

Preclinical tau pathology in the medial temporal lobe relates to eye-movement patterns during memory encoding

BACKGROUND

Medial temporal lobe (MTL) structures are critical for memory and are closely linked to eye-movement-based environmental sampling. Whether subtle, preclinical tau pathology in cognitively unimpaired older adults is already associated with changes in gaze behavior remains unclear.

Aim. To investigate the impact of preclinical MTL tau accumulation on visual exploration during a recognition memory task.

PARTICIPANTS

Cognitively unimpaired older adults (≥ 60 y) were drawn from a large ongoing longitudinal super aging study (CRC1436 – Z03, Behrenbruch et al., 2026) and underwent [^{18}F]PI2620 PET/MR imaging. They were stratified into high- and low-tau groups based on Tau distribution volume ratio (DVR) in an AD-signature meta-ROI covering the medial temporal lobe (MTL, Jack et al. 2017). Data of 29 participants was included in the analysis.

	Low Tau	High Tau	P value
N	13	16	
Age, years	69 (64-88)	68 (62-88)	0.22
Sex (f/m)	7/6	7/9	0.59
Education, years	14.8 (SD 2.1)	15.3 (SD 2.6)	0.59
PACC5	0.6 (SD 0.8)	0.7 (SD 0.7)	0.87
Plasma A β ratio 42/40	0.09 (SD 0.01)	0.09 (SD 0.01)	0.17
Plasma pTau217	0.12 (SD 0.06)	0.16 (SD 0.13)	0.28
MetaROI DVR	0.87 (SD 0.02)	1.01 (SD 0.03)	<.001

Table 1. Sample characteristics by tau group.

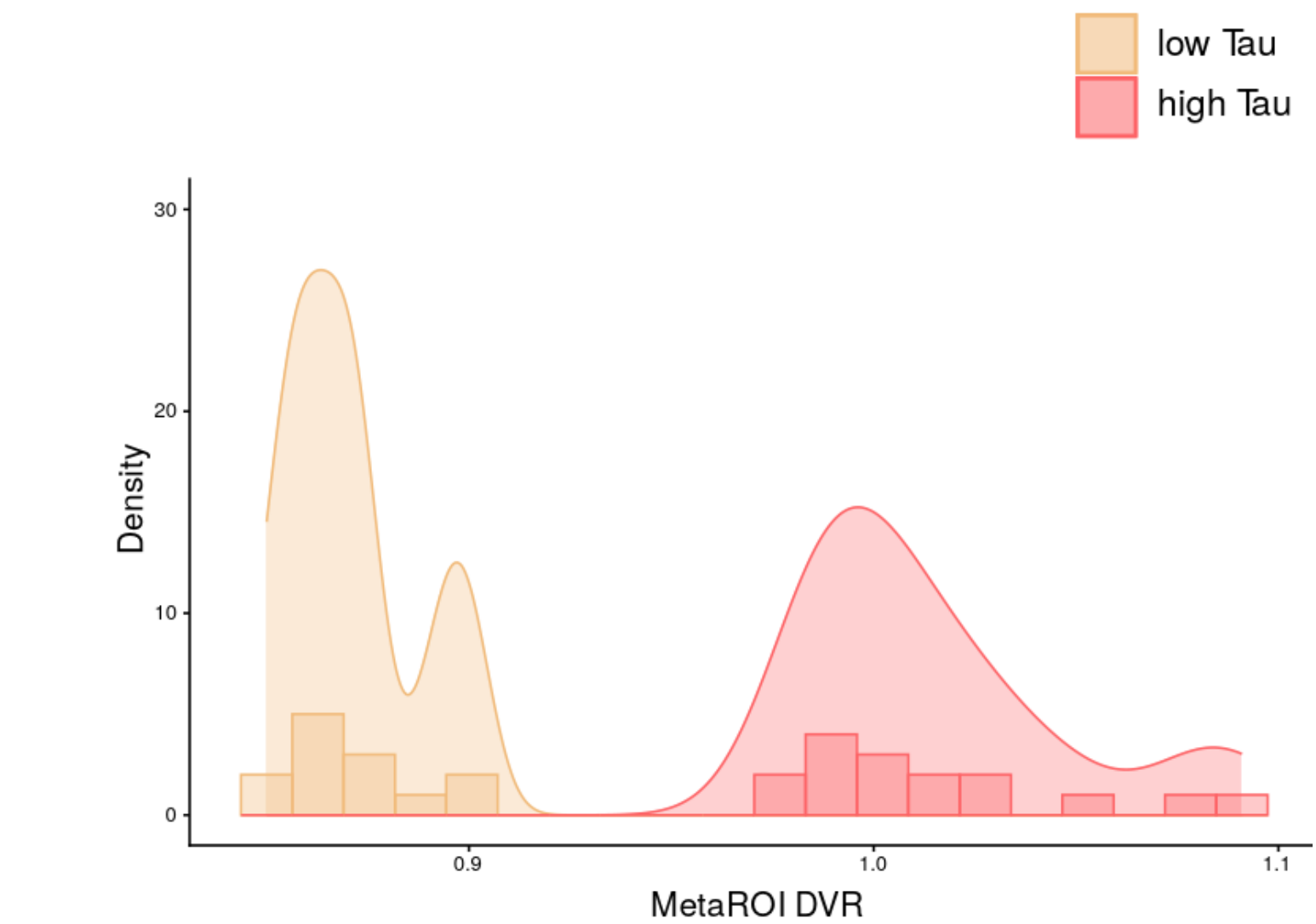


Figure 1. Distribution of MetaROI DVR values defining the Tau groups.

TASK

Participants were presented with 60 face and 60 house images, selected from the Karolinska Directed Emotional Faces (Lundqvist et al., 1998) the DalHouses (Filliter et al., 2016) database, respectively. Each stimulus set was divided into a study set and a test set, containing 54 study images (faces of 9 males and 9 females with neutral, happy, and angry expressions, or 54 house images) and 12 test images (6 old, 6 new). All images were converted to grayscale and equalized in size (image size = $15^\circ \times 9^\circ$). Images were presented on a gray background at a distance of 60 cm from the participant. Before commencing the task, participants completed two practice trials with new stimuli.



Figure 2. Block design. Each trial began with a central fixation cross (≥ 0.5 s), a fixation dot (1–2 s), the 3 s stimulus, and a 1 s blank screen. After each 6-trial block, a 1 s cue (?) preceded the test image; participants responded yes/no with a left or right button within 8 s. 18 blocks per session. Test images were a match to one of the block images in 50% of the cases.

EYE-TRACKING AND ANALYSIS

The dominant eye was tracked with an EyeLink 1000 at 1000 Hz. The eye-tracker was calibrated with 9-point calibration at the start of the experiment and after each break. Fixations and saccades were extracted from the eye-movement data. Blink-adjacent (within 100ms window) saccades were removed. Fixations around small saccades (0.5°) were merged. Trials with extreme blinks or fixation profiles were excluded. We analyzed task performance and eye movement metrics:

- Fixation duration, count, dispersion, saccade amplitude
- Refixation metrics (recurrence quantification analysis)

Group differences were tested using ANOVAs with **group** and **sex** as factors, corrected for multiple comparisons. A linear support vector machine (SVM) classifier using 5-fold cross-validation was trained on fixation coordinates.

RESULTS: EYE-MOVEMENT METRICS

Group differences in fixation duration and fixation count (independent of sex). **No group effects** on fixation dispersion, saccade amplitude, recurrence, determinism, or laminarity ($p > .4$).

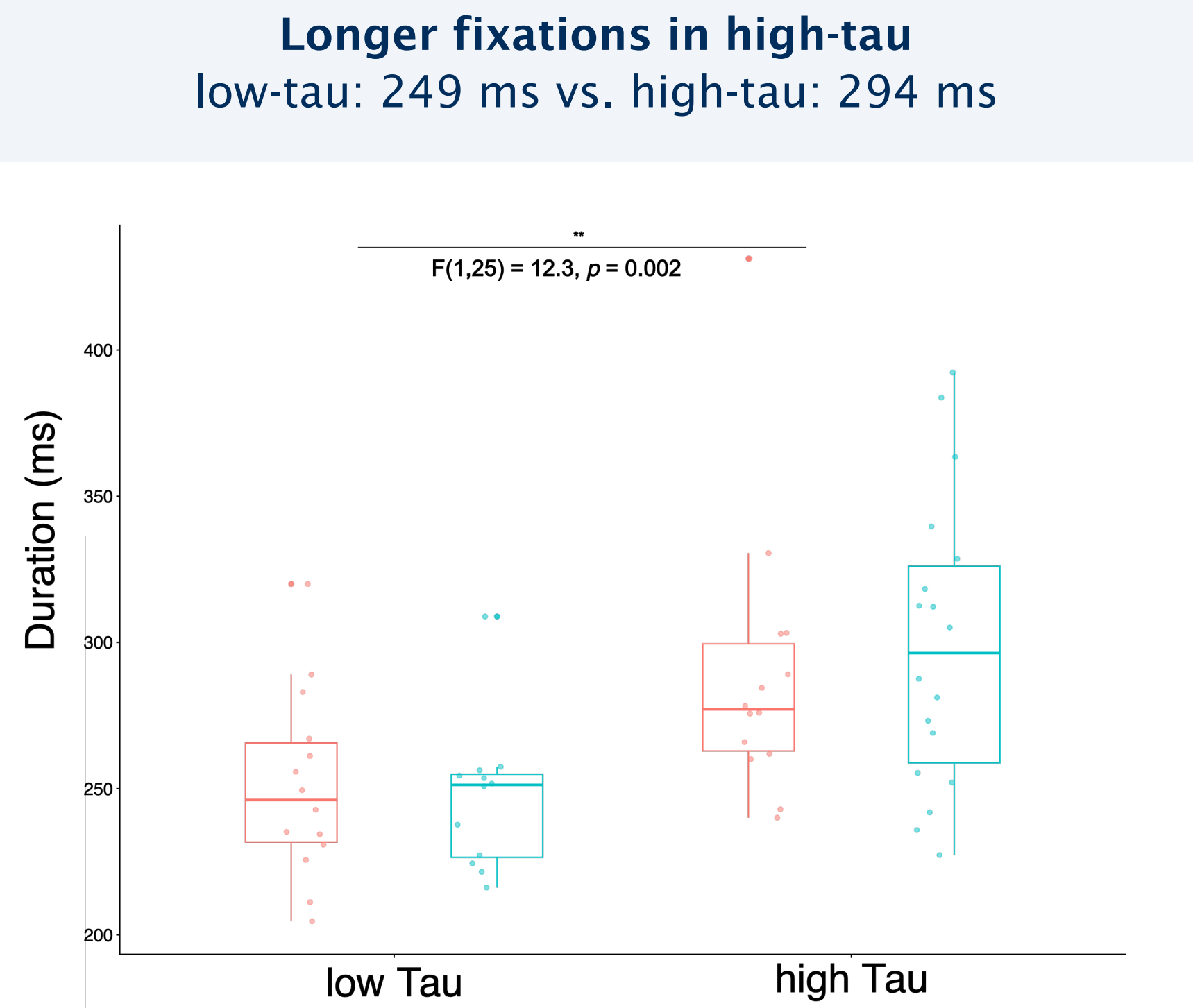


Figure 3. Mean fixation duration per participant by tau group.

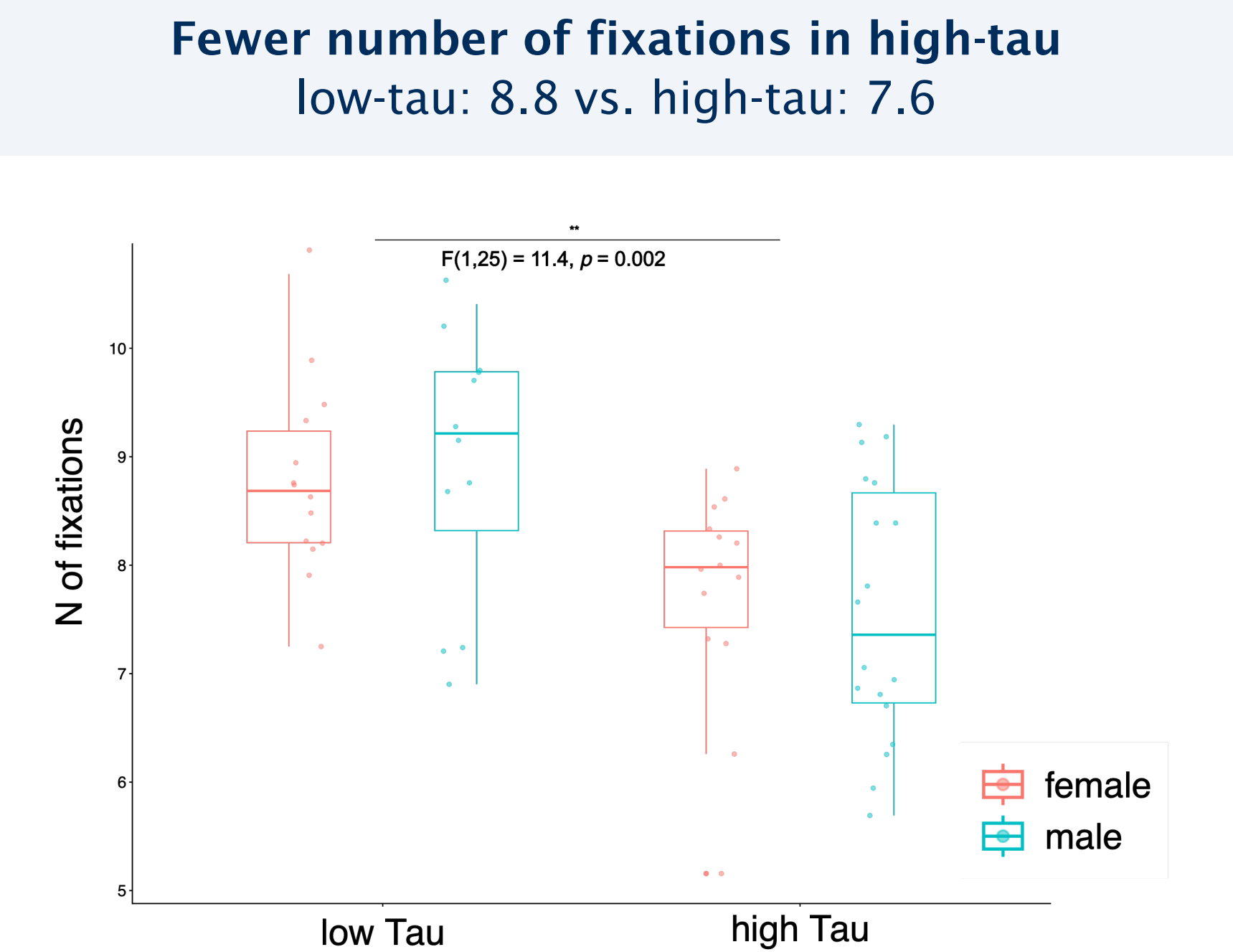


Figure 4. Mean number of fixations per trial per participant by Tau group.

CONCLUSIONS

- Preclinical MTL tau is associated with subtle alterations in gaze behavior during memory encoding.
- High-tau participants made fewer and longer fixations, despite preserved overall task accuracy.
- A SVM successfully identified tau group from the first few fixation coordinates.
- Eye-movement measures, particularly when combined with multivariate approaches, may serve as sensitive markers of early tau-related changes in MTL function in cognitively unimpaired older adults.

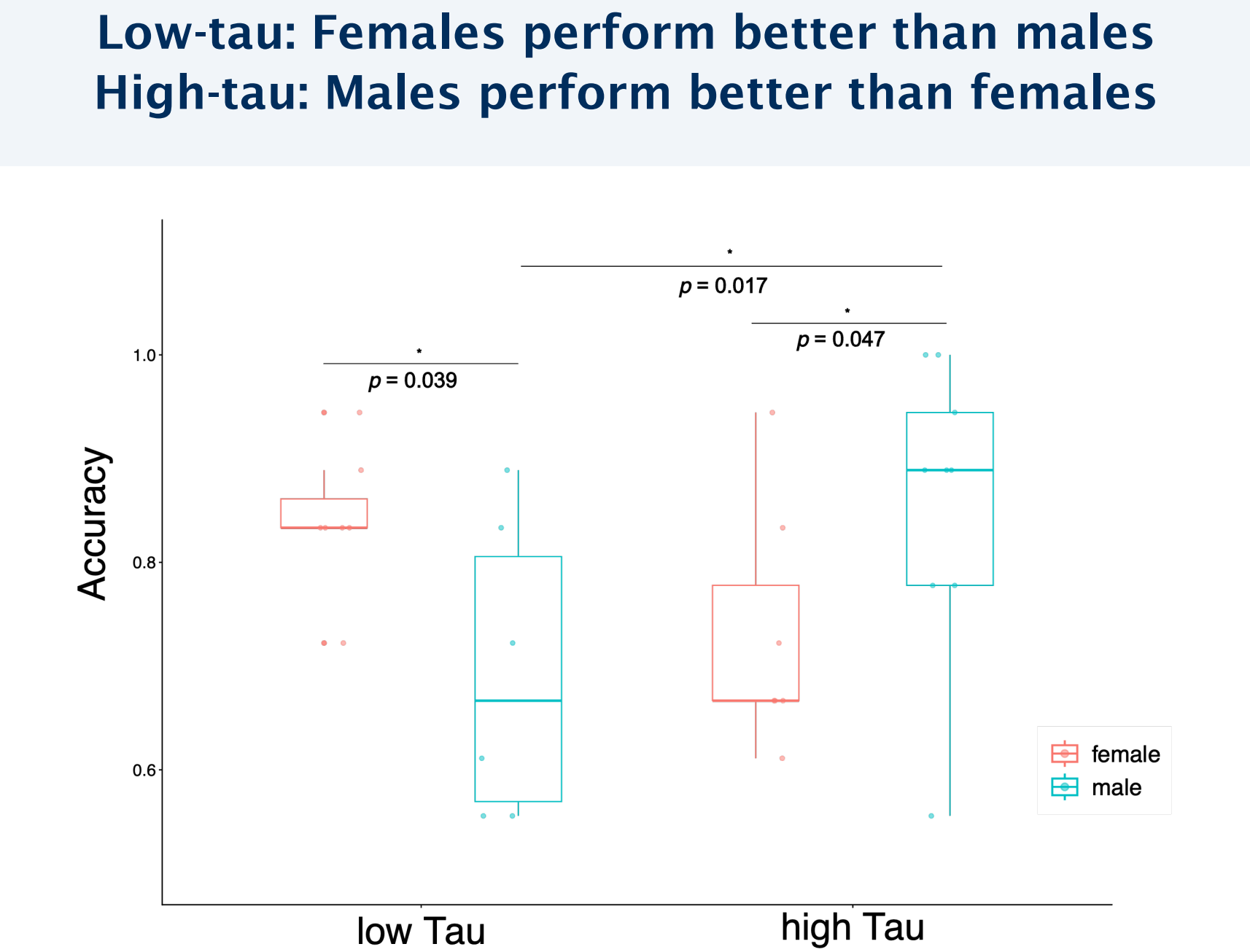
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RESULTS: TASK PERFORMANCE

Overall accuracy did not differ between groups, but showed a group $\times$ sex interaction ($F(1,25) = 9$, $p = .006$).



RESULTS: CLASSIFICATION BY FIXATION

A linear SVM trained on the x,y coordinates of the first N fixations distinguished groups above chance from two fixations onward.

