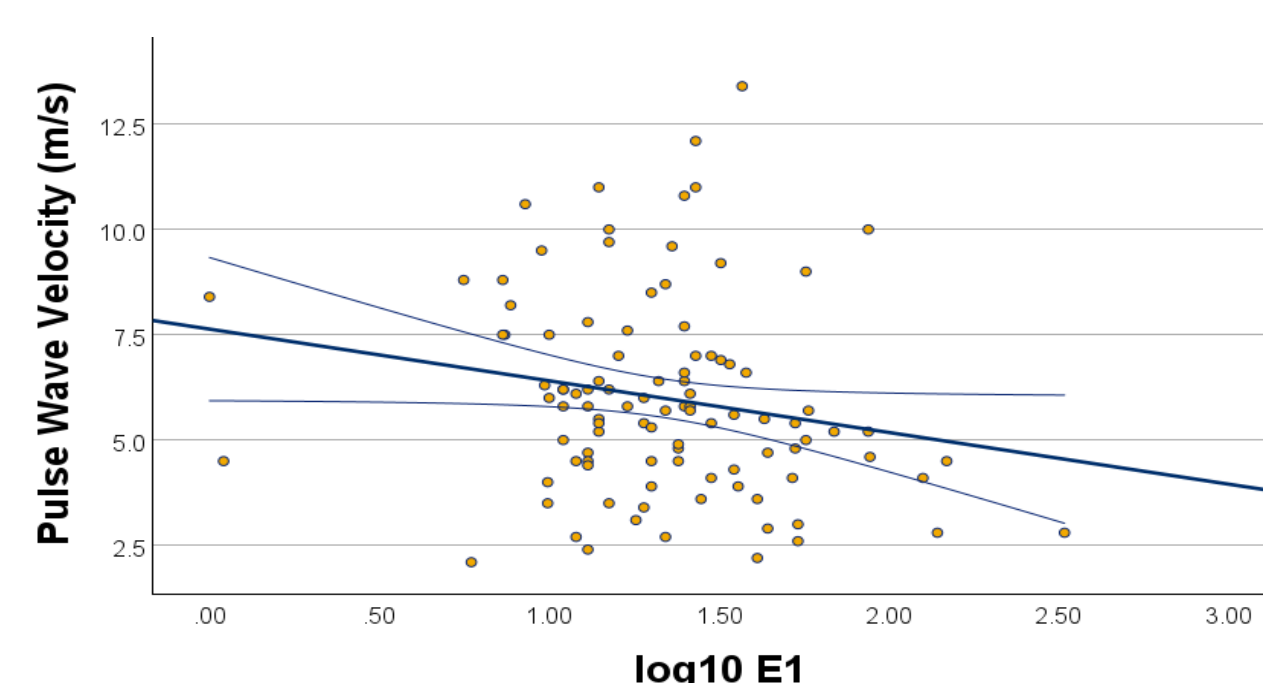
STATISTICAL ANALYSIS:

- Linear regression analyses adjusted for age, gender, race, and education

Results

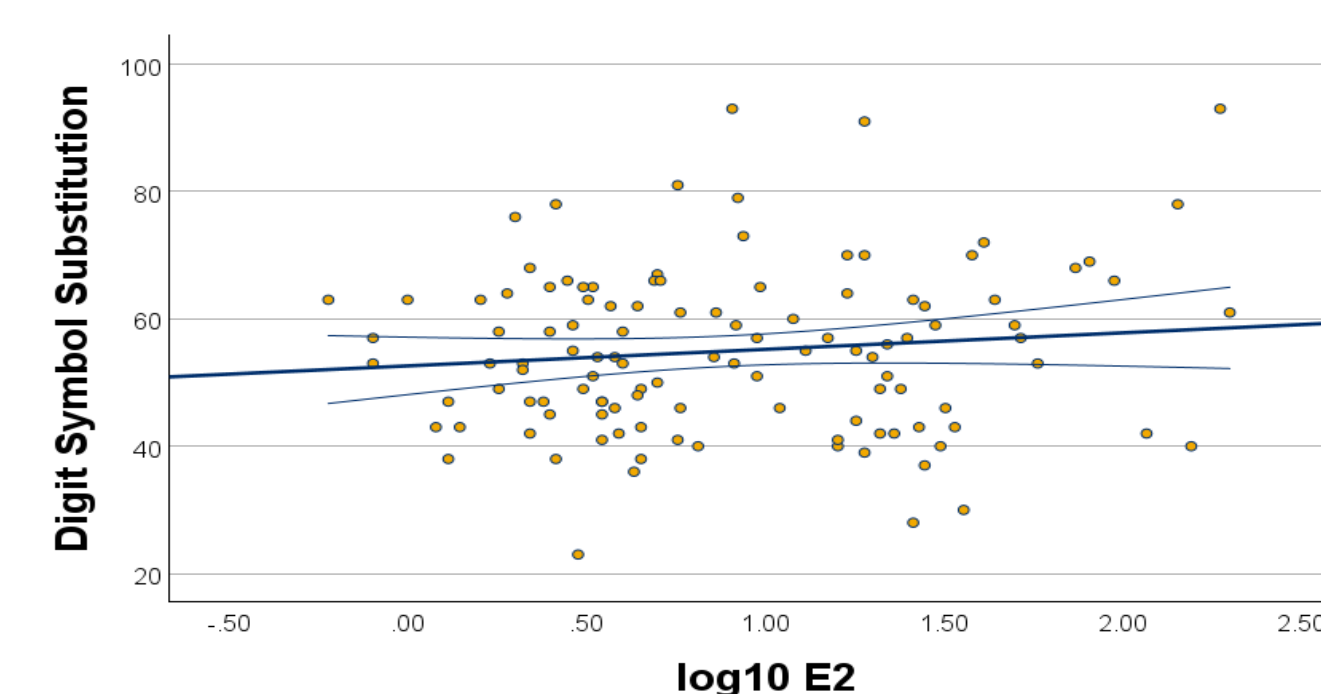
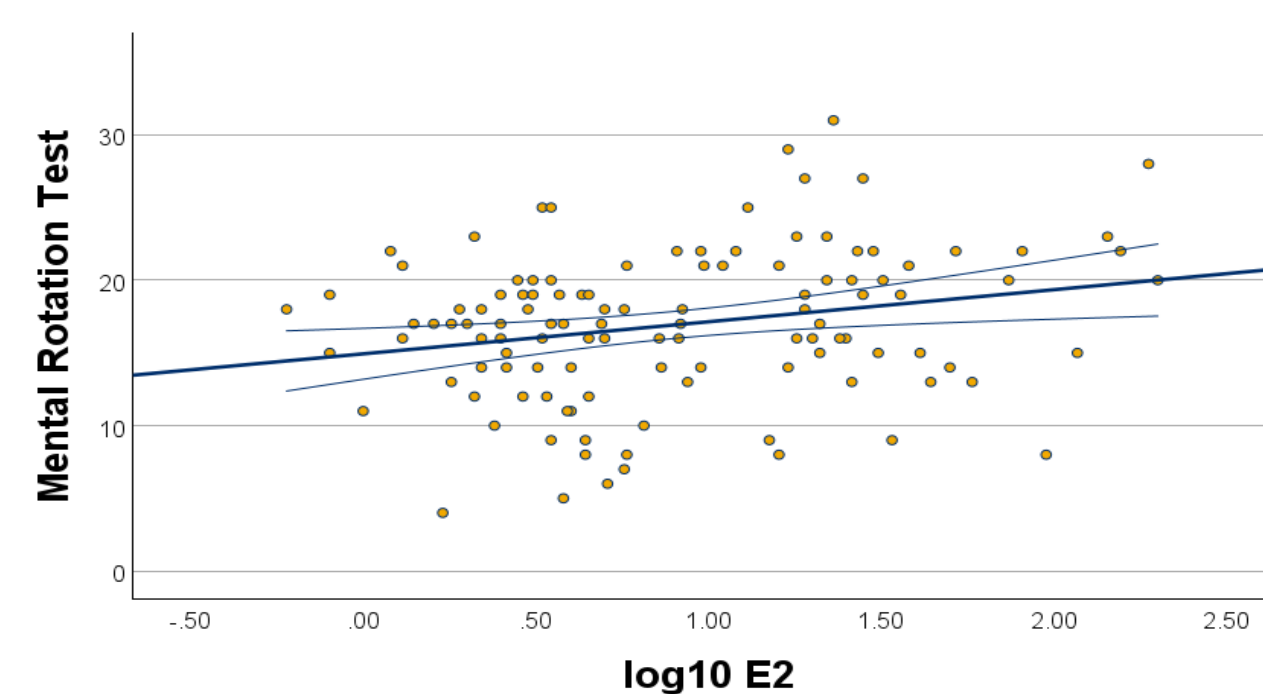
Higher E1 was associated with lower arterial stiffness and higher cognitive test scores.

- E1 was correlated with lower PWV ($r=-0.227$, $p=0.023$) and higher scores on Animal Fluency ($r=0.190$, $p=0.040$) and DSST ($r=0.246$, $p=0.007$).



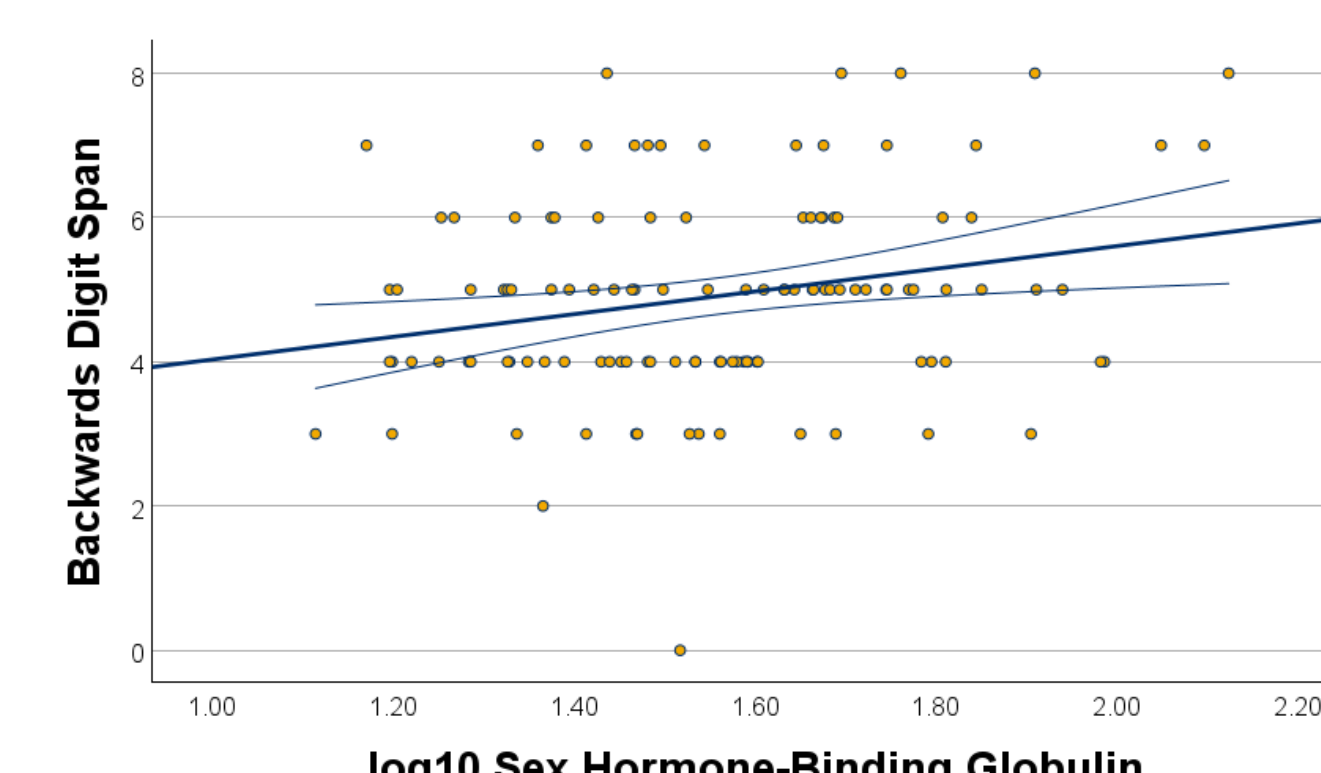
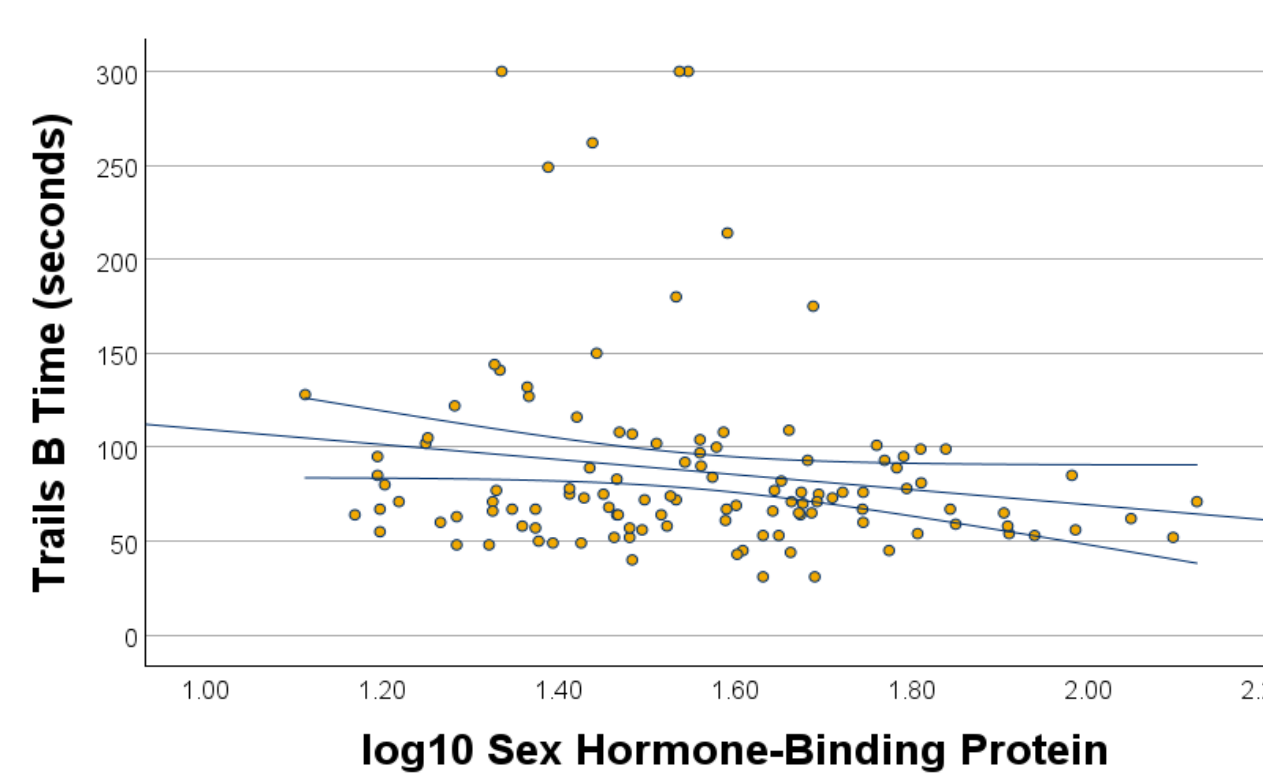
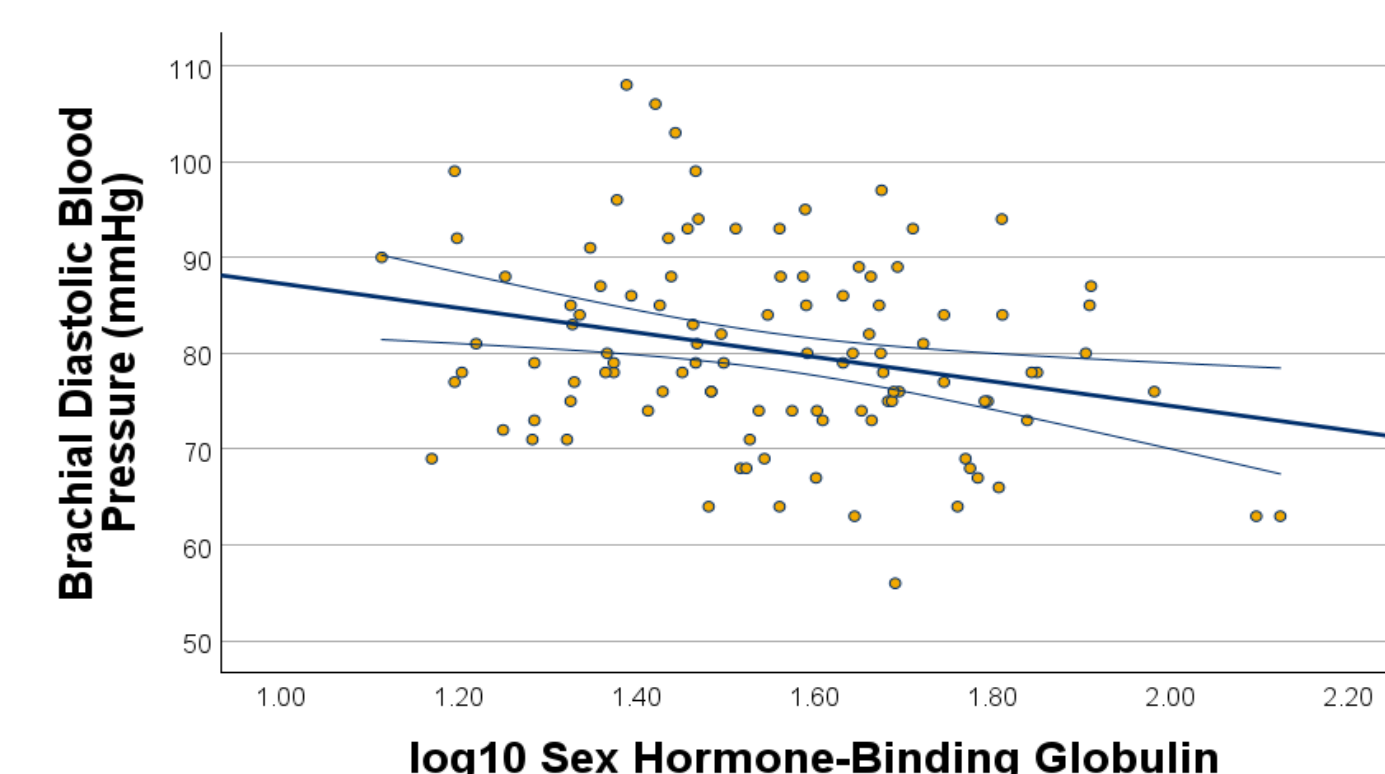
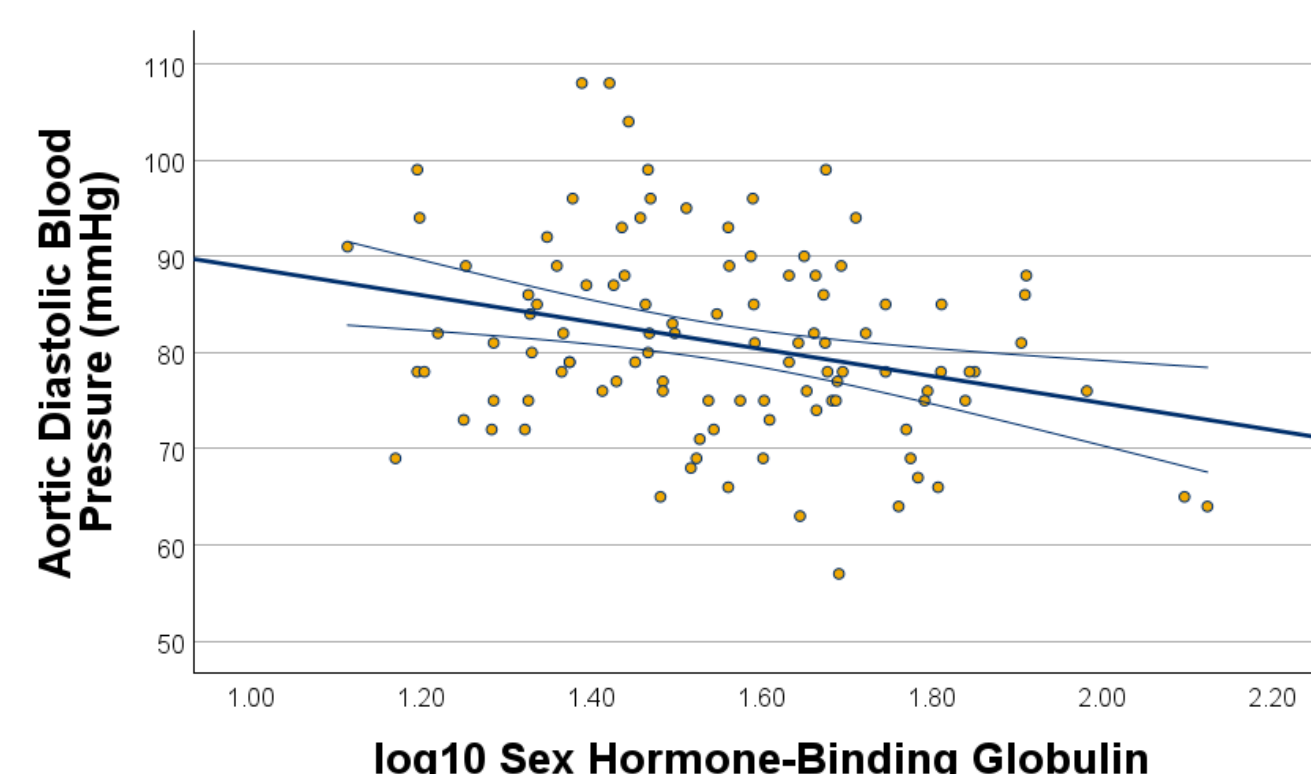
Higher E2 was positively correlated with better cognitive test scores.

- E2 levels were associated with MRT ($r=0.230$, $p=0.013$) and DSST ($r=0.187$, $p=0.046$).



SHBG was associated with lower diastolic blood pressures and better cognitive performance.

- There was a significant negative correlation between SHBG and aortic DBP ($\beta=-0.279$, $p=0.006$), brachial DBP ($\beta=-0.259$, $p=0.011$), and lower Trails B time ($r=-0.186$, $p=0.045$). SHBG was also significantly positively associated with better Backward Digit Span scores ($\beta=0.200$, $p=0.038$).



Demographics

Characteristic	Mean $\pm$ SD / N (%) (N=117)
Age	63 $\pm$ 8 years
Female	88 (75.2%)
Education	17 $\pm$ 2 years
Black/African-American	58 (49.6%)
MoCA	27 $\pm$ 3 points

Conclusion

- Cognitive** domains, including verbal fluency, processing speed, visuospatial ability, working memory, and attention, were differentially affected by sex hormone levels and processes regulating these hormones.
- Sex hormones can help predict **vascular** measures like arterial stiffness and both central and peripheral diastolic blood pressures.
- These results also suggest collinearity that complicates the isolation of sex hormone effects.
- Follow-up will elucidate longitudinal effects and mechanisms of sex hormones on vascular and cognitive changes.
- Further work is needed for a better understanding of sex hormone levels and AD risk factors in diverse life stages and populations.

Impact

- These results suggest that hormone levels play a key role in vascular and cognitive outcomes with implications for women during the menopausal transition.

Acknowledgements

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