INACTIVATION OF THE MEDIAL SEPTAL NUCLEUS DURING A CONDITIONAL DISCRIMINATORY WORKING MEMORY TASK

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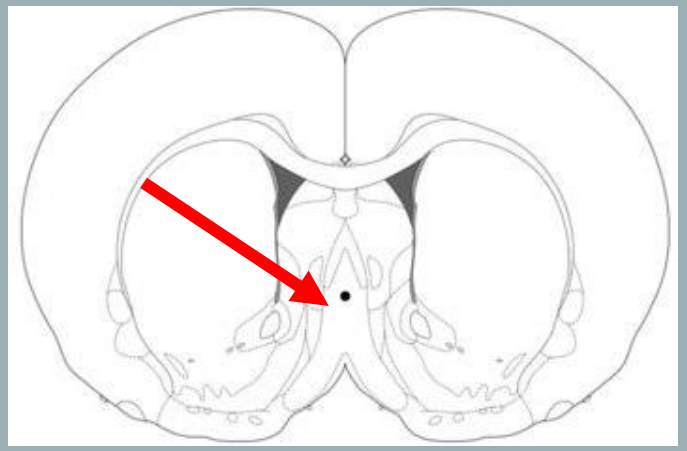
INTRODUCTION

What is the Medial Septum?

- It is widely known that the hippocampus plays an essential role in spatial working memory.
- Projections from the medial septum to the hippocampus are responsible for the generation of hippocampal theta waves (4-12 Hz).
- These theta waves are necessary for the performance of working memory tasks.

Figure 1. Rat medial septum (Ang et. al, 2015).



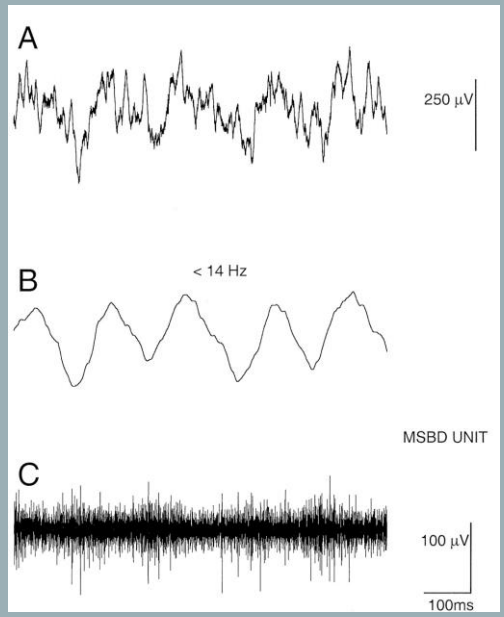


Figure 2. Hippocampal field and septal unit activity during theta waves (Dragoi et. Al, 1999).

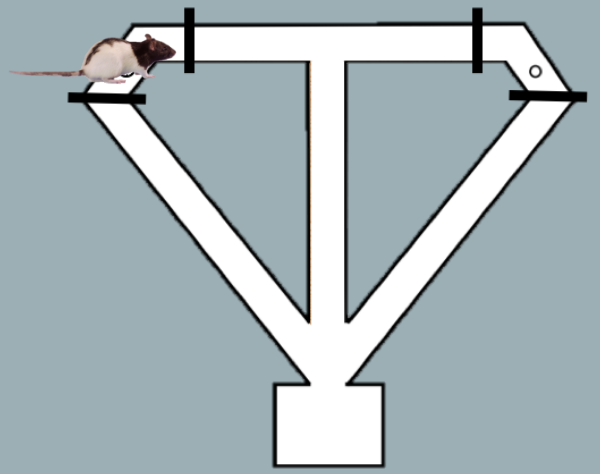
INTRODUCTION

Medial Septum Inactivation

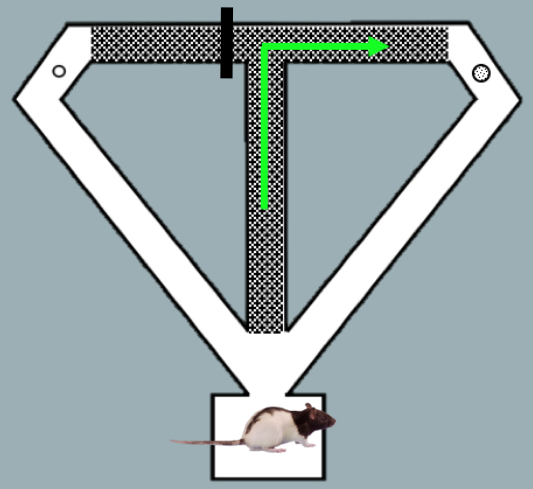
- If hippocampal theta is disrupted, the ability of the hippocampal network to effectively integrate multiple types of task relevant information will also be disrupted.
- In this experiment, we sought to further understand the purpose of hippocampal theta and whether or not it is necessary for encoding and retrieval portions of a conditional discriminatory working memory (CDWM) task.
- To do this we used optogenetic suppression in the medial septum of adult male Long-Evans rats at various points on a T-maze during a CDWM task.
- We also observed opsin-negative rats on a CD task to serve as a control.

PRE-TRAINING

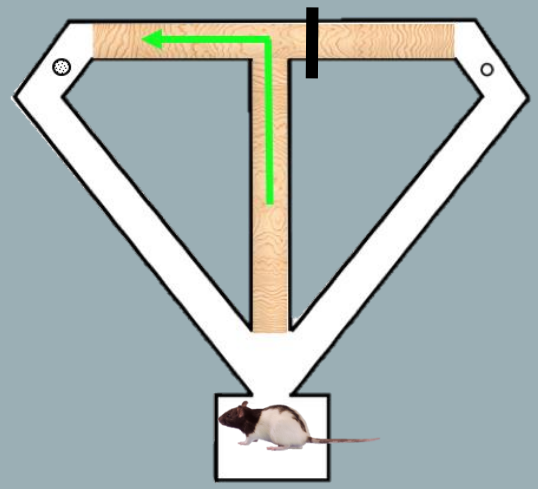
- Rats went through goal box training in which the goal arms were blocked off and the rat sat in each goal box until it ate the cup of sprinkles. This lasted until they consistently ate sprinkles in the reward cups in under 90 seconds.
- They then completed at least two consecutive successful sessions of forced runs on the T-maze in which one arm of the maze was blocked and the rat was forced to traverse down the open arm.



goal box



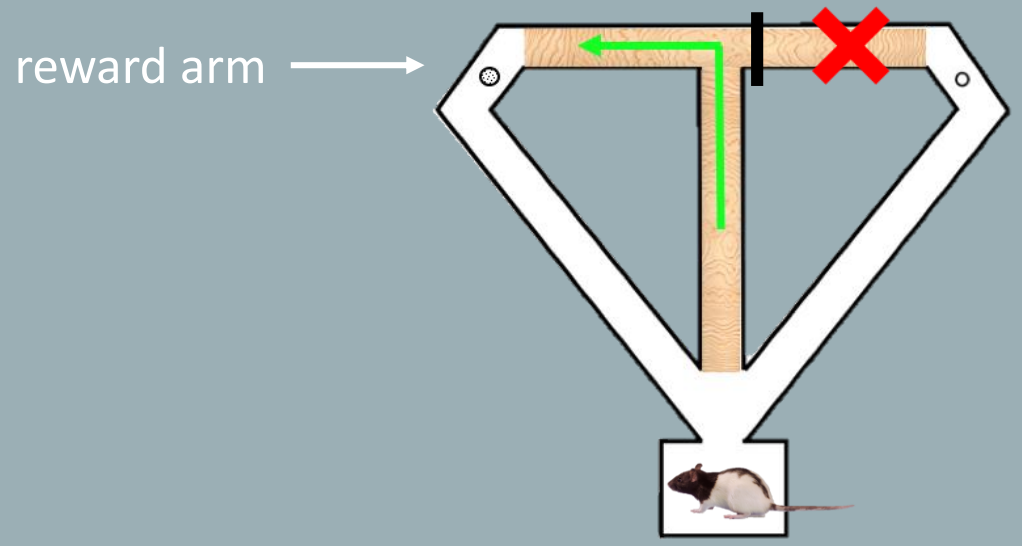
mesh insert

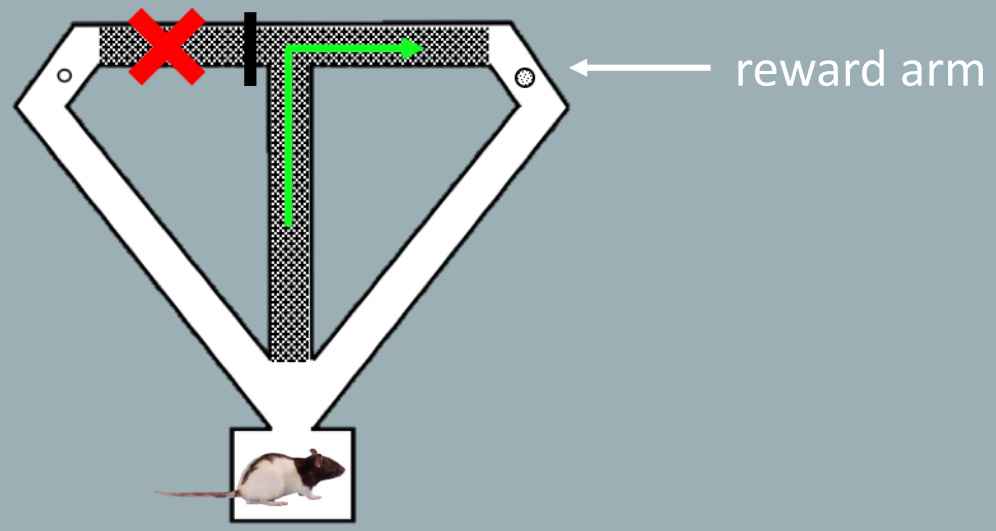


wood insert

TASK TRAINING - CDWM

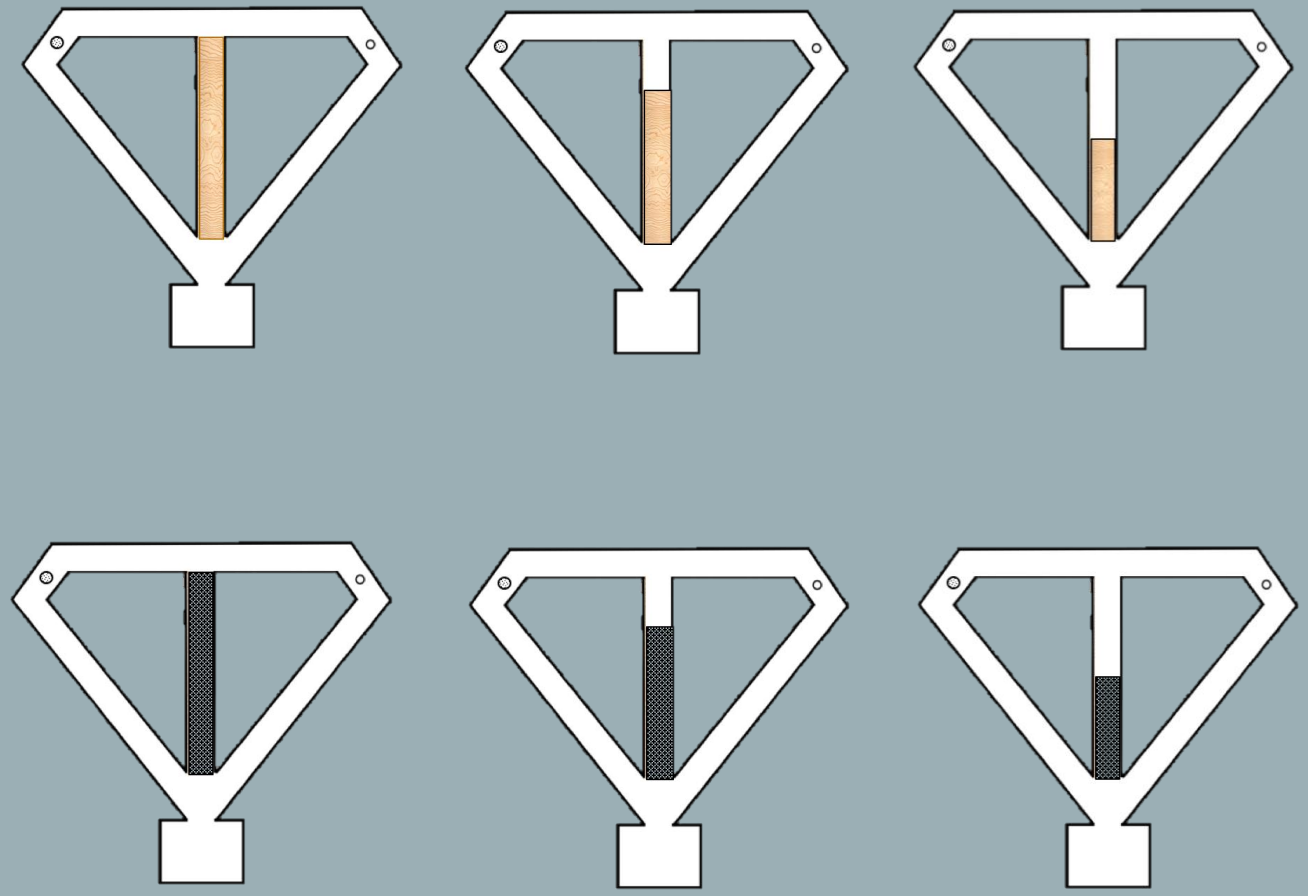
- During CDWM task training, the barrier on the incorrect arm is removed and the rat must remember which way to turn depending on which insert is present
  - mesh insert = turn right
  - wood insert = turn left
- Rats are trained 6 days per week and 24 trials are performed each session.
- To reach criteria, rats must perform the task with $\geq 80\%$ accuracy for at least two consecutive days.





TASK TRAINING - CD

- During CD task training, the same inserts are used as with the CDWM task, but the inserts get shorter as training progresses.
  - mesh insert = turn right
  - wood insert = turn left
- Rats are trained 6 days per week and 24 trials are performed each session.
- To reach criteria, rats must perform the task with $\geq 80\%$ accuracy for at least two consecutive days on the shortest insert.



OPTOGENETIC SUPPRESSION / SURGERY

- We inactivated the medial septum at various points throughout the T-maze using optogenetic suppression.
- The experimental group consists of opsin positive rats injected with AVV5-CAG-ArchT-td-Tomato into the medial septum.
- The control group consists of rats injected with the same non-cell-type specific promotor (CAG) and fluorescent tag, but without ArchT.
- When exposed to green light, ArchT causes the expression of a proton pump which removes protons from the cell causing a 900 pA neural silencing current, therefore creating a temporary lesion in the medial septum.

OPTOGENETIC SUPPRESSION / SURGERY

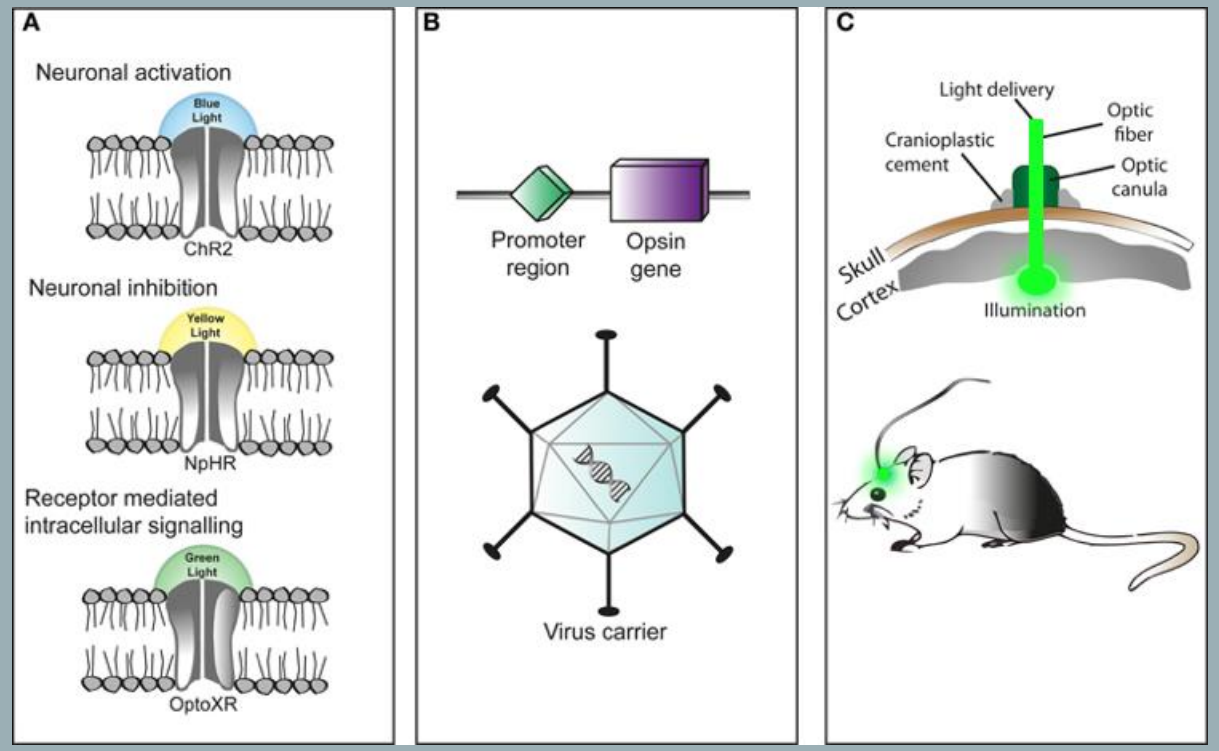


Figure 3. Example applications of optogenetics (Pama, 2013)

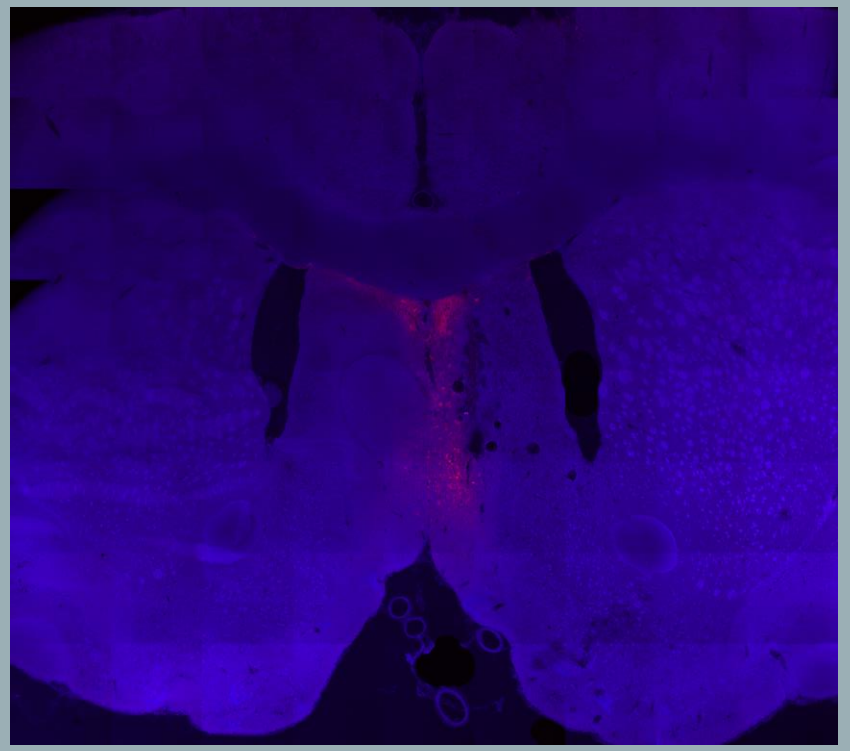
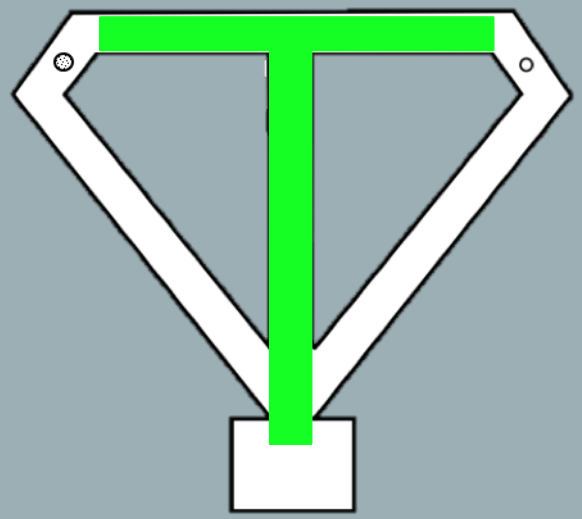


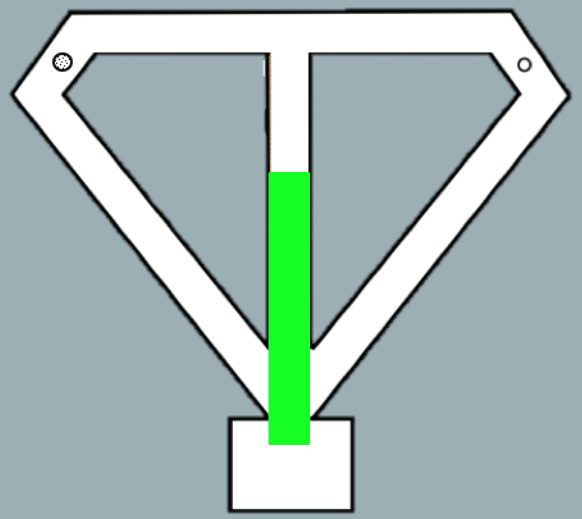
Figure 4. Histology of opsin positive rat brain with fluorescent expression in the medial septum.

TESTING

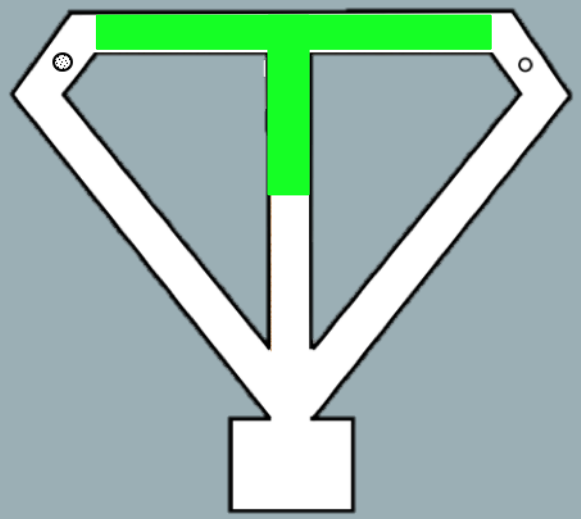
- The green light was turned on at various segments of the T-maze during testing:



Entire



Cued



Uncued

- 12 Light-on and 12 light-off runs were randomly arranged for each session and entire, cued and uncued sessions were shuffled throughout the testing period.

RESULTS (CDWM)

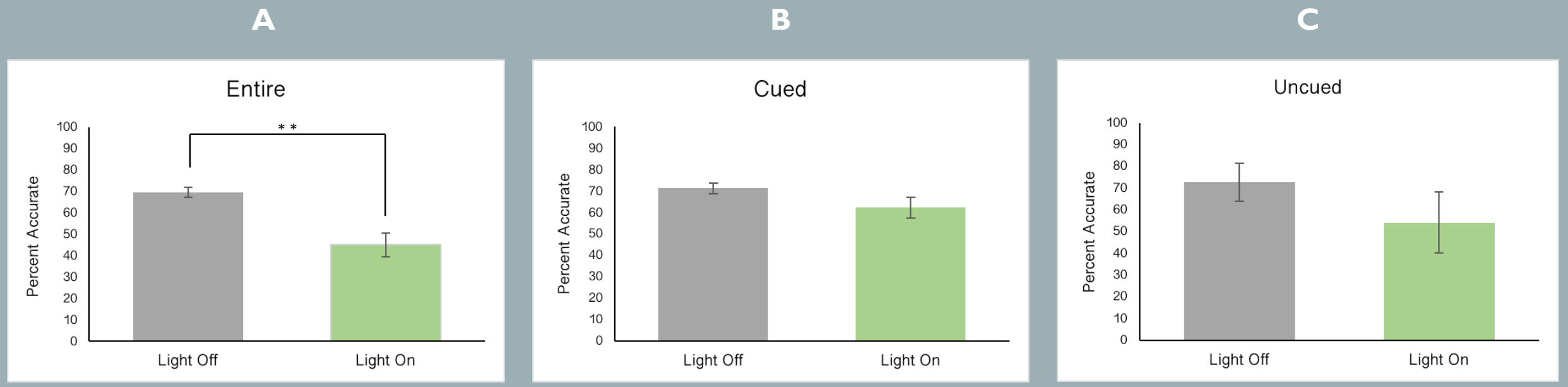


Figure 5. Mean scores for CDWM rats. **A)** n=4; p=0.0166. **B)** n=3; p=0.1975. **C)** n=2; p=0.076

- In the CDWM rats, we only found a significant decrease in maze performance when the light was on for the entire condition (p=0.0166). Performance with the light on was at chance level.
- There were no significant differences between light-on and light-off runs in the cued and uncued conditions.

RESULTS (CD)

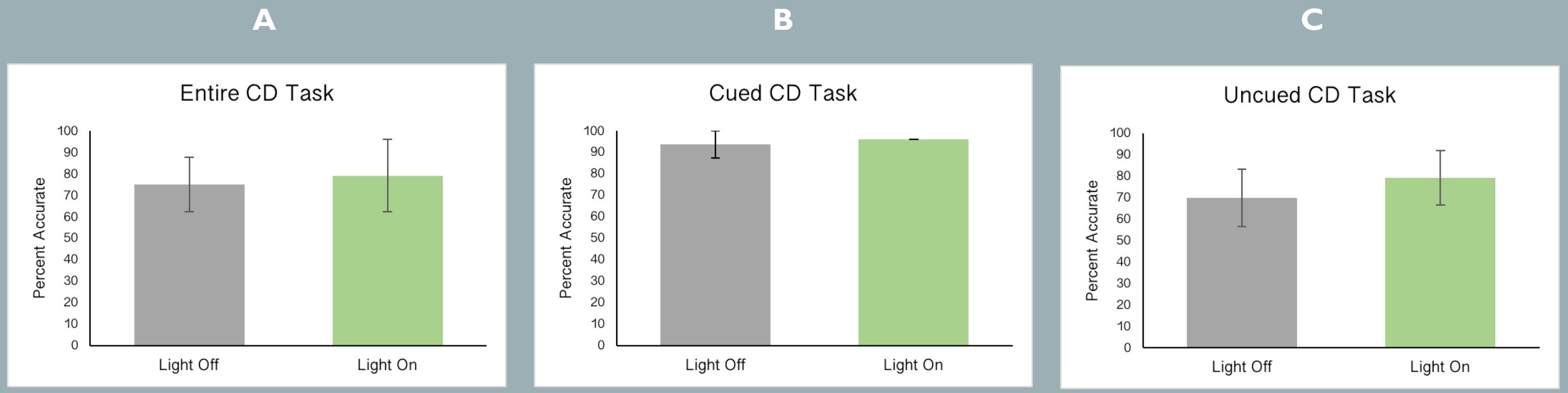


Figure 6. Mean scores for CD rats. **A)** n=2; p=0.8604. **B)** n=2; p=0.6855. **C)** n=2; p=0.6802

- In the CD rats, we found no significant differences between light-on and light-off runs across all conditions.
- This was expected for the control rats.

ACKNOWLEDGEMENTS

Future Work:

- We plan to continue this study and obtain data from a larger sample size of rats in order to delve deeper into the inner workings of the hippocampal network and further understand the mechanisms of spatial working memory .

Acknowledgements:

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