Reference frame utilization as a potential marker of aging-related deficits in spatial navigation

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Introduction

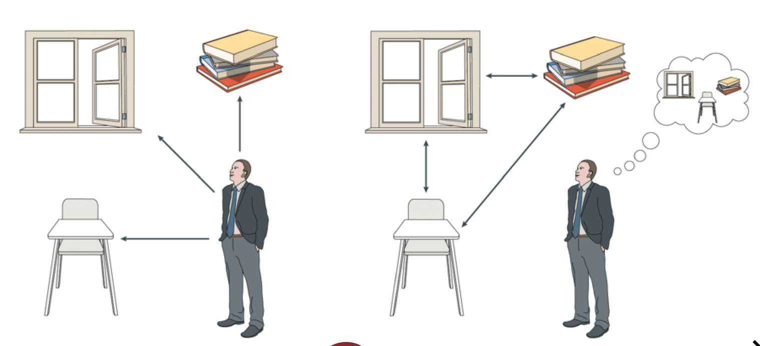
Aging = universal phenomenon

↑ Global age & life expectancy[1]

Aging-related cognitive decline[2,3]

Spatial navigation ability → One of the **earliest indicators** of *aging related cognitive decline & neurodegenerative pathologies*[4-12]

Reference Frame Utilization



- Egoformative and alloformative cues lend to the formation of **egocentric** and **allocentric reference frames** (**RFs**), respectively
- Older adults exhibit **aging-related differences in RF utilization**,[13-17] compared to younger adults
  - Deficits in utilizing allocentric RFs and increased utilization of egocentric RFs

-> Specific behavioral & neurological markers of aging-related deficits in naturalistic navigation?

Study Objectives:

- Validate and measure aging effects of novel virtual reality maze to measure naturalistic navigational ability in lab environments.
- Characterize aging effects on reference frame utilization and associations with naturalistic navigational ability.
- Test circuit mechanisms of aging-related differences in reference frame utilization utilizing concurrent TMS-fMRI.

Methods

Younger adults (YAs): *N*=26, ages 18-35

Older adults (OAs): *N*=21, ages 60+

Simulator Sickness
- Nausea
- Dizziness

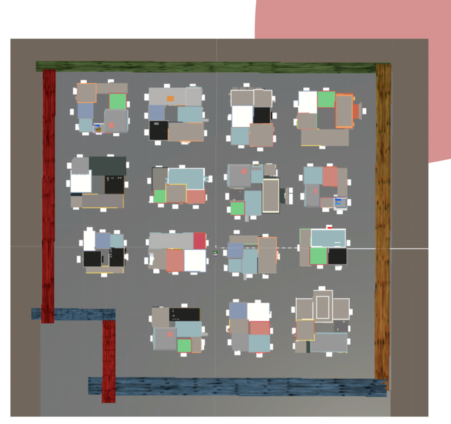
Before & After VR Task

Questionnaire that accounts for Virtual Reality (VR) related sickness, before and after VR measures.[18]

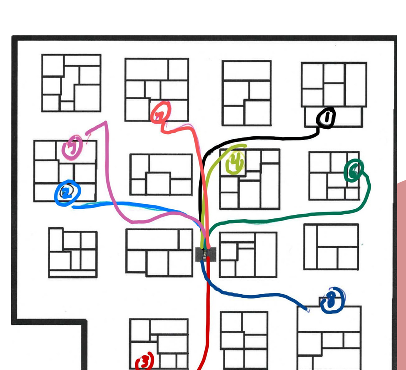
VR Familiarization Task

Task that trains participants in the VR space to correct for baseline differences in utilizing VR equipment. Includes training with handheld controllers, navigating to sample target buildings, and moving around in the VR environment.

VR City-Like Spatial Navigation Maze Task ("NavCity")



Novel VR task, based off prior literature,[19] to assess naturalistic navigational ability. Includes navigating to 8 unique target buildings (8 'trials') and repeating the maze 3 times (3 'blocks').



NavCity Allocentric Representation Assessment (NARA)

Assessment of the formation of allocentric representations post-exposure to NavCity environment. Evaluates ability to recall allocentric reference frames.

Data Analyses:

- Linear mixed models for NavCity outcomes
  - Fixed effect of NavCity outcome, random effect of participant
  - Post-hoc Bonferroni correction for number of outcome measures
- Intraclass correlation for NARA scores
- Pearson's correlation for associations between NARA and NavCity outcomes

Results

1. YAs exhibit improved navigation ability with repeated NavCity exposure.

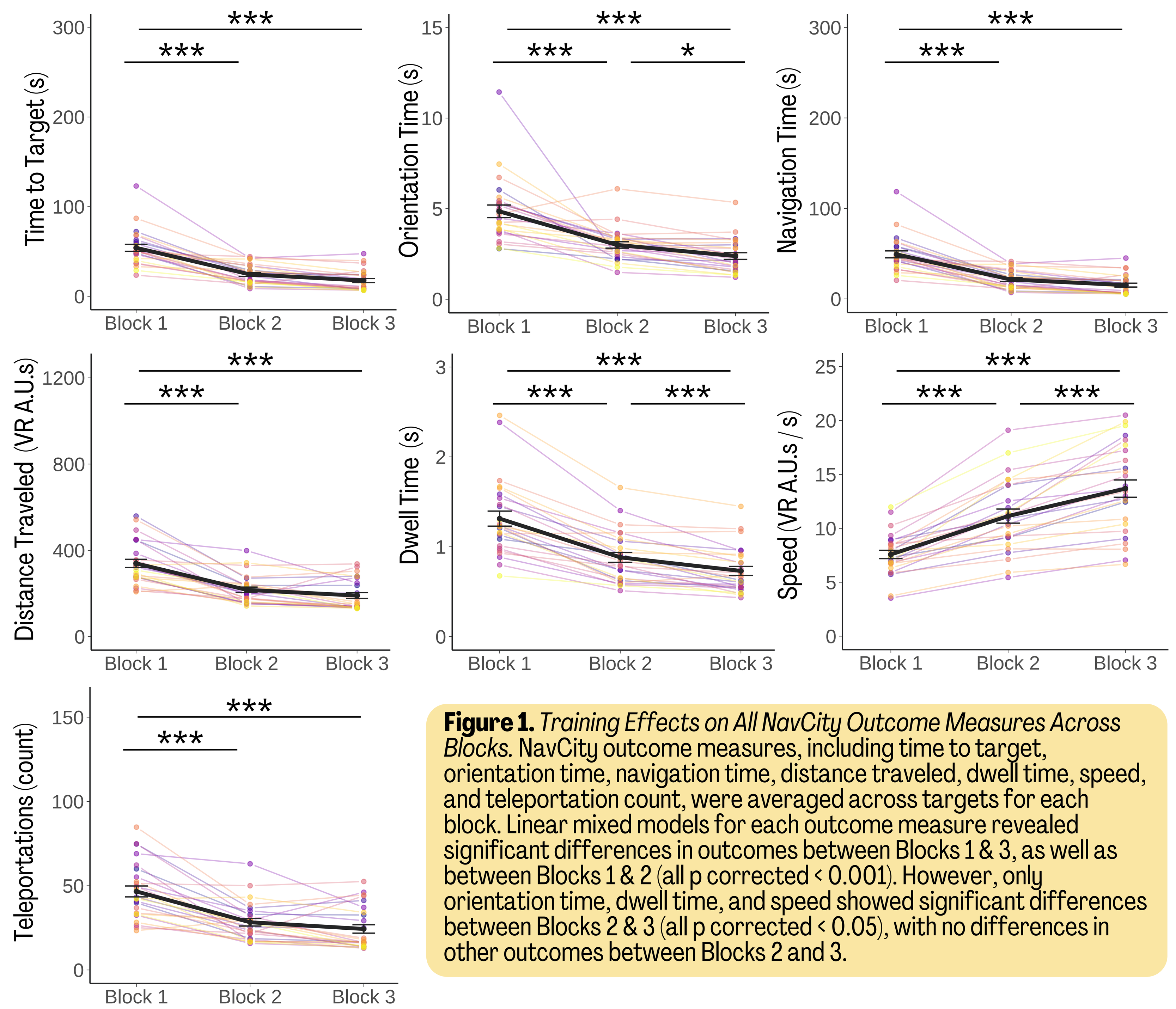


Figure 1. *Training Effects on All NavCity Outcome Measures Across Blocks.* NavCity outcome measures, including time to target, orientation time, navigation time, distance traveled, dwell time, speed, and teleportation count, were averaged across targets for each block. Linear mixed models for each outcome measure revealed significant differences in outcomes between Blocks 1 & 3, as well as between Blocks 1 & 2 (all p corrected < 0.001). However, only orientation time, dwell time, and speed showed significant differences between Blocks 2 & 3 (all p corrected < 0.05), with no differences in other outcomes between Blocks 2 and 3.

2. OAs exhibit lower navigation ability in NavCity, compared to YAs.

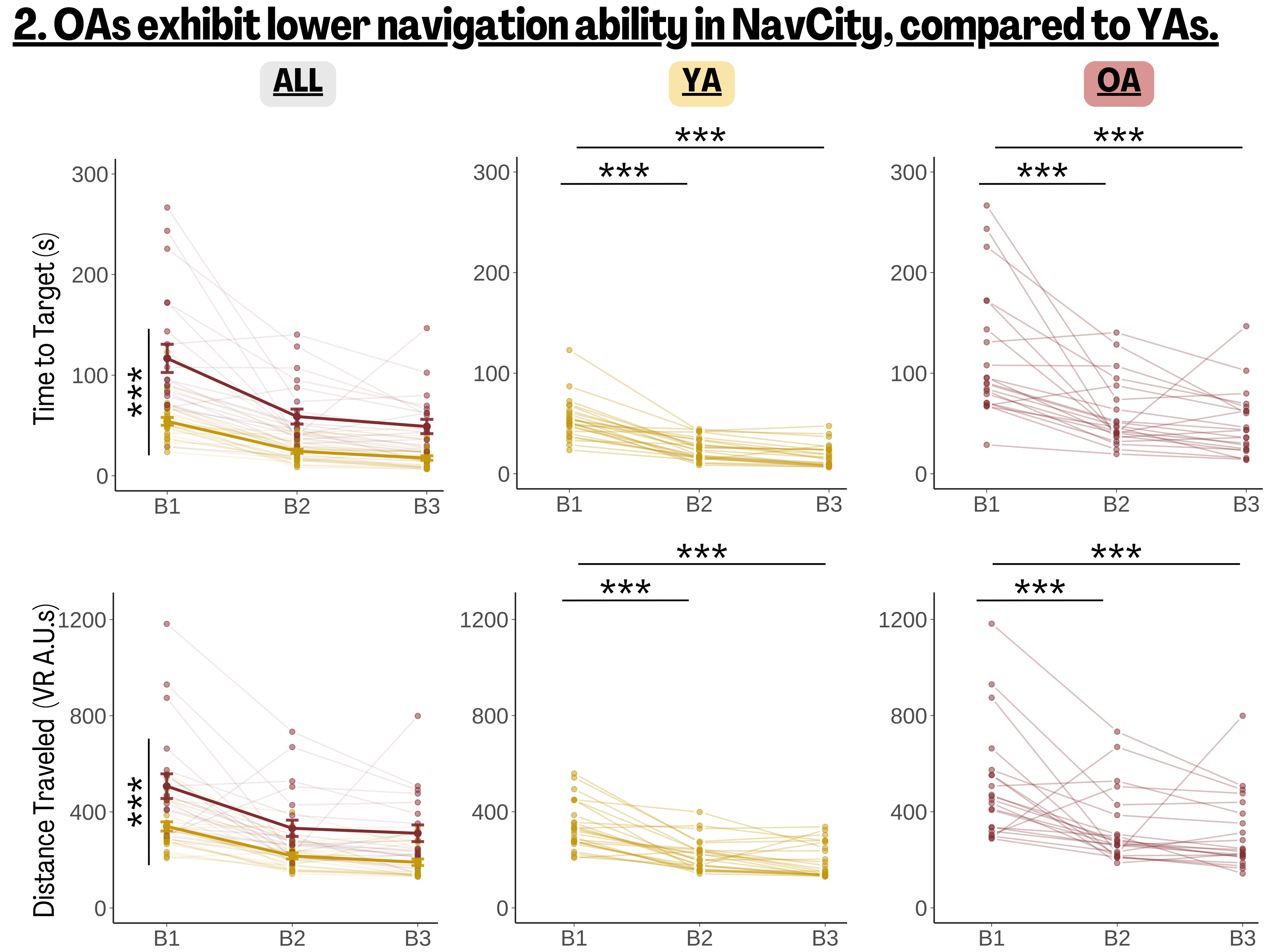


Figure 2. *Aging Effects on Select NavCity Outcomes Across Blocks.* NavCity outcome measures were averaged across targets for each block, per age group. In YA and OA groups, linear mixed models revealed that both time to target and distance traveled decreased significantly between Blocks 1 & 3, as well as Blocks 1 & 2 (all p corrected < 0.001). However, there were no significant differences between Blocks 2 & 3 in YAs (time to target, p = 0.051; distance traveled, p = 0.241) or OAs (time to target, p = 0.650; distance traveled, p = 0.884). Overall, there was a significant aging effect on both time to target and distance traveled between YAs and OAs (p correected < 0.001).

Results (cont.)

3. Higher recall of allocentric reference frames is strongly correlated with better navigational performance.

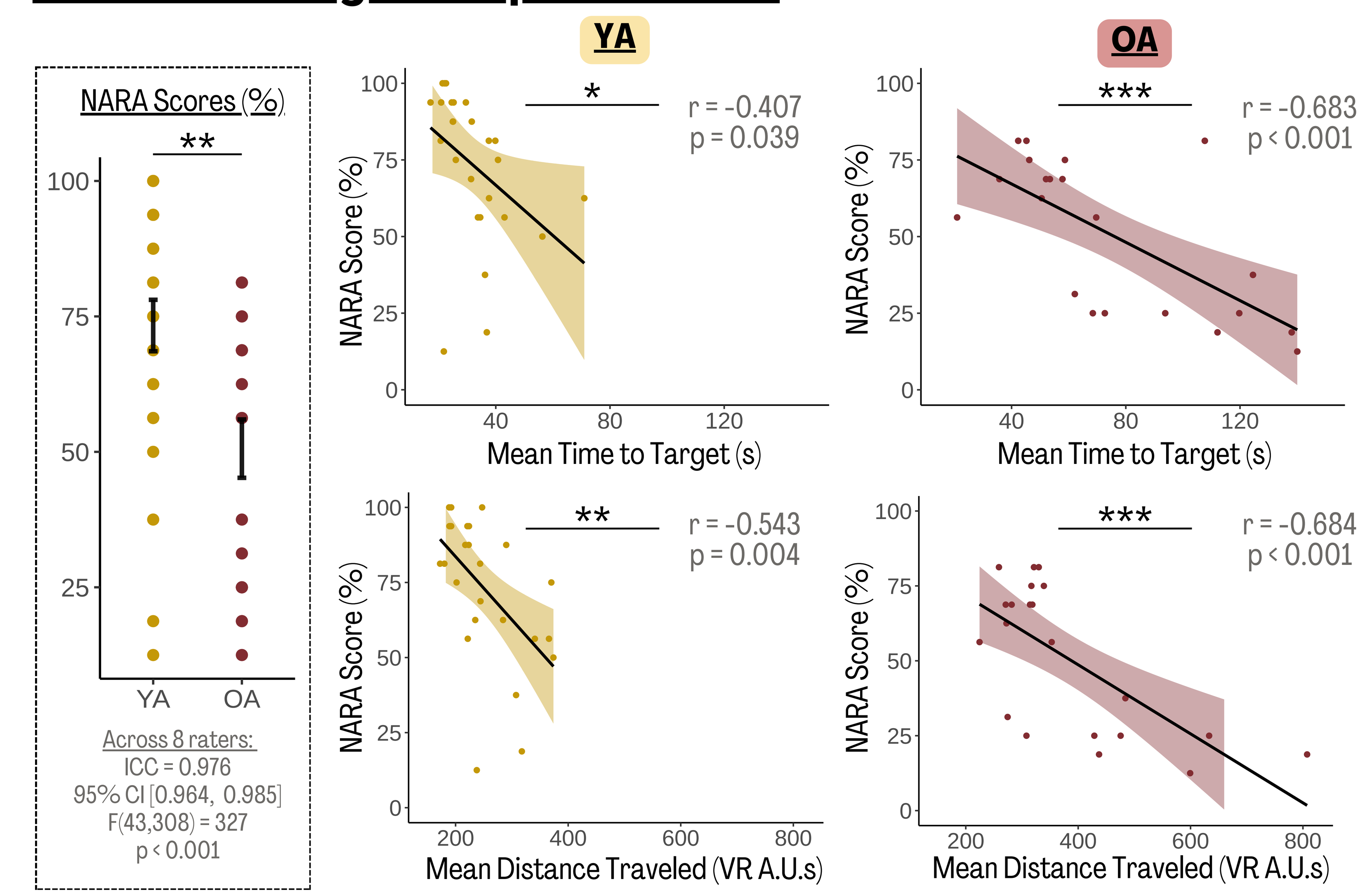


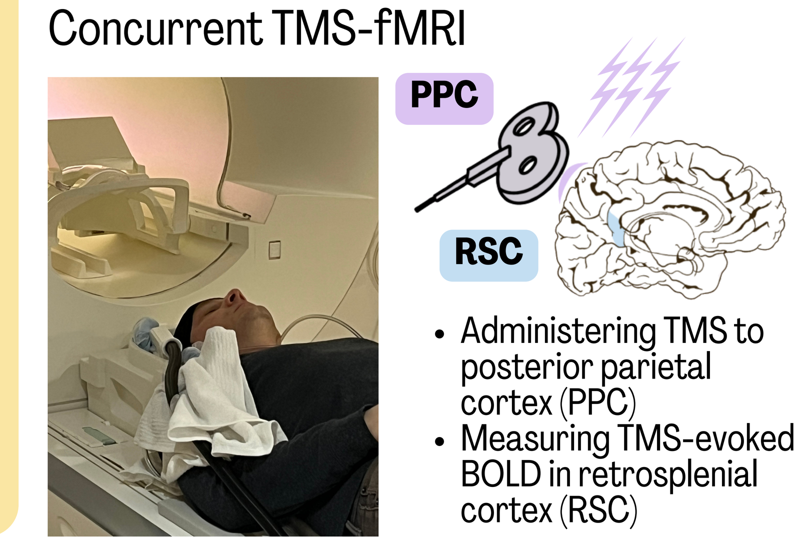
Figure 3. *Correlations between Select NavCity Outcomes and NARA Scores.* NARA outcomes were scored by 8 raters to determine inter-rater reliability and showed a high degree of agreement (ICC = 0.976, 95% CI [0.964, 0.985], F(43,308) = 327, p < 0.001). A one-way ANOVA revealed that NARA scores for YAs were significantly higher than scores for OAs (F(1,45) = 10.06, p = 0.00273), reflecting higher recall of allocentric RFs in YAs and robust aging effects on NARA scores. Additionally, Pearson's correlations revealed significant negative correlations between NARA scores and NavCity outcome measures for YAs (time to target, r = -0.407, p = 0.039; distance traveled, r = -0.543, p = 0.004) and OAs (time to target, r = -0.683, p < 0.001; distance traveled, r = -0.684, p < 0.001). This indicates that a stronger NARA score (higher recall of allocentric RFs) is associated with decreased NavCity outcomes (higher navigational ability).

Discussion & Future Directions

Main Takeaways:

- The novel NavCity task allows for sufficient navigational training and captures individual naturalistic navigational ability (Fig. 1)
- Rates of improvement across blocks are similar for both YAs and OAs, indicating that aging does not affect the rate of navigational training (Fig. 2).
- NARA reveals aging-related deficits in the recall of allocentric RFs, which may serve as a potential biomarker of aging-related cognitive decline (Fig. 3).

Future Directions:
Concurrent TMS-fMRI



- Administering TMS to posterior parietal cortex (PPC)
- Measuring TMS-evoked BOLD in retrosplenial cortex (RSC)

References

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