

Investigating the Role of the ATN-PPC Pathway

Introduction

- This research project focuses on egocentric and allocentric spatial navigation and its impact on neurodegenerative diseases, specifically Alzheimer's disease, in both humans and animals.
- Egocentric navigation uses your own perspective to navigate, while allocentric uses environmental cues and landmarks, with egocentric being "turning right then going straight" and allocentric being "going north then turning west."
- Alzheimer's disease impairs spatial navigation, causing individuals to get lost or end up in unintended places, highlighting the importance of spatial memory and navigation in cognitive function.
- These experiments on rats are **studying the link between the anterior thalamic nuclei (ATN) and the parietal cortex (PC) to better understand their role in spatial navigation and Alzheimer's disease, as damage to the anterior thalamic nuclei could affect both navigation methods.**

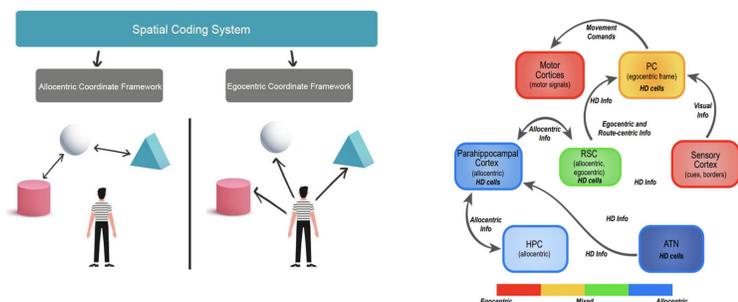
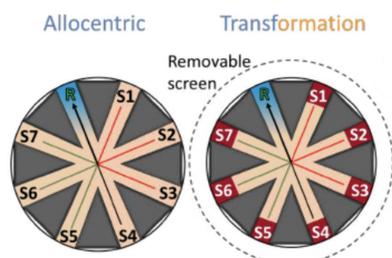


Figure showing the difference between allocentric and egocentric spatial navigation.

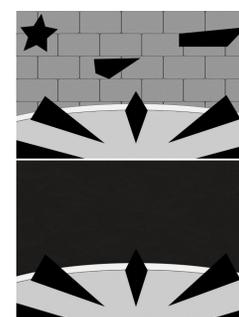
Brain stimulation in different structures in regard to egocentric and allocentric navigation patterns.

Methods

- A circular maze with 8 arms was constructed, and 5 rats (3 female, 2 male) were randomly assigned to arms to receive a food reward upon entry.
- For the allocentric task, 20 starting points were randomly assigned, and rats were placed in a box for 5 seconds to view distal cues, then navigated to their reward.
- After achieving a behavior score of 80% for 20 trials over 3 days, rats transitioned to the transformation task, where distal cues were blocked after the 5-second exposure.
- The rats were kept at a food restriction maintaining around 85% of their body weight.



Sample model of maze used to order to test the rats' spatial navigation.

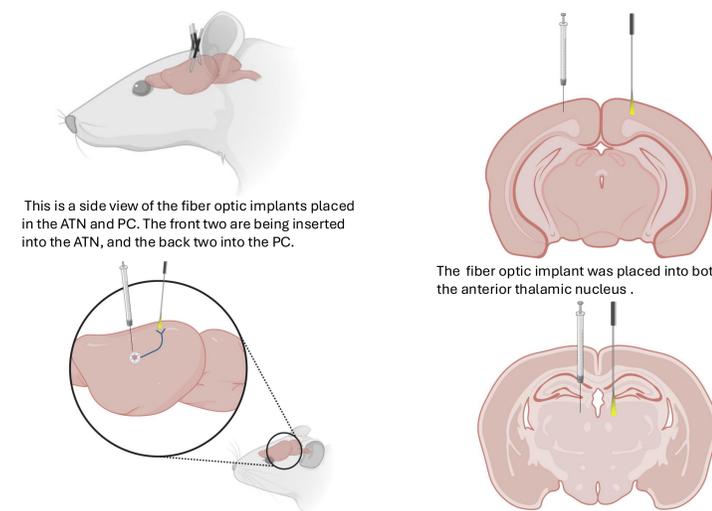


The environment with distal cues from the rats' point of view, where they exhibit allocentric spatial navigation techniques.

The environment where the distal cues are blocked by a curtain, forcing the rats to rely on egocentric navigation rather than allocentric.

Methods (Cont.)

- 4 fiber optic implants were placed in both lobes of the ATN and PC. Optogenetics was then used to inhibit these sections of the brain.



This is a side view of the fiber optic implants placed in the ATN and PC. The front two are being inserted into the ATN, and the back two into the PC.

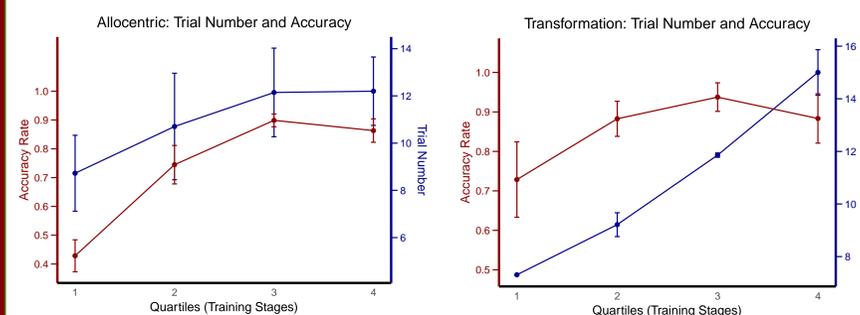
The fiber optic implant was placed into both lobes of the anterior thalamic nucleus.

This image shows a different approach that we are building up to optogenetics. In this approach a specific projection is inhibited by allowing the virus to transport to the projection site of the cells that are infected.

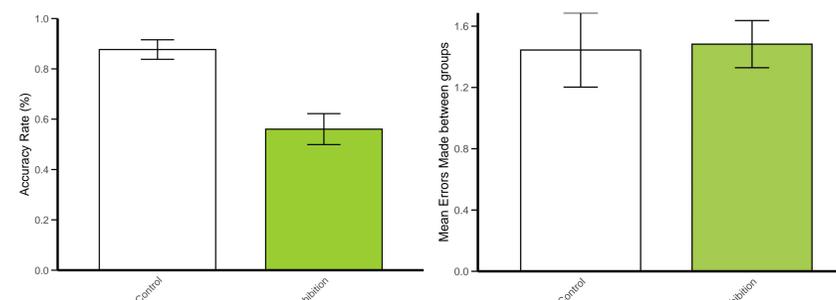
The last two fiber optic implants were inserted into the right and left lobe of the parietal cortex.

Results

Current Results



Pretraining contains two phases, the allocentric (left) and transformation (right). Graphs showing the increase in accuracy rate (left y-axis in dark red) and number of trials (right y-axis in dark blue) as pretraining progresses.



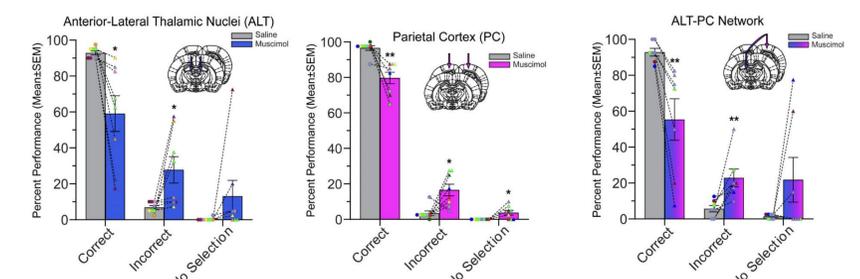
The accuracy rate significantly decreased when optogenetically inhibit unilateral ATN ($t = 4.23$, $p = 7.02 \times 10^{-5}$).

The deviation from the goal arm (i.e. the absolute distance between the observed and expected arms) is not significantly different between inhibition and control conditions.

Results (Cont.)

Expected Results

- Unilateral inhibition of the PC will have no effect, while bilateral, contralateral inhibition of ATN, and inhibition of the PC will impair performance.
- These impairments might be due to the disruption of animals' different reference frames, resulting in slower response times and less accuracy.



Muscimol compared to control (saline) causes a decrease in performance.

Muscimol has less of a deviation from the control in terms of performance level, suggesting the PC has less involvement with egocentric navigation.

When both the ALT and PC is blocked, there is a decrease in performance showing that the connection between the 2 networks is essential for spatial navigation.

Future Directions

- Expand the Sample Size
 - We will incorporate additional rats into our experiment to get more generalizable results
- Examine Inhibition Timing
 - Rather than applying inhibition throughout the whole session, inhibition at different phases can help identify the timing of the transformation from allocentric to egocentric
- Improve the Optogenetic technique used
 - Infect ATN neurons with a viral vector and inhibit in its axonal terminal at the PC, such that we can better identify the function of this circuitry

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References

Simmons, C. M., Moseley, S. C., Ogg, J. D., Zhou, X., Johnson, M., Wu, W., Clark, B. J., & Wilber, A. A. (2023). A thalamo-parietal cortex circuit is critical for place-action coordination. *Hippocampus*, 33(12), 1252–1266. <https://doi.org/10.1002/hipo.23578>