

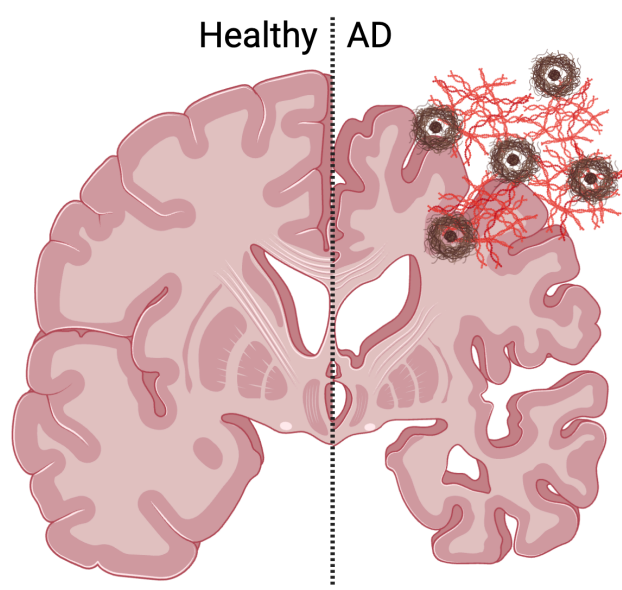
Fine Motor Dysfunction As An Early Indicator Of Alzheimer's Disease: Evidence From A Novel Rodent Reaching Task

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Background

Alzheimer's disease is the most common form of dementia and the 6th leading cause of death amongst individuals 65 years and older. The disease is characterized by amyloid aggregates, tau tangles, and brain-wide inflammation, atrophy, and cell-death, with insomnia, personality changes, and memory deficits being key behavioral symptoms.

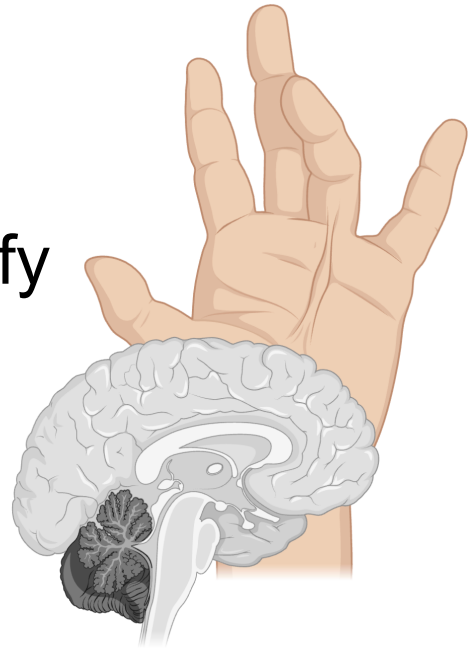


6th

leading cause of death amongst Americans and seniors 65 & older.

Emerging disease staging frameworks highlight that pathology can develop ~ 15 years prior to clinical symptom onset, such that individuals may be cognitively asymptomatic while still at risk for dementia. Thus, diagnostic tasks capable of detecting early, pre-clinical disease shifts are critical.

Notably, fine motor performance appears to decline earlier than gross motor capabilities. Functional fine motor assessments can identify and predict decline and subsequent disease progression in individuals with Mild Cognitive Impairment, pointing the specificity of these tasks to early AD-related dysfunction.

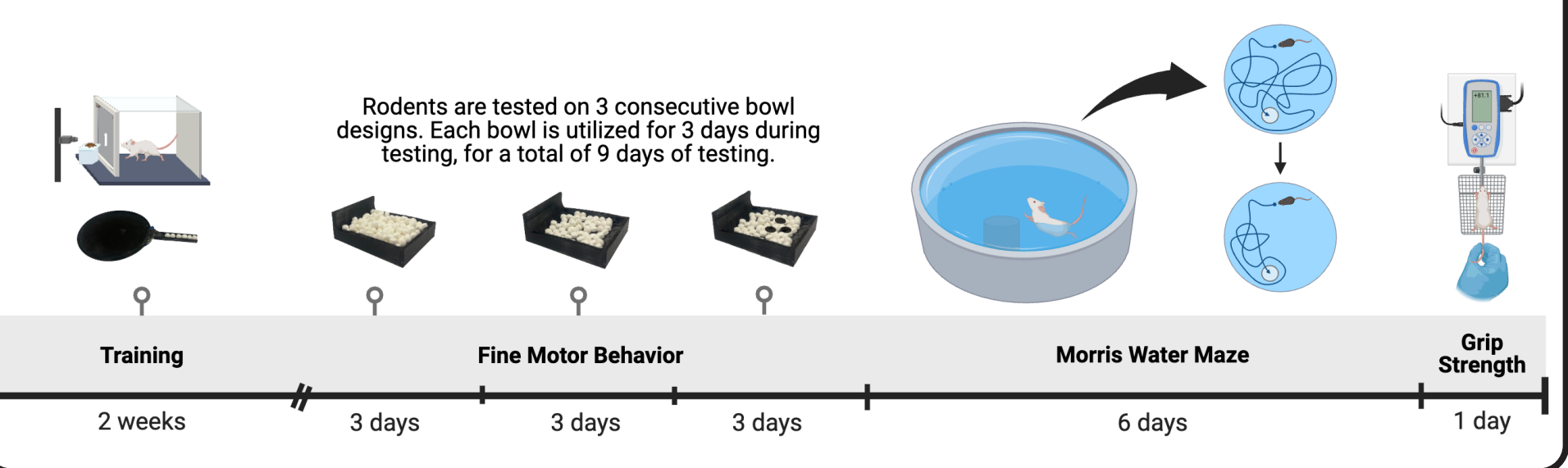


Here, we examine the specificity of a novel fine motor task in identifying early shifts in AD pathology across the lifespan of the TgF344-AD rat model. By taking advantage of these early fine motor changes, we aim to transition from diagnostic tools that emphasize deficits in cognition and executive function that largely occur at late stages, to motor biomarkers that detect early pathological anomalies.

Overview

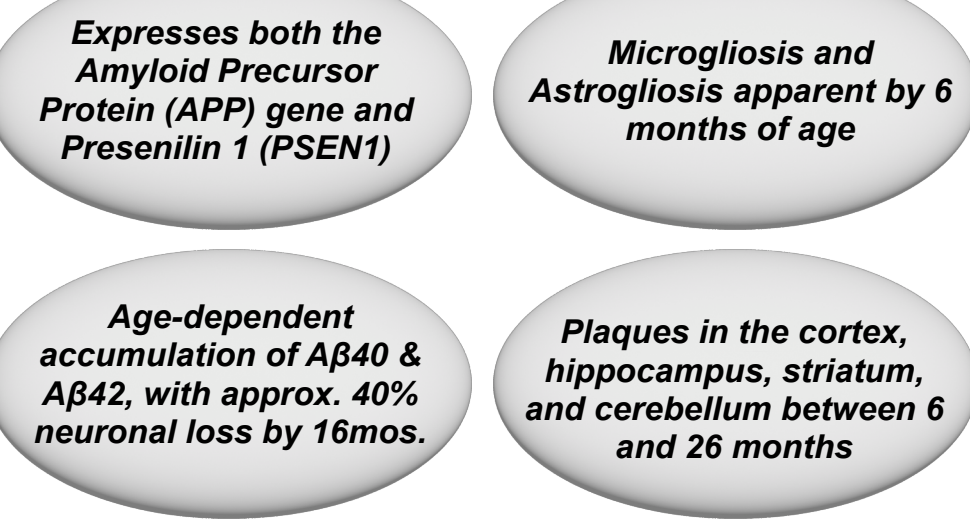
To examine the impact of pathology accumulation and its effects on both fine motor function and cognition, male and female rats were tested in a fine motor task (see Melick et al., 2025), the Morris Water Maze, and a grip strength task at 6 and 12 months of age. These time points capture both the commencement and early progression of disease state in the TgF344-AD rat.

Experimental Timeline



TgF344-AD Model

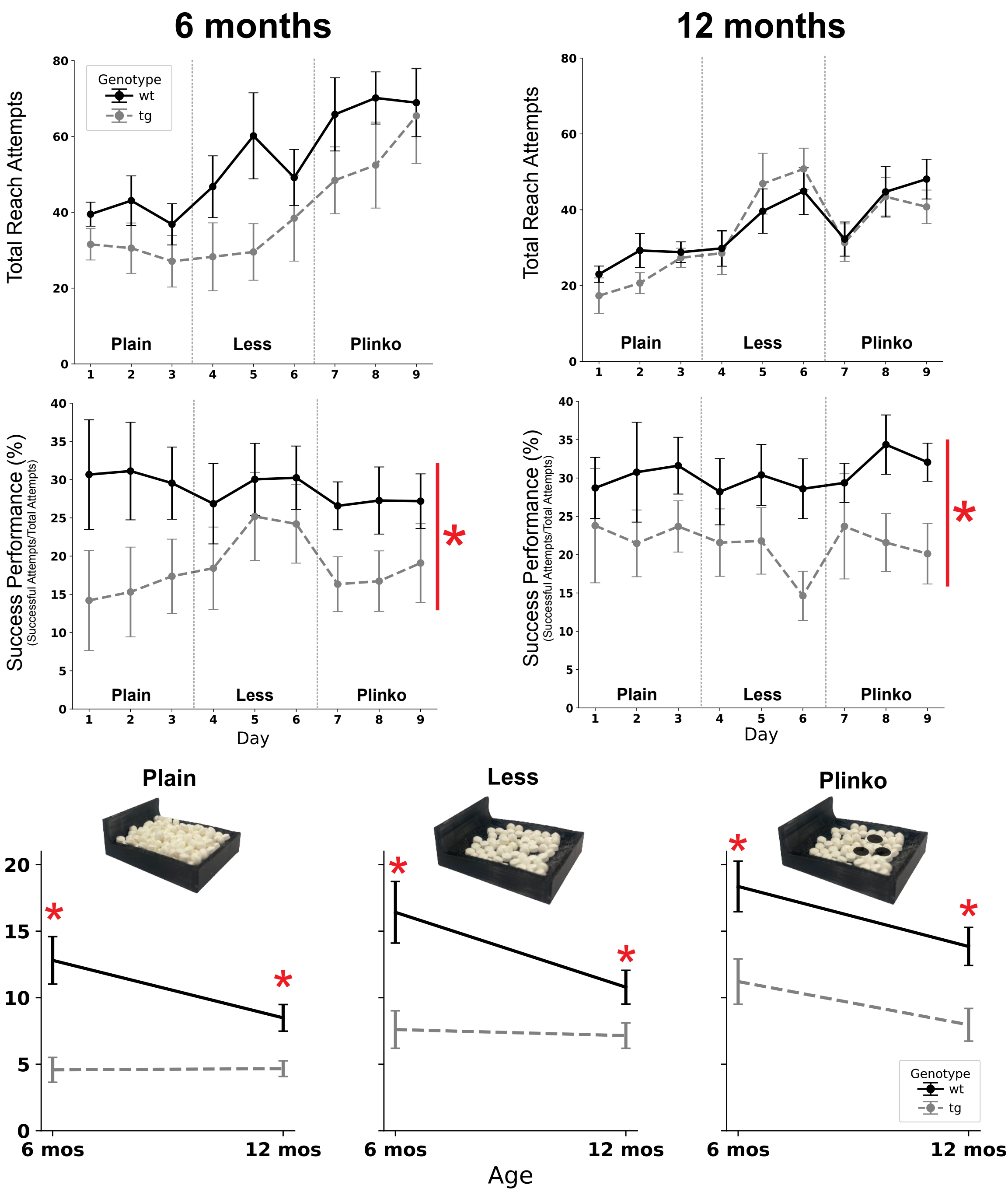
(Cohen et al., 2013)



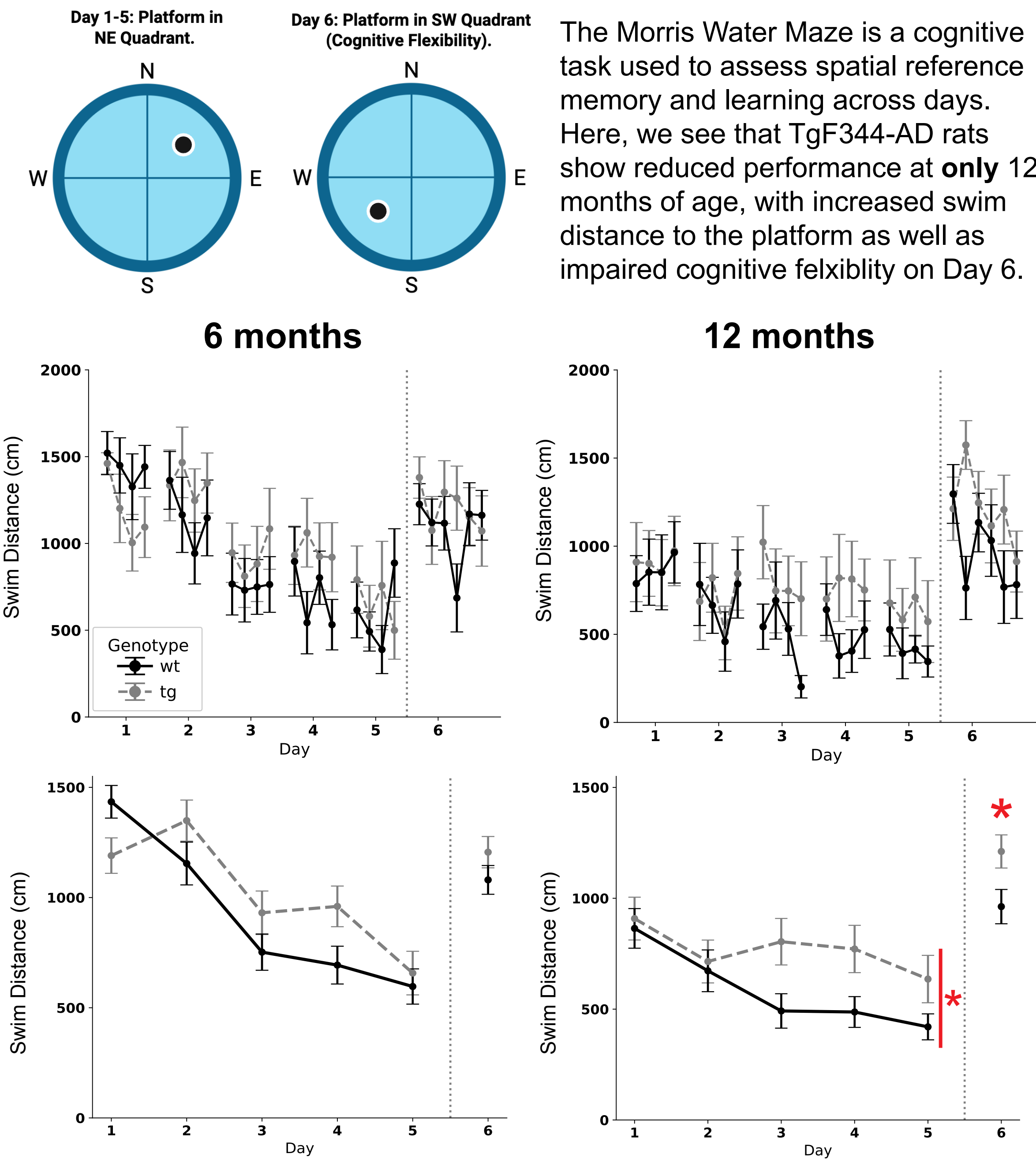
Age	6 mos.	12 mos.
Wildtype	12	12
TgF344-AD	12	12

Fine Motor Deficits Precede Cognitive Decline in the TgF344-AD Rat

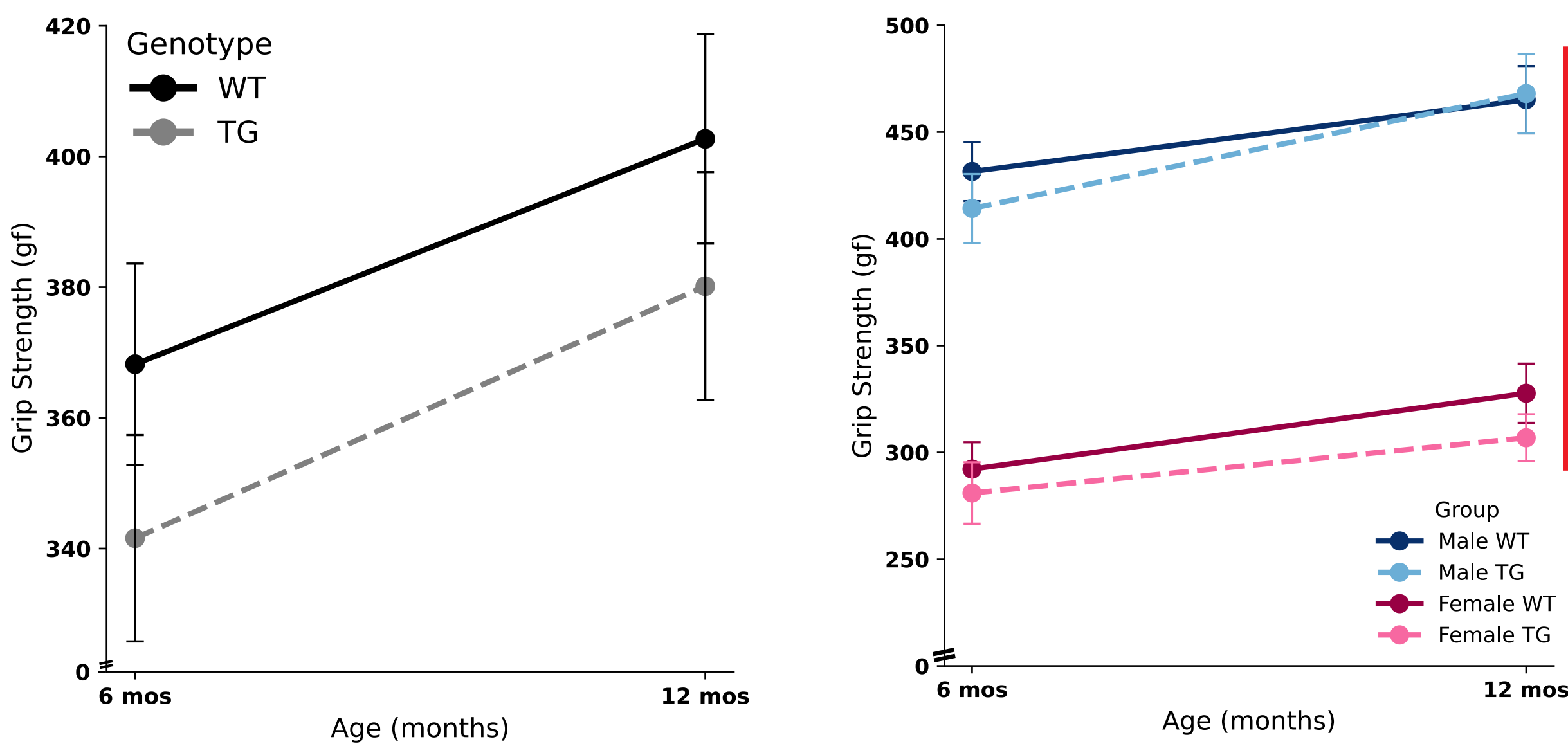
Fine Motor Deficits Arise at 6 Months of Age



Cognitive Deficits Arise at 12 Months of Age



Grip Strength Remains Comparable Between Genotypes at 6 and 12 Months of Age



Grip strength tasks can distinguish cognitively impaired older adults from their unimpaired counterparts, but there is a weak association between cognitive function and grip strength, which cannot distinguish Mild Cognitive Impairment from dementia (Hooyman et al., 2021). Thus, grip strength is considered **less specific to AD pathology**.

Conclusions and Future Directions

- Fine motor dysfunction was detectable earlier in disease progression than cognitive deficits, as demonstrated by reduced fine motor performance at both 6 and 12 months of age, and cognitive deficits arising only at 12 months of age in the Morris Water Maze.
- These findings suggest that functional fine motor assessments may provide greater specificity in distinguishing disease-related decline as well as early disease-related changes.
- At both 6 and 12 months, grip strength remained comparable between genotypes, with only sex impacting grip strength scores. This matches the human literature which suggests that changes in grip strength, a gross motor measure, are indicative of normal aging but lack specificity to AD.
- Future directions include testing animals at 18 and 24 months of age to evaluate if these deficits persist. Longitudinal tissue analysis will be conducted to examine the trajectory of pathology across the lifespan alongside behavior. Additionally, machine learning analysis of behavior (including fine motor function, gait, and swimming trajectory in the Morris Water Maze) is ongoing.

Acknowledgments

We would like to express our gratitude to our funding sources: Institute for Mental Health Research, Institute for Social Science Research, Nancy Eisenberg Junior Faculty Scholar Award, Arizona Department of Health Sciences (ADHS14-052688), US Department of Health and Human Services and State of Arizona (ADHS Grant No. CTR057001), National Institute on Aging (NIA) of the National Institutes of Health (NIH) (P30AG019610), Arizona Alzheimer's Disease Research Center REC Fellows Program and Arizona Alzheimer's Consortium. We would like to thank graduate student Nelson Yamada for colony management. Images created with Biorender.com.

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