Developing an Experimental Test to Determine Cognitive Flexibility in Rats in a Reward Motivated Task

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FSU UNDERGRADUATE RESEARCH OPPORTUNITY PROGRAM

Introduction

- Cognitive flexibility is defined as the ability to adapt to environmental changes by changing responsiveness, tasks, and strategies. This is tested through tasks that require switching effectively in response to deterministic task response rules (Zühlsdorff,2023).
- The nucleus reuniens, prefrontal cortex, and the thalamus are associated with learning, memory, and behavior (Linley, 2003)(Rojas, 2024).
- The goal of this experiment was to form a new method and experimental test to study cognitive flexibility, memory, and recognition in rats for a reward motivated task by bridging the gap between old and new studies.
- This task uses visual cues (LEDs and cues on the wall), rewards (sugar pellets), and slow progression for the rats to learn the task.

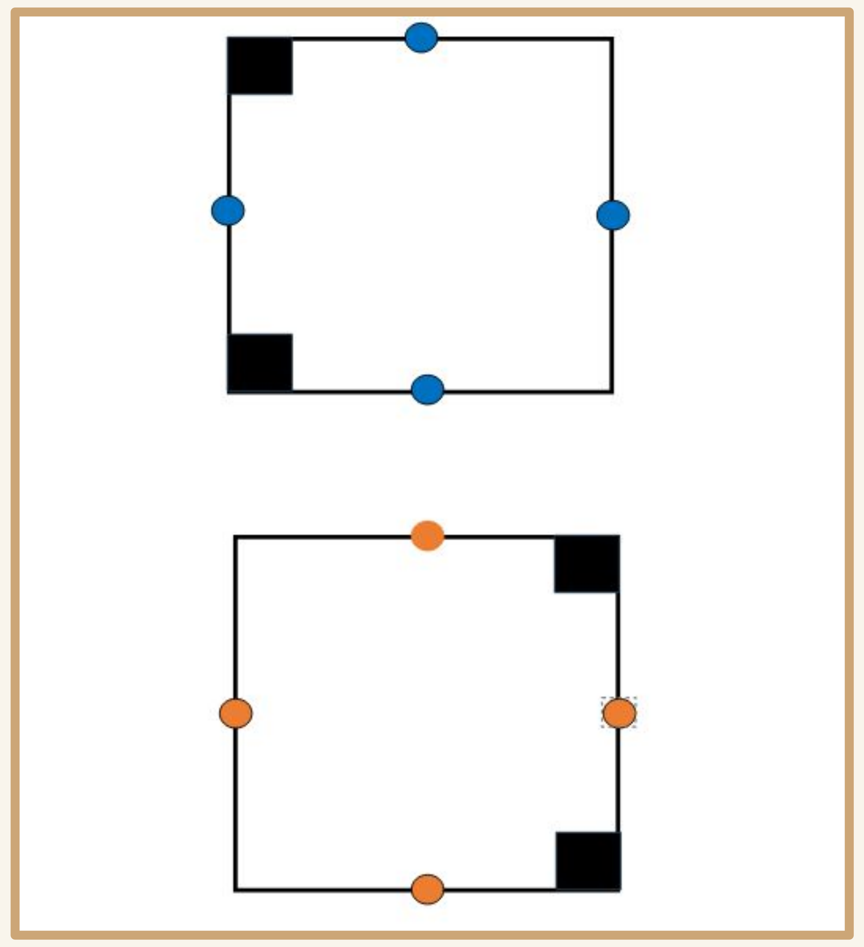

Figure 1: LED color associated with the corner that is considered a correct response.

Resources:

- Linley, S. B., Gallo, M. M., & Vertes, R. P. (2016). Lesions of the ventral midline thalamus produce deficits in reversal learning and attention on an odor texture set shifting task. *Brain research*, *1649*(Pt A), 110–122. https://doi.org/10.1016/j.brainres.2016.08.022
- Rojas, A. K. P., Linley, S. B., & Vertes, R. P. (2024). Chemogenetic inactivation of the nucleus reuniens and its projections to the orbital cortex produce deficits on discrete measures of behavioral flexibility in the attentional set-shifting task. *Behavioural brain research*, *470*, 115066. https://doi.org/10.1016/j.bbr.2024.115066
- Zühlsdorff, K., Dalley, J. W., Robbins, T. W., & Morein-Zamir, S. (2023). Cognitive flexibility: neurobehavioral correlates of changing one's mind. *Cerebral cortex (New York, N.Y. : 1991)*, *33*(9), 5436–5446. https://doi.org/10.1093/cercor/bhac431

Methods

- **Setup:**
- Feeders were received, assembled, placed, and secured on each of the corners of the experimental box with tubing attached to deliver the reward.
- An Arduino circuit was implemented to control the motors and LEDs through soldered wires, switches, and buttons.
- **Shaping**:
- The purpose of shaping is to accustom the rats to the experimental box, the noises of the feeders, the food dropping, and the LEDs.
- These trials took place over a span of 20 minutes, with 30 seconds for each trial: 10 seconds of the LED being on in intervals of 20 seconds between each trial. There was an alternation between blue and orange for each trial. The rat was rewarded if they went to any corner.
- **Training:**
- After approximately 5 days of shaping, the training began for each rat.
- The purpose of the training is for the rat to learn the correct corners associated with the color LED (Figure 1).
- Rat 1 was trained on the blue LED with its associated two corners, and rat 2 was trained on the orange LED with the other two corners (Figure 1).
- The training session lasted for 30 minutes using the same 30 second interval as shaping, with only one color LED (blue for 1 and orange for 2) being switched on and the rat only being rewarded if going to the correct corner associated with that LED.
- This continued until they learned each rule independently, by going consistently (80%) to the correct corner associated with the color LED that they were training on (Figure 2).
- **Testing:**
- The purpose of testing is to connect both rules learned in the training portion, and for the rat to learn how to consistently switch between the LED and correct corners associated.
- Starting with one LED, the rat would get rewarded if going to the correct corner associated with that color LED. After 6 consecutive correct trials, the color and corners would switch (Figure 3 and 4)
- The purpose of this is to see how quickly they can switch between rules to determine rate and ability of cognitive flexibility.

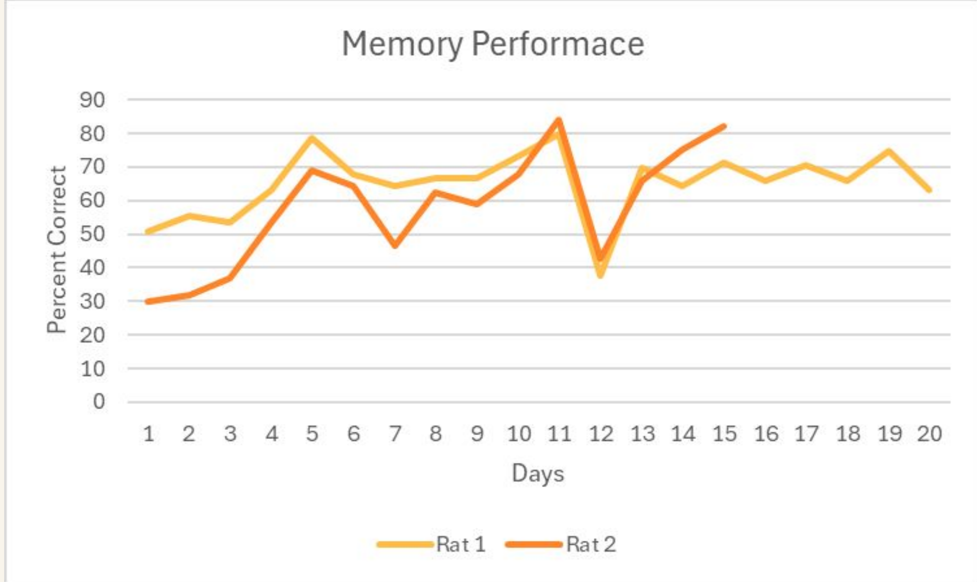

Figure 2: Memory performance based on day of training and percent of correct responses.

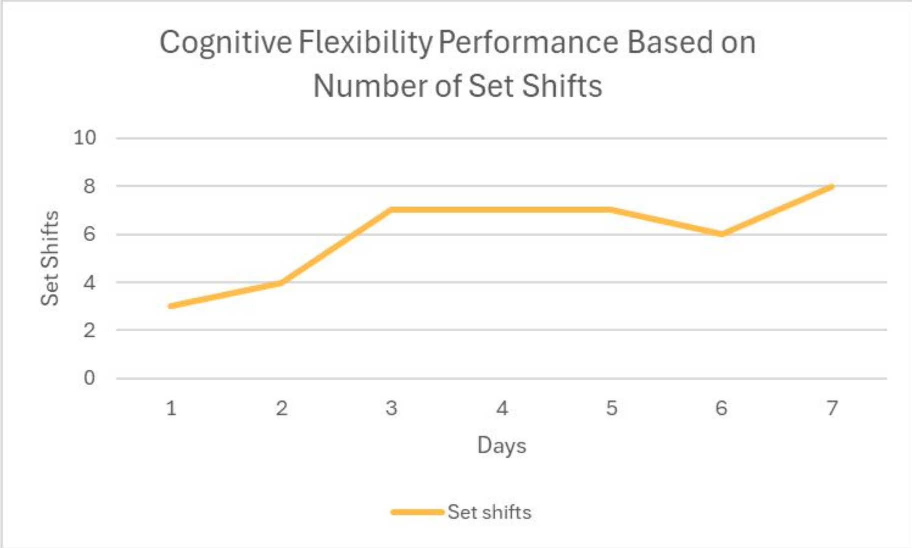

Figure 3: Performance of cognitive flexibility for rat 2 by number of set shifts per day.

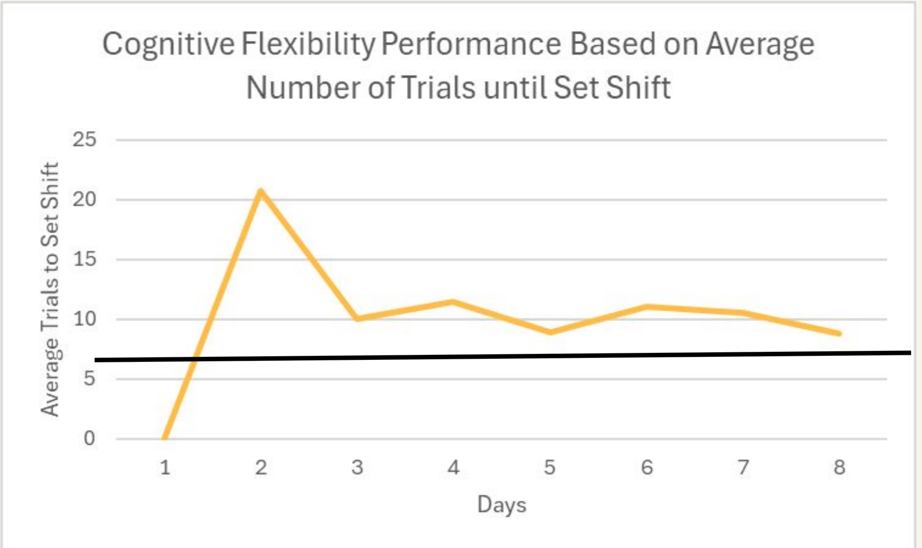

Figure 4: Performance of cognitive flexibility for rat 2 by average number of trials until set shift.

Conclusion

Based on the results, we can conclude that both rat 1 and 2 showed consistent positive trends in learning. While rat 1 was unable to get to the final testing stage of the experiment, through more time it will eventually be reached. There was still positive learning trends in the data from rule 1. Rat 2 was able to complete the experiment to the full extent, with consistent positive trends through each stage. This ended with the final testing stage, and the ability to switch efficiently between rules to complete the cognitive flexibility task.

Results

- Through this test, a full experiment was ran on two pilot rats.
- In the process of shaping, training, and testing the rats there was a positive learning curve throughout the process.
- **Figure 2** correlates the training day to the percent of correct responses for both rules:

The steep decline in day 11, accounts for the rats hitting 80% correct responses, and then switching to the other rule.

In rat 2, between days 2-5 there was a 40% increase in correct response, before decreasing 25% between days 5-7. Then rising 40%, with a consistent gradual increase of 20% from days 9-11 to hit 80% and the rule switch. There was a consistent positive trend from days 12-16 and then hitting 80% correct to go into the testing portion (Figure 3 and 4) of the experiment.

In rat 1 between days 1-5, there was a 30% increase in correct response, before decreasing 15% and then rising back to hit the 80% correct mark for rule switch. After the rule switch there was a consistent 5% alternating fluctuation in response per day.

- **Figure 3** depicts the number of times the animal was able to switch rules (number of set-shifts) for each testing day:

On days 1-3, there is an increase of 4 set shifts, before plateauing on days 3-5. There is a decrease in 1 set shift on day 6, before rising again by 2 on day 7.

- **Figure 4** depicts the average number of trials it takes per day before a set shift. The horizontal black line indicates the criterion used to switch the rule for the rat (6 consecutive correct trials). Day 7 was the closest to perfect average, only being off by an average of 2.75 trials.