

# Examining whether Estrogen Hormone Therapy Modifies the Association between Depressive Symptoms and Cognition among Latino/x/e Females

Marco Santoscay<sup>1</sup>, Carlos E.E. Araujo-Menendez<sup>1-2</sup>, Ariana M. Stickel<sup>1</sup>

<sup>1</sup>San Diego State University, Department of Psychology

<sup>2</sup>SDSU/UC San Diego Joint Doctoral Program in Clinical Psychology

## Introduction

- Females who are Latino/x/e (henceforth Latina adults) are more likely to experience higher levels of depressive symptoms than non-Latina White females during menopause<sup>1</sup>
- Depression has been associated with declines in cognition across different domains and is a risk factor for dementia<sup>2,3</sup>
- Some studies suggest that estrogen therapy is associated with less cognitive decline and reduced risk for dementia<sup>5</sup>
- The association between depression, estrogen hormone therapy, and cognition is unclear and understudied among Latina adults

## Research Goal

We aimed to investigate whether estrogen hormone therapy modifies the association between depressive symptoms and cognition among Latina adults

## Methods

**PARTICIPANTS:** Participants included 3,161 Latina adults (mean age=70.4 years) from the National Alzheimer's Coordinating Center (NACC)

**DEPENDENT VARIABLES:** Cognitive scores on the Craft Story 21 Delayed Recall, Trails Making Test Parts A and B, Digit Symbol Substitution, semantic fluency (Animals), and Digit Span Forward and Backward

**INDEPENDENT VARIABLE:** Total score on the Geriatric Depression Scale (GDS)

**MODERATOR:** Estrogen hormone therapy use (Yes/No categorical variable)

**COVARIATES:** Hispanic/Latino origin, primary language, education, and age

**STATISTICAL ANALYSES:** Linear regression models tested the association between GDS and Cognition. Also, the interaction between estrogen hormone therapy and depression symptoms on each cognitive outcome separately in fully adjust models

Table 1. Sample descriptives

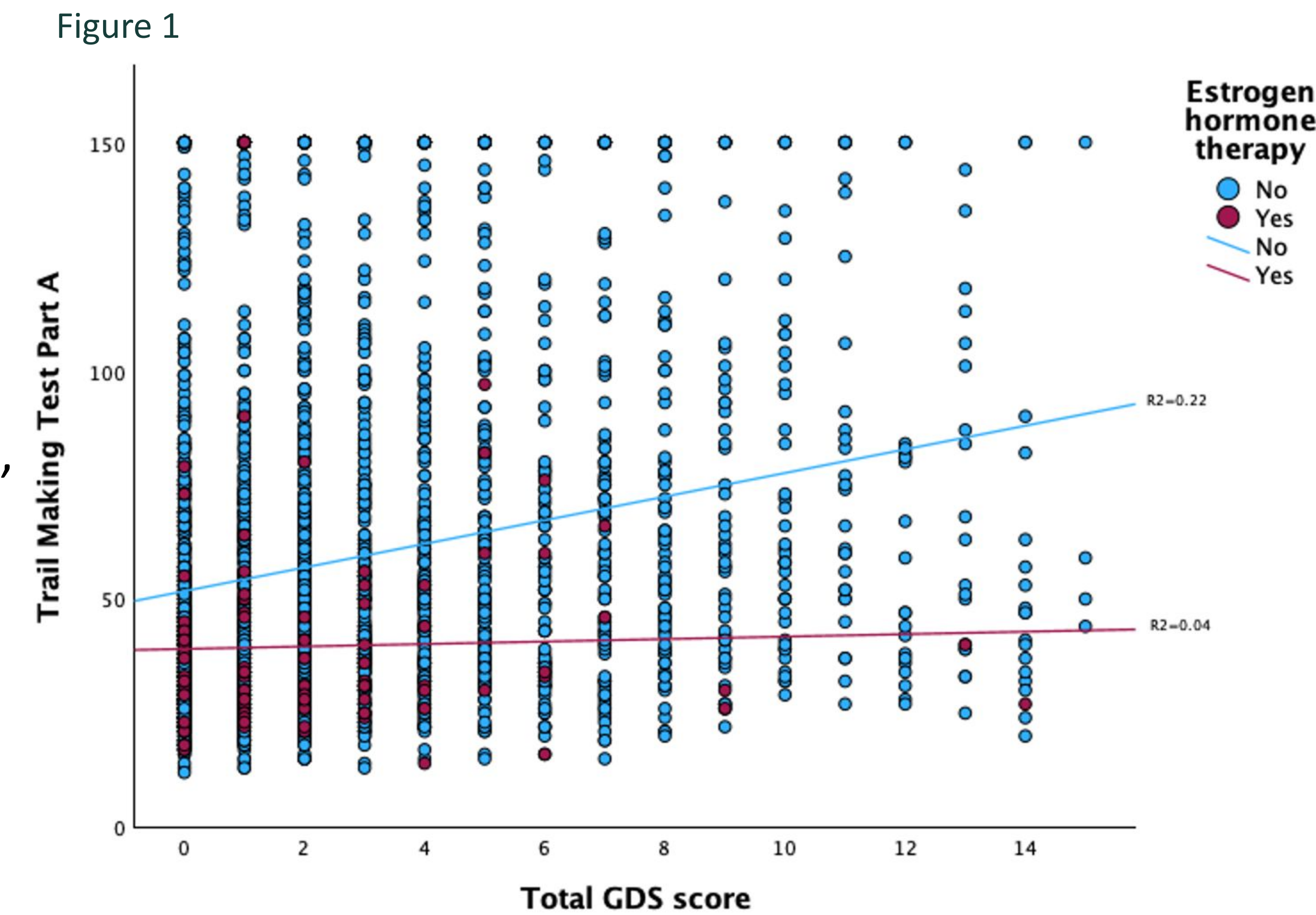
|                                                  | Estrogen Hormone Therapy |             | Total        |
|--------------------------------------------------|--------------------------|-------------|--------------|
|                                                  | No (n=3028)              | Yes (n=113) |              |
| Age (years), mean (SD) **                        | 70 .5 (9.3)              | 67.9 (8.9)  | 70.4 (9.3)   |
| Education, mean (SD) ***                         | 11.5 (5)                 | 14.2 (4)    | 11.6 (5)     |
| Latino heritage ***                              |                          |             |              |
| Mexican, Chicano, or Mexican-American            | 1134 (38.3%)             | 60 (54%)    | 1194 (38.9%) |
| Puerto Rican                                     | 522 (17.6%)              | 8 (7.2%)    | 530 (17.3%)  |
| Cuban                                            | 265 (8.9%)               | 9 (8.1%)    | 274 (8.9%)   |
| Dominican                                        | 289 (9.8%)               | 3 (2.7%)    | 292 (9.5%)   |
| Central America                                  | 214 (7.2%)               | 11 (9.9%)   | 225 (7.3%)   |
| South America                                    | 432 (14.6%)              | 13 (11.7%)  | 445 (14.5%)  |
| Other                                            | 105 (3.5%)               | 7 (6.3%)    | 112 (3.6 %)  |
| Primary language: English ***                    | 1011 (33.4%)             | 69 (61%)    | 1080 (34.4%) |
| Geriatric Depression Scale (GDS) *               | 3 (3.2)                  | 2.3 (2.7)   | 3 (3.1)      |
| NOTE: * = p<0.05, ** = p<0.01, and *** = p<0.001 |                          |             |              |

## Results

Table 2. Main associations among depressive symptoms, estrogen hormone therapy, and cognitive tests

|                                                                         | Geriatric Depression Scale (GDS)     | Estrogen Hormone Therapy         | GDS*Estrogen Hormone Therapy         |
|-------------------------------------------------------------------------|--------------------------------------|----------------------------------|--------------------------------------|
| Craft Story 21 Delayed Recall                                           | $\beta = -0.35$ [ -0.48 - -0.22] *** | $\beta = 1.4$ [ -1 - 3.8]        | $\beta = 0.40$ [ -0.87 - 0.95]       |
| Trails Making Test A                                                    | $\beta = 1.49$ [1.06 - 1.2] ***      | $\beta = -1.31$ [ -6.36 - 3.75]  | $\beta = -2.41$ [ -3.65 - -1.17] *** |
| Trails Making Test B                                                    | $\beta = 4.25$ [ 3.18 - 5.31] ***    | $\beta = -9.33$ [ -27.34 - 8.68] | $\beta = -0.29$ [ -8.03 - 7.44]      |
| Digit Symbol Substitution                                               | $\beta = -0.7$ [ -0.9 - -0.51] ***   | $\beta = 1.64$ [ -3.34 - 6.62]   | $\beta = 0.45$ [ -0.69 - 1.59]       |
| Semantic Fluency (Animals)                                              | $\beta = -0.29$ [ -0.36 - -0.23] *** | $\beta = -0.31$ [ -1.64 - 1.01]  | $\beta = 0.23$ [ -0.12 - 0.57]       |
| Digit Spin Forward                                                      | $\beta = -0.10$ [ -0.13 - -0.07] *** | $\beta = 0.24$ [ -0.7 - 1.17]    | $\beta = -0.08$ [ -0.28 - 0.13]      |
| Digit Spin Backward                                                     | $\beta = -0.08$ [ -0.11 - -0.05] *** | $\beta = -0.04$ [ -0.66 - 0.58]  | $\beta = 0.01$ [ -0.16 - 0.18]       |
| NOTE: *** = p<0.001; No estrogen hormone therapy is the reference group |                                      |                                  |                                      |

**MAIN ASSOCIATIONS:** Lower scores on the GDS scale were associated with better performance on all cognitive tests (ps<0.001). There were no associations between estrogen hormone therapy use and cognitive scores. See Table 2.



**INTERACTIONS:** Estrogen hormone therapy modified the relationship between depressive symptoms (GDS) and Trails Making Test A ( $\beta=-2.4$ ,  $p<0.001$ ). Estrogen hormone therapy was associated with weaker association between GDS scores and cognitive scores on the Trails Making Test A See figure 1.

## Conclusion

- Overall, lower depressive symptoms were associated with better performance across all cognitive tests
- Estrogen hormone therapy use largely did *not* appear to differentially modify associations between depressive symptoms and cognition in Latina adults
  - This may be due to our limited number of participants using estrogen hormonal therapy
  - Despite this, estrogen hormone therapy use seemed to mitigate the association between current depressive symptoms and processing speed
  - Processing speed tends to be one of the first cognitive domains affected by ageing, thus making it more receptive to estrogen hormone therapy
- Future research should consider whether dosage or starting age of estrogen hormone therapy impacts the relationships between depressive symptoms and cognition

## Acknowledgments

We thank the NACC and their participants. The NACC database is funded by NIA/NIH Grant U24. AG072122. AMS is supported by NIH grants: K08AG075351 and U54CA267789.

## References

- Cortes et al (2020). <https://doi.org/10.1080/13697137.2020.1834529>
- Ou et al (2025). <https://doi.org/10.1016/j.jad.2025.02.115>
- Livingston et al (2024). [https://doi.org/10.1016/S0140-6736\(24\)01296-0](https://doi.org/10.1016/S0140-6736(24)01296-0)
- Conde et al (2021). <https://doi.org/10.5498/wjp.v11.i8.412>
- Oughli et al (2022). <https://doi.org/10.1177/08919887221090216>