

Prolonged Sitting and APOE-ε4 Interact to Influence Episodic Memory in Adults at Risk for Alzheimer's Disease: Findings from PAAD2

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BACKGROUND

- Sitting time (ST) and Apolipoprotein E epsilon 4 (APOE-ε4) are linked to Alzheimer's Disease (AD) risk¹, and APOE-ε4 carriers may be more vulnerable to lifestyle risk factors like prolonged ST².
- Middle age is a key period for preclinical cognitive changes²⁻³.
- We tested whether ST (from International Physical Activity Questionnaire, IPAQ) and APOE-ε4 interact to influence episodic memory (EM) in cognitively unimpaired middle-aged adults with a family history of AD (FH+).



METHODS

- Cross-sectional pre-test data from the PAAD2 clinical trial (NIH-R01AG058919)⁴.
- 151 cognitively unimpaired adults aged 40–65 years (55.93 ± 6.4 years; 89% female).
- APOE-ε4 status determined from saliva samples (87 non-carriers; 64 carriers).
- ST assessed via IPAQ and categorized as < 8 vs. ≥ 8 hours/day (low ST: n = 93; high ST: n = 58).
- EM outcomes: AVLT Immediate (AVLT_IR) & Delayed Recall (AVLT_DR); Logical Memory Immediate (LM_IR) & Delayed Recall (LM_DR).
- Two-way ANCOVAs tested APOE-ε4 × ST interactions, adjusting for age, sex, education, sleep duration, and BMI.



RESULTS

APOE-ε4 carrier ■ Yes ■ No

Figure 1. ST × APOE-ε4 for AVLT_IR

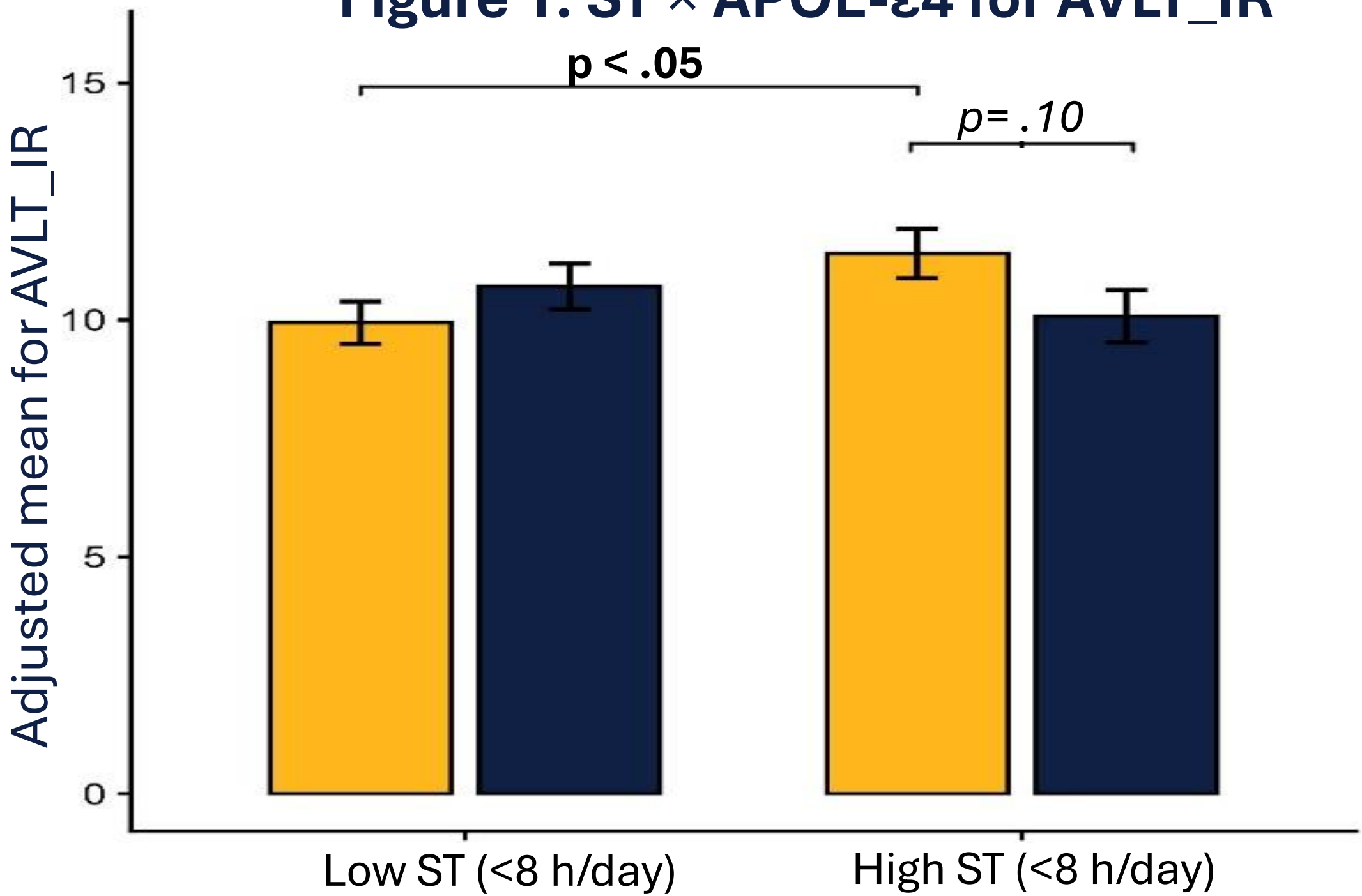


Figure 2. ST × APOE-ε4 for AVLT_DR

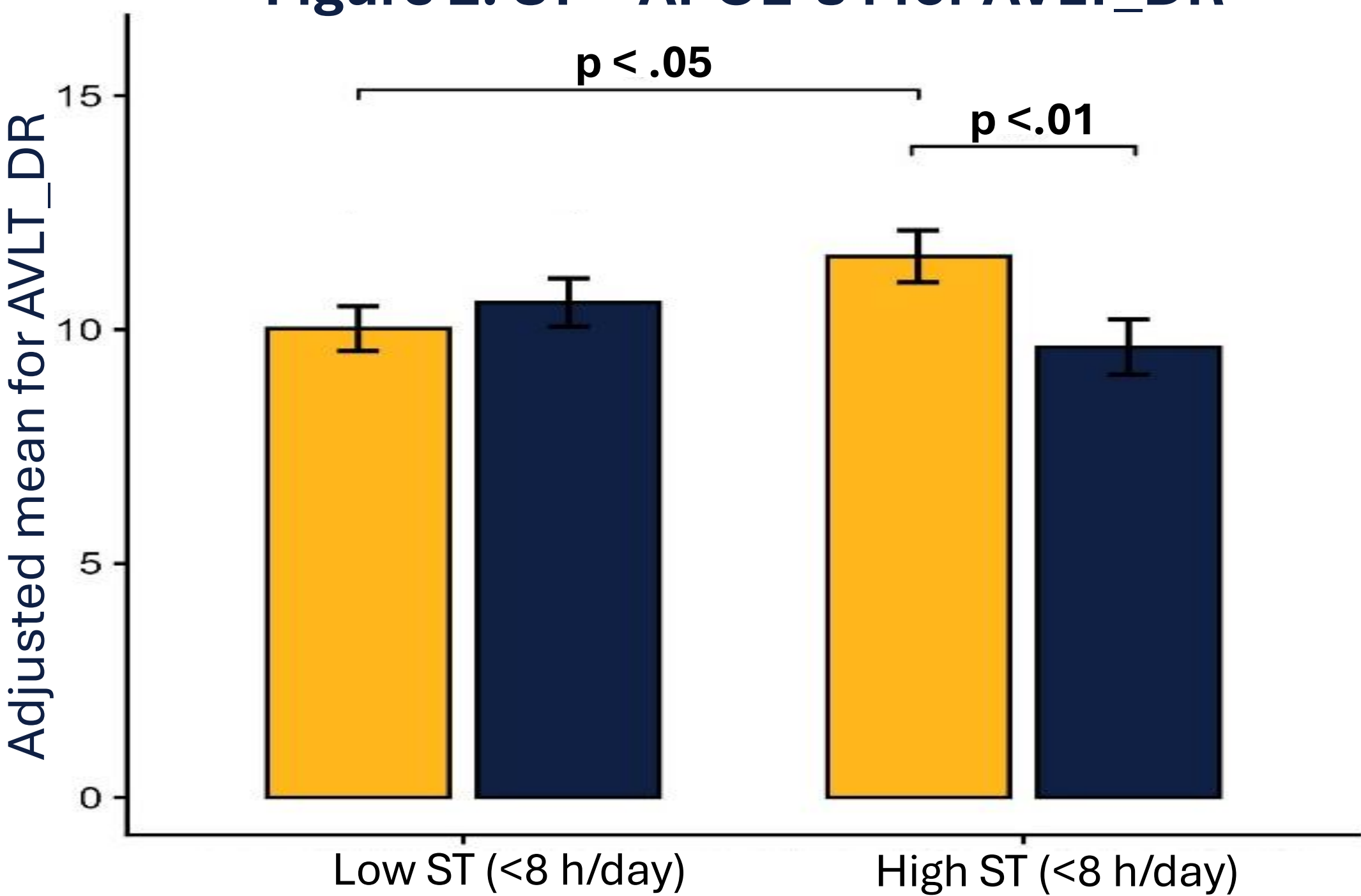


Figure 3. ST × APOE-ε4 for LM_IR

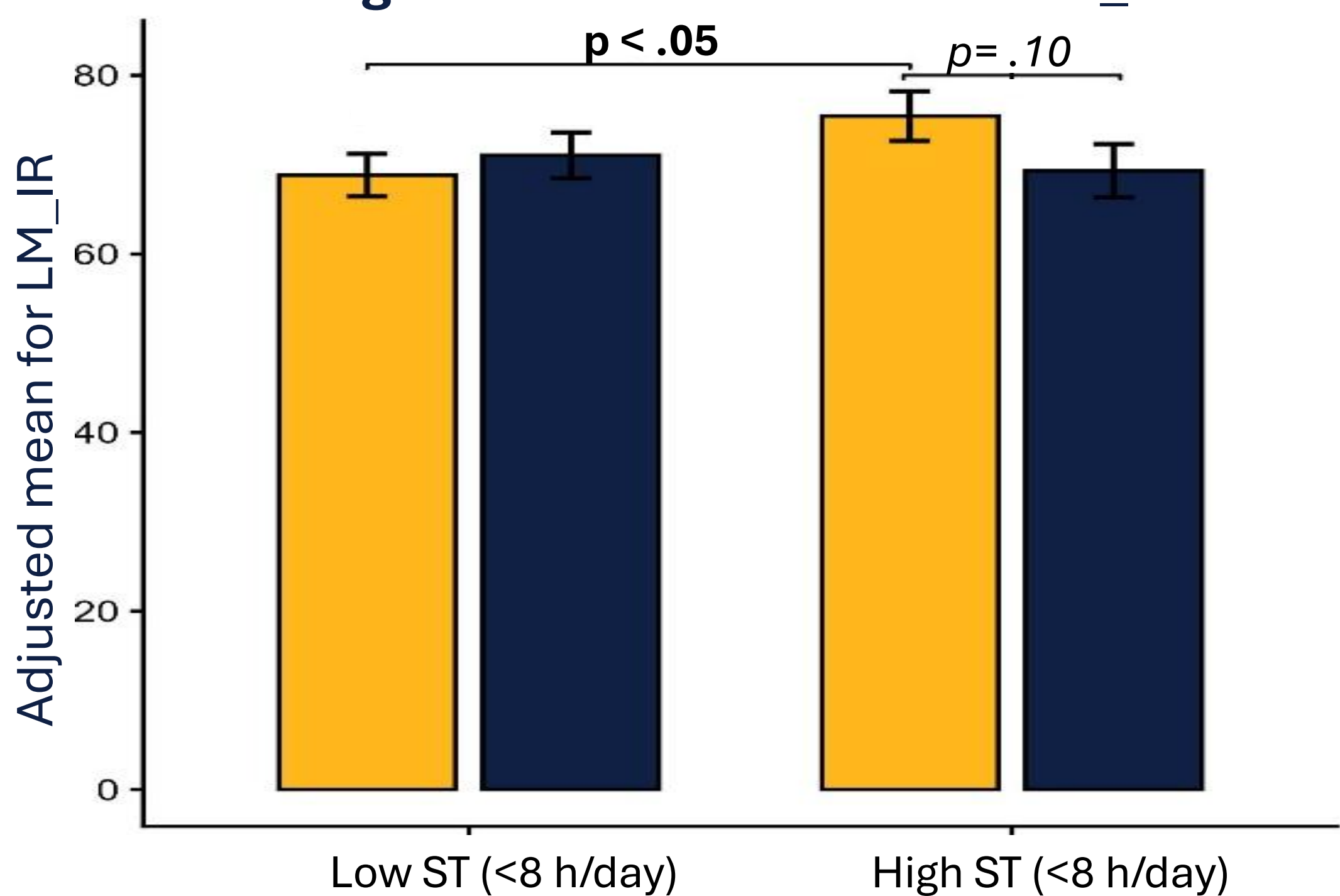
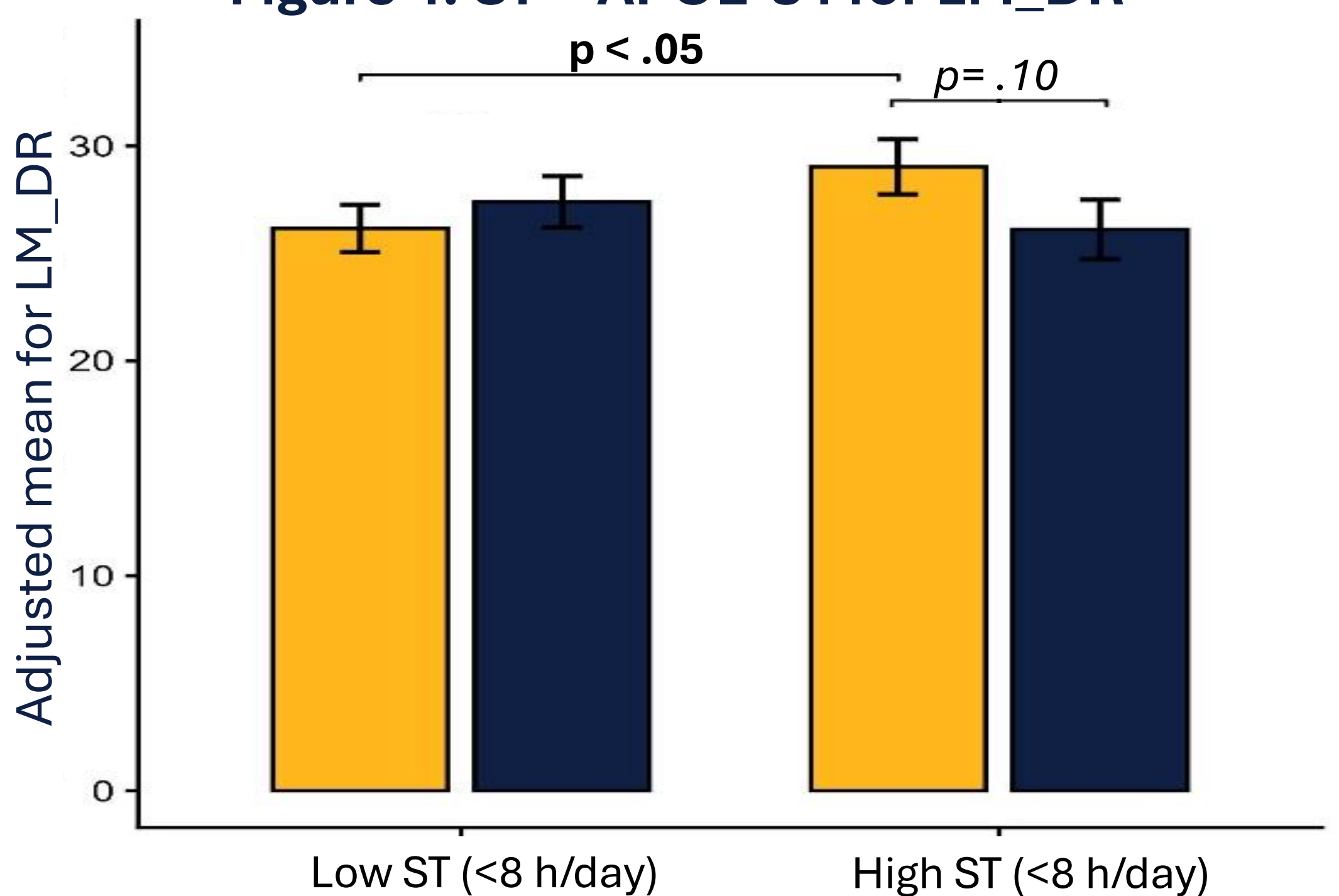


Figure 4. ST × APOE-ε4 for LM_DR



• No main effects of ST or APOE-ε4 status were detected for AVLT or LM.

• Significant APOE-ε4 × ST interactions for:
✓ AVLT_IR (p = .020) → Figure 1
✓ AVLT_DR (p = .009) → Figure 2

• APOE-ε4 × ST trends were observed for:
✓ LM_IR (p = .083) → Figure 3
✓ LM_DR (p = .062) → Figure 4

When ST was low, differences in memory as a function of carrier status were not observed. When ST was high, APOE-ε4 carriers performed worse than non-carriers. Non-carriers with high ST performed better than those with low ST.



DISCUSSION

- ST moderated the association between APOE-ε4 carriage and EM, suggesting that ST may be a modifiable factor influencing cognitive vulnerability.
- APOE-ε4 carriers appeared more susceptible to the negative association between higher ST and memory performance, particularly during midlife.
- Future studies should determine whether reducing or interrupting ST influences longitudinal cognitive trajectories and whether these effects differ by APOE-ε4 carriage.



GLOBAL TARGET

Reducing ST may be an important target for those at elevated genetic risk of AD



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