Spatial Navigation in Rodent Models of Alzheimer's Disease During Reference Frame Transformation

Kelsey Coss, Alfonso Brea Guerrero, Aaron Wilber

Introduction

Spatial navigation is the ability to navigate through space and find one's way to a desired location.
In rodents, spatial navigation is crucial for survival and involves the use of various sensory cues to create a mental map of the environment.

In the present project, we will use rodent models to understand the neurophysiology of spatial navigation, and how some disorders, such as Alzheimer´s disease (AD), interfere with its normal physiology.

Our objective is to train rats to complete a series of spatial orientation tasks. We focus on obtaining behavioral data while developing electrophysiological recordings to measure neuronal activity in the hippocampus and parietal cortex using two approaches, tetrodes and silicon probes.

We use the Map to Action Transformation Task (MATT) to investigate egocentric and allocentric reference-frames as well as the transformation between them. We are looking to identify navigation deficits in AD animals and further our understanding of the navigation system's physiology when spatial memory is tested, and what changes there are in spatial memory deficit/ disease models.

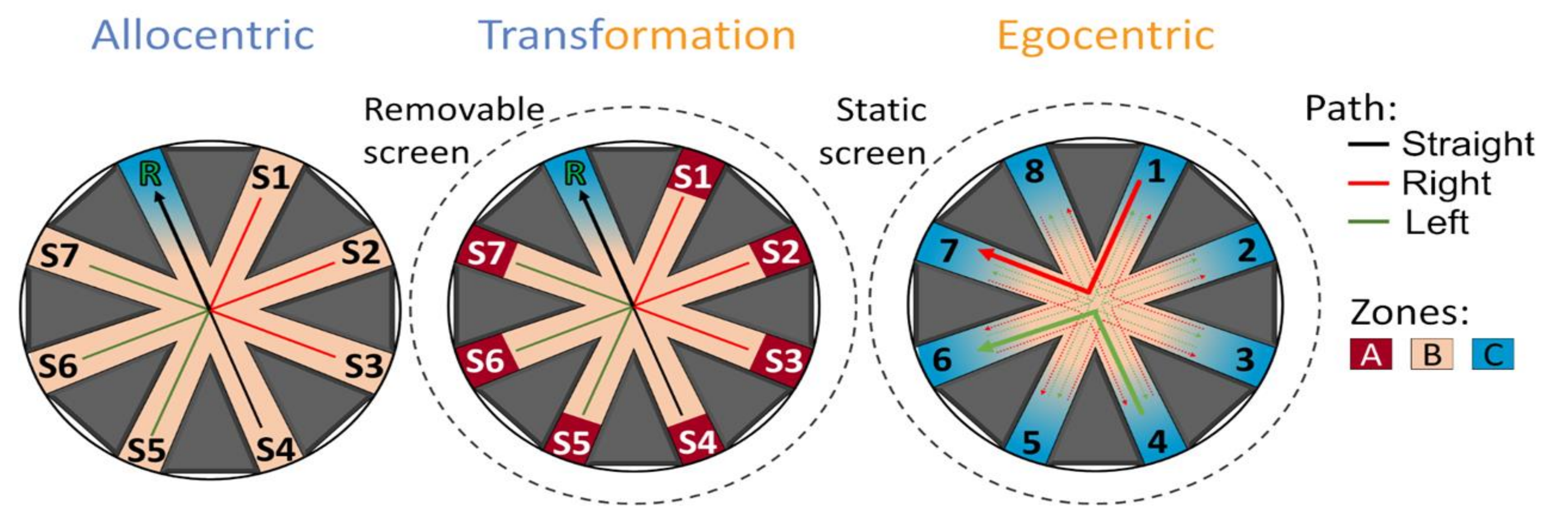
Methods

The Map to Action Transformation Task (MATT) is a three-part behavioral paradigm carried out on a circular platform with 8 zones.

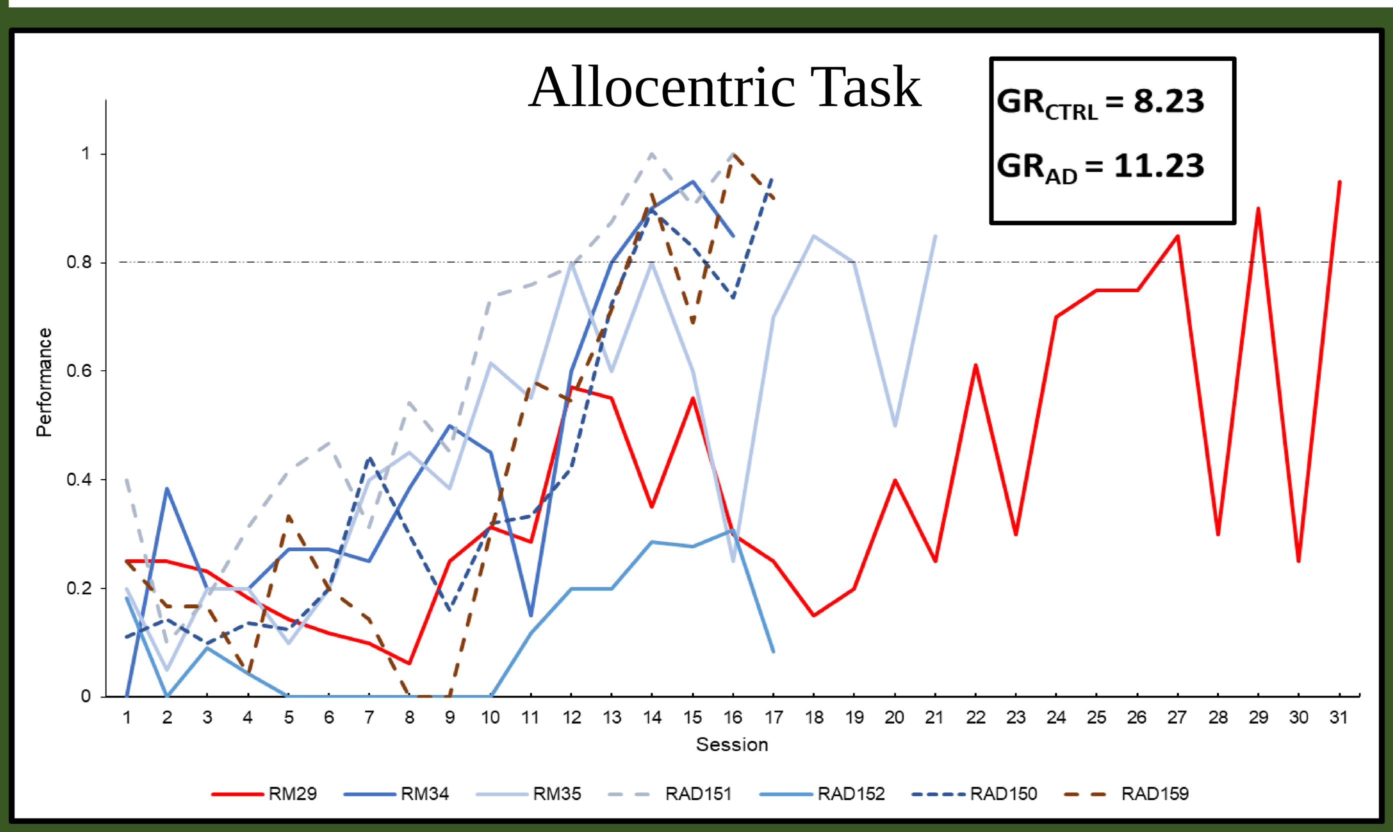
In the first paradigm, Allocentric, the animal must learn and remember which of the eight arms is rewarded using distal cues (cues on the walls surrounding the platform) and navigate to the rewarded arm from seven possible starting locations. The reward can be either food or stimulation to the medial forebrain. Once the animal performs over 80% correctly for 3 out of 4 days, they move on to the next paradigm.

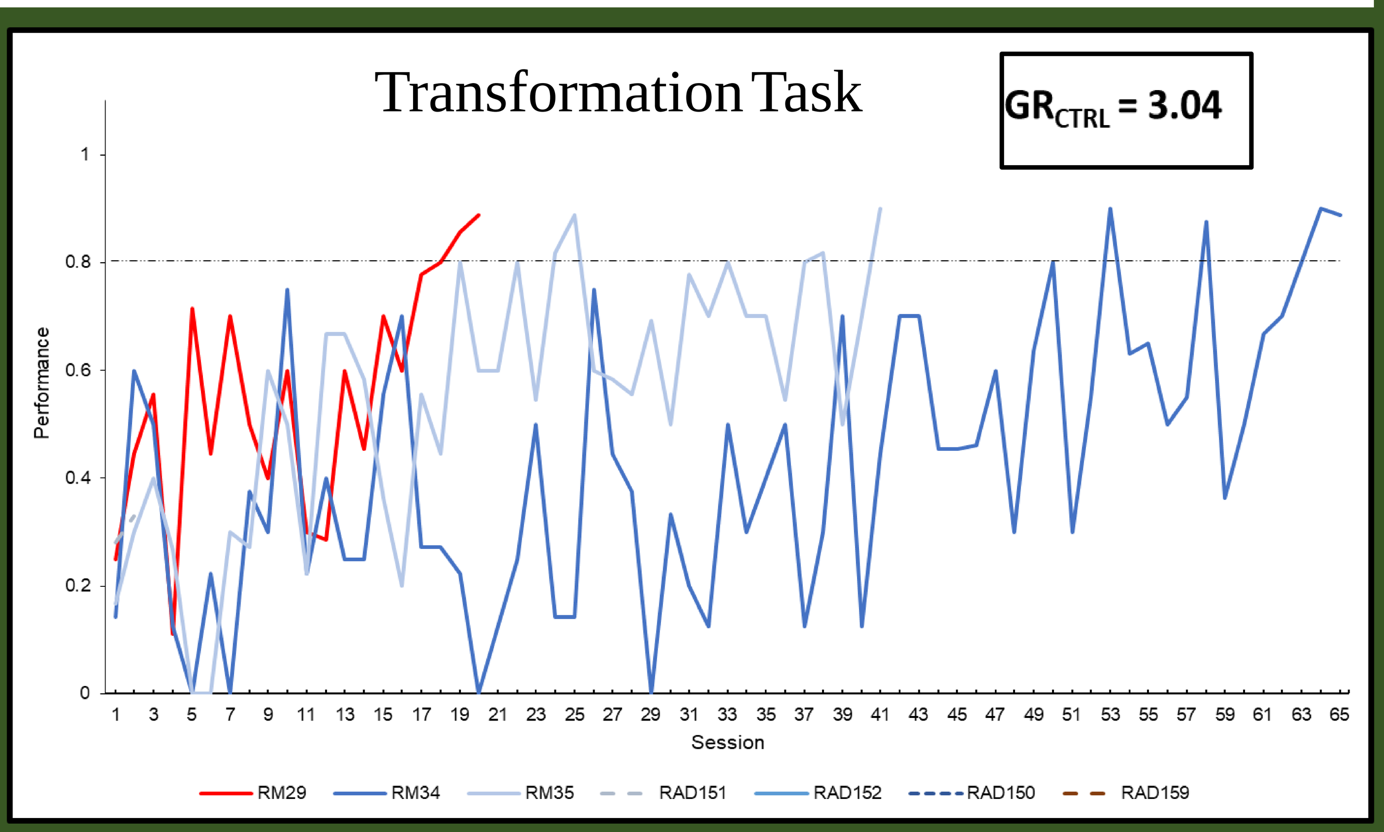
The second paradigm, Transformation Task, requires the animal to use self-centered motion plans based on their previous knowledge of the surroundings. The animal is placed in a translucent plexiglass box andis allowed to view distal cues, then an opaque box is placed over the animal and dark curtains are pulled around the platform to cover the distal cues. After each trial, the curtains are removed, and the next trial starts with the cues being visible.

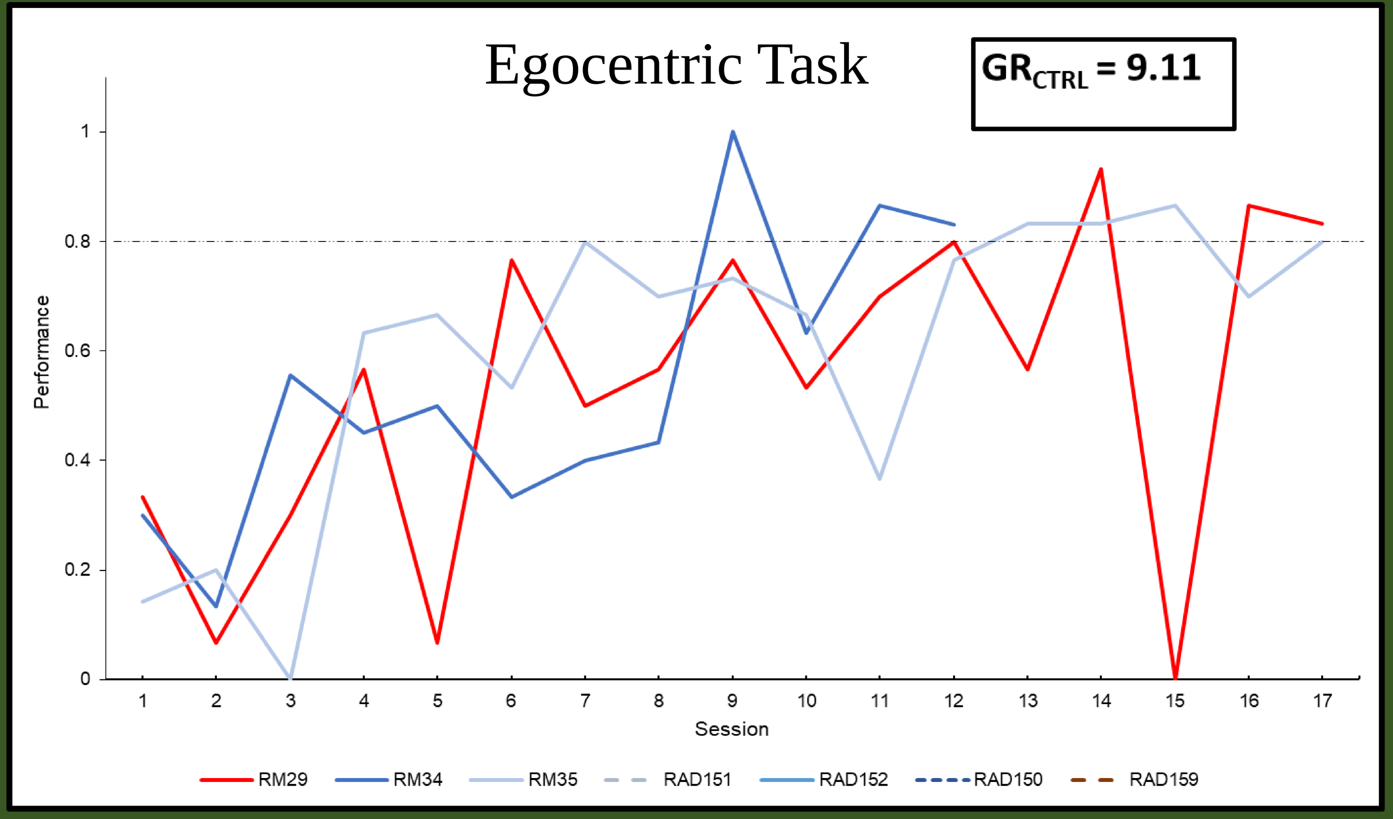
The third and final paradigm, Egocentric, involves the curtains being present at all times and the animal not having access to the distal cues. The rewarded arm is determined in reference to the starting arm and not to a position in the room. For example, the rewarded arm may be randomly determined to be two zones to the right of the starting zone. The animal must learn the motion path to obtain the reward. The starting point is randomized in each trial, and the animal must reach the same performance criteria as before.



Results







Blue. Males
Red. Females
Solid. Control
Dash. AD

Growth rate:

$$GR = \left(\frac{Performance_f}{Performance_i}\right)^{\frac{1}{t}} - 1$$

Results Summary

Through the Map to Action Transformation Task (MATT), we have found that animals are able to learn and progress through all 3 steps. The Transformation paradigm seems to present the highest level of complexity, as shown by the lower Growth Rate across sessions.

Alzheimer's Disease (AD) animals are found to be not impaired in the allocentric task at 3 months old when compared to the control group.

Future directions

In the context of the presented project, we will obtain brain tissue to investigate the AD pathology at 3-months-old. We will reassess MATT performance at 6-months-old in a subset of animals following a longitudinal study design. We will also investigate neural activity in the parietal cortex and hippocampus and the role they play in reference frame transformation during MATT. We will also obtain electrophysiological data during behavior and sleep cycles in order to look into memory replay and its correlation with task performance.

References

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