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Identification and Characterization of Response Selection and Response Inhibition in Mice Performing a Two Paddle Whisker Detection Task

A Thesis submitted in partial satisfaction
of the requirements for the degree of

Master of Science

in

Biomedical Sciences

by

Christian Michael Delgadillo

June 2024

Thesis Committee:
Dr. Edward Zagha, Chairperson
Dr. Milton Hamblin
Dr. David Lo

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2024

The Thesis of Christian Michael Delgadillo is approved:

Committee Chairperson

University of California, Riverside

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DEDICATION

I would like to first dedicate this piece to my family. To my mother and father: Terrie Jean Jones-Delgadillo and Michael Cannon Delgadillo. Throughout my undergraduate and graduate career, you have been by my side every step of the way. For six consecutive years, you have supported me as I navigated and continue to navigate through my mission of becoming a physician. I would not be where I am today without your love, the sacrifices you gave to aid me, and your everlasting commitment to seeing me succeed in anything I put my mind to. Thank you for everything and I love you both with all my heart.

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To my Aunt: Karen Terry Delgadillo. Thank you for all the support you have provided me over the past years. Your support means the world to me and I am thankful to have you in my life.

I would also like to dedicate this piece to Dr. Venugopala Reddy Gonehal and my lab members in the Dr. Venugopala Reddy Gonehal lab. Thank you, Dr. Gonehal, for accepting me into your research lab in July of 2021. Joining your research lab has been an amazing experience and I learned so much under your guidance and instruction. It was from your lab that I was able to learn the foundations of research and gained inspiration to pursue research at the graduate level. To my fellow lab members, I would like to thank you for your unwavering support during my tenure in the lab and throughout my graduate studies. I look forward to working with you in completing our many experiments and moving ahead.

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ABSTRACT OF THE THESIS

Identification and Characterization of Response Selection and Response Inhibition in Mice Performing a Two Paddle Whisker Detection Task

by

Christian Michael Delgadillo

Master of Science, Graduate Program in Biomedical Sciences
University of California, Riverside, June 2024
Dr. Edward Zagha, Chairperson

Everyday we are presented with choices that require us to make decisions. How we understand these choices and the processes that guide us in making decisions are important aspects of cognition. Cognition with respect to decision making has been previously studied using goal-directed behavioral tasks such as Go/No-Go tasks. In Go/No-Go tasks, participants are required to make decisions in providing responses to presented stimuli, where one stimuli is a ‘go’ signal and one stimuli is a ‘no-go’ signal. Previous research has looked into the performances of participants completing Go/No-Go tasks (e.g. do participants respond highly to ‘go’ stimuli or ‘no-go’ stimuli). Such observations of behavior are at the core of response selection and response inhibition. Response selection and response inhibition are cognitive strategies utilized by individuals to complete stimulus-based tasks. Response selection is present when a subject's behavior is determined by the subject’s ability to select and execute appropriate behavioral responses. Response inhibition is present when a subject's behavior is determined by the subject’s ability to withhold the execution of inappropriate behavioral responses. The learning of either cognitive strategy and the behavioral mechanisms that drive such learning is not yet fully understood. To identify and characterize the cognitive strategy being learned by our mice, we analyzed behavioral variables (hit rate, false alarm rate, discrimination, target detection, distractor detection, pretrial spontaneous rate, and target reaction time) that were recorded when mice trained to master our Go/No-Go whisker detection task. Our task is a goal-directed behavioral task that requires mice to learn to respond to whisker deflection stimuli and distinguish target detection from distractor detection. We found that mice learned and exhibited response selection across learning and mastery of the task. During mastery of the task, target detection drives increases in Hit Rate, and Pretrial Spontaneous Rate drives increases in False Alarm Rate. Lastly, reduction in target reaction times confirmed that mice were exhibiting response selection. The approaches used in this study to characterize response selection can serve as a model for explaining behavioral trends exhibited by individuals with behavioral deficits, such as ADHD.

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LIST OF ABBREVIATIONS

ADHD - Attention Deficit Hyperactive Disorder
D DP - Distractor Detection D-prime
Disc - Discrimination D-prime
FAR - False Alarm Rate
GCaMP6s - Calmodulin M13 Protein 6 Slow
HR - Hit Rate
PSR - Pretrial Spontaneous Rate
T DP - Target Detection D-prime
T RT - Target Reaction Time

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Chapter 1: Introduction

Every day we are faced with events or situations that require us to respond to them in some way. Simple examples of this include responding to a traffic light turning green when we are at a red light. When you see the light turn green, do you push on the gas pedal to accelerate your vehicle or do you not? Most people would say that if you pushed on the gas pedal, you provided a correct appropriate response to green traffic light stimuli. If you saw the green light but did not push on the gas pedal, you would have responded incorrectly. Situations like this where a correct and wrong response can be provided in response to a presented stimulus can be described by Signal Detection Theory.

Signal Detection Theory

Signal Detection Theory, as adapted to psychology by David M. Green and John A. Swets, is a framework that describes behaviors in the context of stimulus-dependent tasks. To elaborate, Signal Detection theory, in the context of its adaptation to behavioral psychology, provides means to qualitatively define decision making and consequential behaviors (Heeger & Landy, 2009). Signal Detection Theory states that actions provided in response to certain stimuli can be classified as being either Hits, False Alarms, Correct Rejections, and Misses. Hits are defined as providing a correct response associated with the correct detection of a particular (target) stimulus. False Alarms are defined as providing a response when the target specific stimulus is not present. Correct Rejections are defined as the providing of no response when there is no target stimulus presented.

Misses are defined as the providing of no response when there is a target stimulus presented. These different types of behaviors, particularly hits and false alarms, under Signal Detection Theory, can be attributed to and correlated with a mouse's ability to detect stimuli and a mouse’s bias in responding (e.g. do the mice have response rates generally). Under Signal Detection Theory, a subject can have high response rates without high levels of detection. Subsequently, a subject can have high response rates that are caused by a general tendency to respond to anything.

Two of these response classifications, Hits and False Alarms, have been widely used by behavioral psychologists and researchers to characterize behaviors that can be exhibited by participants completing goal-directed tasks. Additionally, behaviors that can be characterized as being hits and false alarms have also been used in behavioral studies that focus on how behaviors change across learning. Such studies have looked at how rates of hits (Hit Rate) and false alarms (False Alarm Rate) change over time as a participant learns to complete and master a goal-directed task.

Goal-Directed Tasks and Behaviors

Previous studies looking into behavioral changes that occur during learning have often utilized various forms of behavioral goal-directed tasks to study such behavior changes. Such tasks, often referred to as Goal-directed behavior tasks (Marrero et al., 2023), can be exist in many forms: stop-signal, go–no-go, Stroop, flanker, single-response selection, psychological refractory period, and attentional blink tasks (Bender et al., 2016). In these goal-directed tasks, participants may be required to identify and detect stimuli and provide an appropriate response. Additionally, depending on the nature and setup of the goal-directed task being used, a participant may be required to learn to ignore distractor stimuli. Generally, the execution of the task correctly results in the receiving of a reward and incorrect performance of the task results in no reward or a punishment. Some tasks have been developed to enact punishments upon participants that engage in inappropriate performance (e.g. punish subjects that engage in false alarms). Punishments serve as a means to teach subjects to withhold inappropriate responses or behaviors.

Participants that are learning to master these tasks have their performance characterized by changes in their Hit Rates and False Alarm Rates. Hit Rate can be defined as the rate of which a correct response is provided in response to the detection of the correct corresponding stimuli. False Alarm Rate can be defined as the rate at which incorrect responses are provided when a wrong stimulus is presented. Previous research reviewing Hit Rate and False Alarm Rate exhibited by participants completing goal-directed studies has connected these response rates to two cognitive strategies: response selection and response inhibition.

Response Selection v.s. Response Inhibition

Response Selection is a behavioral strategy that can allow an organism to carry out and improve goal-directed behaviors. To elaborate, when an organism exhibits a response selection behavioral strategy, they will show increases in correct response behaviors

(Goghari & MacDonald, 2009). Response Inhibition is a behavioral strategy that can allow an organism to carry out and improve goal-directed behaviors. To elaborate, when an organism exhibits a response inhibition behavioral strategy, they will show decreases in incorrect response behaviors (Mostofsky & Simmonds, 2008). There is also the possibility that both response selection and response inhibition can take place at the same time. If this were to occur, subjects would show increases in correct response behaviors and decreases in incorrect response behaviors simultaneously.

Previous Response Selection Studies & Response Inhibition Studies

Previous studies that have studied response selection and response inhibition have primarily studied the intensity of response selection in subjects completing goal-directed behavioral tasks. To elaborate, most studies have utilized reaction times to measure strength of response selection and false alarm rate to measure the strength of response inhibition (Bender et al., 2016; Waring et al., 2019). Regarding reaction times as a means to measure response selection, previous studies have suggested that shorter reaction times are associated with strong utilization of response selection as a strategy, the idea being that if an individual is proficient in responding to a particular stimulus, they will also show an improved target trial reaction times. With respect to false alarm rate as being a measure of response inhibition, previous studies have suggested that high levels of false alarm rates are associated with poor inhibitory response, the idea being that a false alarm rate indicates a failure to withhold inappropriate responses (Congdon et al., 2012; Mostofsky & Simmonds, 2008). Despite many studies using paradigms to study response selection and response inhibition, the paradigms themselves do not provide information beyond measuring the intensity of response selection or response inhibition behaviors. There are many questions that cannot be answered using these current paradigms. What underlying behavioral mechanisms (behaviors caused by stimuli detection and impulsive tendencies) drive changes in response selection or response inhibition behaviors? How do behavioral measures reflective of response selection or response inhibition change across the learning of stimuli-dependent tasks? Part of this current study aims to address these previously unanswered questions.

The Investigation Outlined in This Study

In this study, we answer five main questions. What cognitive strategy (response selection or response inhibition) is being learned and exhibited in mice training to master a Go/No-go selective whisker detection task? Does detection-induced behaviors and/or impulsive tendencies drive changes in observed response rates? How do behavioral variables used to identify a response selection or response inhibition cognitive strategy differ across naïve performance status and expert status days? What behavioral mechanisms, if any, drive changes in observed response rates during the naïve and expert periods and how do they differ across periods? How do target reaction times change across the learning and mastery of a response selection and response inhibition cognitive strategy? To address and answer these questions, this study utilizes a Go/No-Go selective whisker detection task previously used in other behavioral studies conducted in the Dr. Edward Zagha

Research Lab to record specific mouse behavioral variables that can help us answer these questions (Marrero et al., 2023).

Experimental Mice

Mice used in this study were acquired from The Jackson Laboratory. The mice ordered and used in the study were designed to express GCaMP6s under the Snap25-2A-GCaMP6s-D promoter (JAX #025111). Six mice in total were used in the experiment. Mice used in the experiment were either male or female.

Mouse Care and Surgical Procedures

All experiments conducted in this study received approval from the Institutional Animal Care and Use Committee (IACUC) of the University of California, Riverside. Mice were housed in the designated Zagha Lab mouse care room in one of the University's vivariums. Each mouse included in this study had their own mouse cage, each of which contained hydrogels and mouse food. The mice cages had an opening that allowed for the insertion of a water sipper into the cage, thus providing another source of water for the mice. The room in the vivarium that housed the mice living in their cages had programmed lighting settings; the room utilized a 12-hour light/12-hour dark cycle.

Prior to the training and running of mice in the behavioral apparatus to collect behavioral data, mice first underwent cranial headpost implantation surgery necessary for the mice to be placed into the behavioral apparatus. This surgery was performed on the mice when they were aged 2 to 5 months. Mice were first anesthetized using a combination of isoflurane (1-2%), ketamine (100 mg/kg), and xylazine (10 mg/kg). Scissors were used to remove as much hair as possible from the head post implantation site. Once enough hair was removed, a separate set of scissors were used to remove a 10 mm x 10 mm section of the scalp and expose the skull. Any connective tissue covering the exposed skull was thoroughly removed. Once all connective tissues had been removed, a clean custom-built headpost was acquired and disinfected. Custom-built headposts were made of lightweight titanium or stainless steel, 3 cm in length, and weighed approximately 1.5 grams. Each headpost had a 5 mm x 7 mm central window that could be used for vivo widefield Ca2+ imaging and recording (in vivo widefield Ca2+ imaging and recording are not utilized in this study). Disinfected headposts then had a layer of cyanoacrylate glue placed on the parts of the headpost that would be in direct contact with the exposed skull. Once the glue was applied, the headpost was meticulously placed onto the center of the exposed skull area. A thin layer of cyanoacrylate gap-filling medium was subsequently applied to the window to seal the exposed skull. Post-surgery, mice were placed on a heating pad to awaken from being anesthetized and recover. Additionally, meloxicam (0.3 mg/kg) and enrofloxacin (5 mg/kg) were administered post-surgery. Daily administrations of meloxicam and enrofloxacin occurred up to three days post-surgery. Mice were given a minimum of three days to recover from surgery before undergoing water restriction and behavioral training.

Mice that successfully recovered from the surgery were then placed into water restricted mouse cages. In these cages, there is no opening for any type of water dispenser or bottle. Mice that began the water restriction process had their initial weight measured in grams on the first day of water restriction. Every day that the mice underwent water restriction, their weight was monitored and recorded until they reached a weight that was between 85 to 90 percent of the original recorded weight. Once the weight of the mice was within the range, they then began the process of training.

Two Paddle Go/No-Go Whisker Selective Detection Task

This study used a Go/No-go selective whisker detection task previously utilized in previous studies conducted in the Zagha Lab at the University of California, Riverside (Aruljothi et al., 2020; Marrero et al., 2022; Zareian et al., 2021, 2023; Zhang & Zagha, 2023). Headposted water-restricted mice engaging in the task are placed into a behavioral apparatus controlled by custom MATLAB scripts and Arduino software. The headposts were compatible with the physical setup of the behavioral apparatus which allowed for the mice to be secured into the behavioral apparatus. Once mice were secured into the behavioral apparatus, two paddles were placed within the vicinity of their whisker detection fields (Figure 1A). One paddle was placed in the whisker detection field on the right side of the mouse's face and the other paddle was placed in the vicinity of the opposite whisker field (Figure 1C). One paddle was designated as the target stimulus and the other paddle was designated as the distractor stimulus. A lick port was placed just below the area where the mouth of the mice were located. Additionally, the lick port was positioned so that the tongue of the mouse could lick the lick port.

When the task was initiated, either the target or distractor stimulus would deflect within their respective whisker detection field. The deflection of a target stimuli is known as a target trial and the deflection of the distractor stimuli is known as a distractor trial. Throughout the task, trials would be presented in the following order: Trial, Intertrial Interval, Trial, Intertrial Interval. The intertrial interval (ITI) is a period of time between the end of one trial and the beginning of the next upcoming trial. The intertrial interval was variable and could range between 5.5 and 9.5s. The implementation of the ITI aimed to reduce spontaneous sampling before the onset of an upcoming trial. Following the onset of any stimulus deflection, the mice are required to wait 200 ms after stimulus onset before licking the lick port. If the mouse licked the lick port between 200 ms and 1,200 ms after the onset of a target stimulus, they received a 5 uL water reward and their behavior was recorded as a hit (hits are rewarded with water delivery). If the mouse licked the lick port between 200 ms and 1,200 ms after the onset of a distractor stimulus, they received no water reward, and their behavior was recorded as a false alarm (false alarms are not rewarded). If mice do not lick in response to a distractor trial, their behavior was recorded as a correct rejection. The correct rejection of a distractor stimulus initiated a target trial preceded by a shortened 0.2 to 1.9 s ITI. Overall, mice must withhold licking during the ITI (which has a range of 5.5 s (ITImin) to maximum 14.6 s (ITImax) to be presented with a target trial. Any licks detected during the ITI resulted in a resetting of the ITI period. Additionally, any licks detected during the last 1 second of an ITI preceding any trial were defined as the Pretrial Spontaneous Rate (PSR).

Animal Behavioral Variables Recorded and Analyzed from This Study's Two Paddle Go/No-Go Whisker Selective Detection Task

The setup of the behavioral apparatus and behavior recording custom MATLAB code allowed for the collection and measuring of various different behavioral measures and mechanisms: Hit Rate, False Alarm Rate, Discrimination, Target Detection, Distractor Detection, Pretrial Spontaneous Rate, and Target Reaction Time. Behavioral measures include Discrimination, Hit Rate, and False Alarm Rate. Behavioral mechanisms include Target Detection, Distractor Detection, and Pretrial Spontaneous. We also study Target Reaction Time throughout this study. Below are the descriptions and mathematical equations used to calculate each of these behavioral variables.

1. **Hit Rate**
    a. Equation: Hit Rate = (# of Target Trial induced responses with a RT between 0.2 & 1.20 sec) / (# of target stimulus trials presented during a session day)
    b. Description: Hit Rate is a measure of how often the mice are able to correctly respond to a target stimulus. Hit Rate is calculated as the number of target trials where a mouse licked the lick port 200 ms to 1,200 ms after

stimulus onsent divided by the number of target trials provided during a daily training session.

2. **False Alarm Rate**

    a. Equation: False Alarm Rate = (# of Distractor Trial induced responses with a RT between 0.2 & 1.20 sec) / (# of distractor stimulus trials presented during a session day)

    b. Description: False Alarm Rate is a measure of how often the mice respond to a distractor stimulus. False Alarm Rate is calculated as the number of distractor trials where a mouse licked the lick port 200 ms to 1,200 ms after stimulus onsent divided by the number of distractor trials provided during a daily training session.

3. **Pretrial Spontaneous Rate**

    a. Equation: Pretrial Spontaneous Rate = % of trial types where a lick was detected within 1 second before an impending stimulus.

    b. Pretrial Spontaneous Rate is classified as an impulsivity behavioral mechanism that can affect and proportionally drive both Hit Rate and False Alarm Rate behavioral performance. Pretrial Spontaneous Rate is calculated as the percentage of trial types in which the mouse licked within the final 1 second of an ITI that precedes any impending stimulus (target or distractor stimulus).

4. **Discrimination**

    a. Equation: Discrimination = zHit Rate - zFalse Alarm Rate

b. Description: Discrimination is a measure that provides information regarding an individual mouse’s ability to discriminate between target and distractor stimuli and provide appropriate responses to them. Discrimination is calculated as the normative inverse of Hit Rate minus the normative inverse of False Alarm Rate.

5. **Target Detection**

a. Equation: Target Detection = zHit Rate - zPretrial Spontaneous Rate

b. Description: Target Detection is a measure of how many hits recorded during a daily training session were most likely induced by the mouse actually detecting the target stimuli. Target Detection is calculated as the normative inverse of Hit Rate minus the normative inverse of Pretrial Spontaneous Rate. Target Detection is classified as one of two detection-based behavioral mechanisms that can affect and proportionally drive Hit Rate behavioral performance.

6. **Distractor Detection**

a. Equation: Distractor Detection = zFalse Alarm Rate - zPretrial Spontaneous Rate

b. Description: Disaster Detection is a measure of how many false alarms recorded during a daily training session were most likely induced by the mouse actually detecting the distractor stimuli. Distractor Detection is calculated as the normative inverse of False Alarm Rate minus the normative inverse of Pretrial Spontaneous Rate. Distractor Detection is classified as one of two detection behavioral mechanisms that can affect and proportionally drive False Alarm Rate behavioral performance.

7. **Target Reaction Time**

   a. Equation: Target Reaction Time = mean target reaction time during one session day.

   b. Description: Target Reaction Time is a measure of behavior that reveals how fast the mice are able to respond to a target stimulus trial.

Definitions of Naïve and Expert Periods

Throughout chapters 4, 5, and 6 of this thesis, behavioral analyses conducted used specific sets of data from the naïve session periods and expert session periods observed in each mouse. The expert session period is defined as the first three consecutive days a mouse achieves a Discrimination value of 1 or greater. All the session days that precede a mouse's expert period is considered to be the naïve period of that particular mouse.

Behavioral Data Analysis

Data analyses were performed using functions in Excel, Google Sheets, and custom scripts in MATLAB. Linear regression analyses were used to determine slopes of behavioral variables (response rates, behavioral mechanisms, and reaction times) across sessions per mouse (Figures 2-7); the slopes of individual linear regressions for each behavioral variable were averaged to determine mean linear slopes for the behavioral variables. If the mean linear slope for a behavioral variable across mice was significantly positive, the behavioral variable was identified as ‘increasing’. In contrast, if the mean linear slope for a behavioral variable across mice was significantly negative, the behavioral variable was identified as ‘decreasing’. Pearson correlation coefficient tests were used to determine levels of association between various behavioral variables during all session days, during naïve session days, and during expert session days. Reported correlations are calculated from the mean correlation using the individual correlations from each mouse. All mean values reported as the mean ± standard error of the mean (SEM). All values reported are rounded to three significant figures.

Statistical Tests Used

One sample t-tests were used to determine if slopes across mice were significantly different from zero (Excel and Google Sheets Functions). One sample t-tests were also used to determine if the correlation coefficient values for two behavioral variables was significantly different from zero. Paired t-tests were used to determine whether individual mean slopes for naïve and expert behavioral variables were significantly different from each other. Additionally, a two-way ANOVA with replication was used to study whether observed changes in Discrimination and Behavioral Responses were significantly driven by response behavior type, performance status, and/or both. The two-way ANOVA with replication was used to see if there is any interaction between response behavior type and performance status. The following statistical tests were used in each of the chapters outlined in this thesis.

1. Chapter 2: one sample t-test

2. Chapter 3: one sample t-test
3. Chapter 4: one sample t-test, two-way ANOVA with replication, paired t-test
4. Chapter 5: one sample t-test, paired t-test
5. Chapter 6: one sample t-test, paired t-test

Data Inclusion Criteria

We trained and examined 9 mice with potential learning data but included only 6 mice who met all criteria described below. First, mice were included if they transitioned from naïve status to expert status. The status level of a mouse was defined by discrimination performance. A mouse was considered to have reached expert status when they achieved a Discrimination value (normalized separation between hit rate and false alarm rate) greater than one for three consecutive days. Second, mice were included if they transitioned from naïve to expert performance status within 21 days of training ($\mu_{mNaiveStatusDays}$ = 11.83 days). Third, the data required a minimum of fourteen training sessions with no more than a 7-day gap between sessions ($\mu_{mTrainingSessionDays}$ = 16 days).

Figures

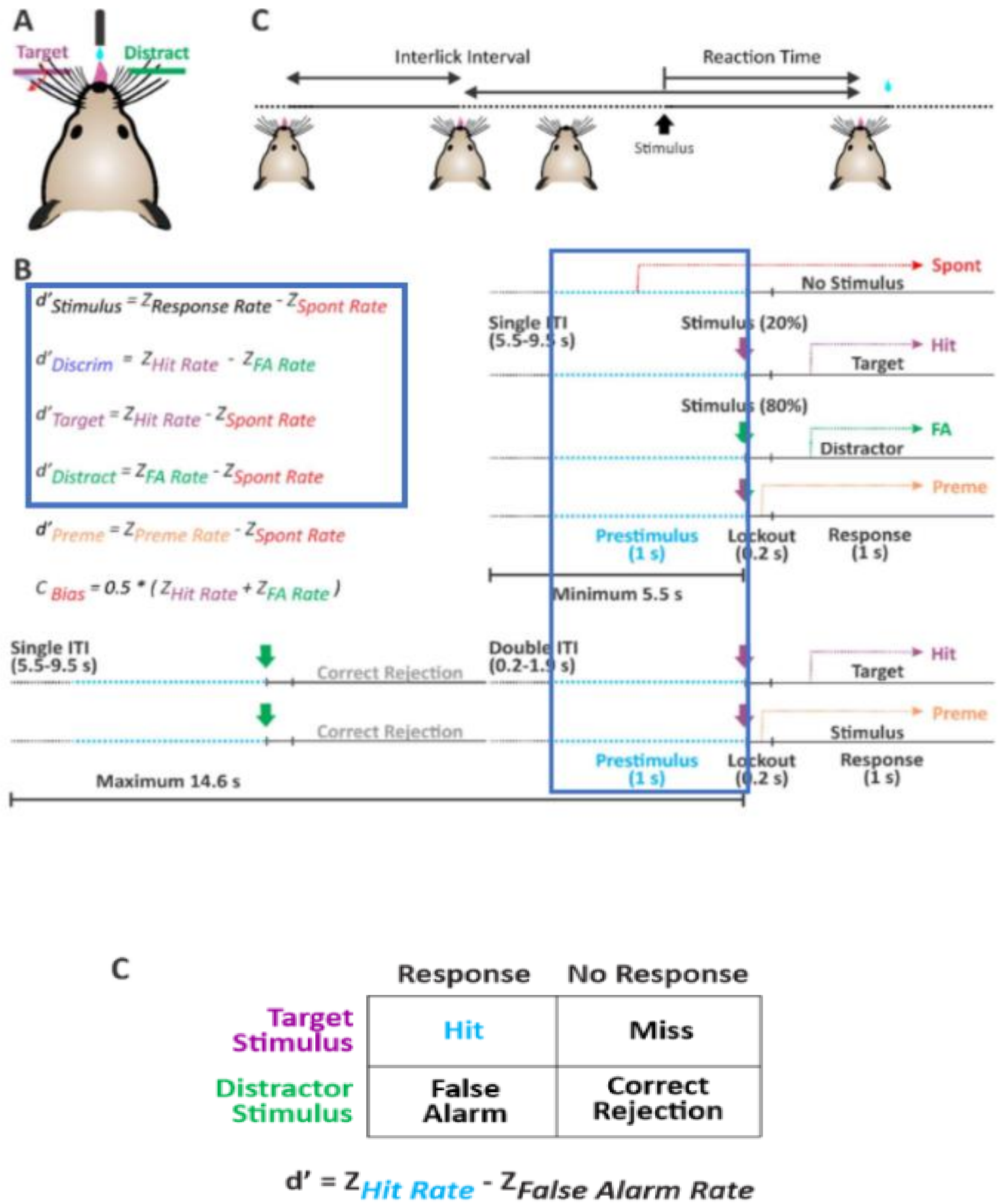


Figure 1: A. Placements of Paddles and Lick Port **B.** Visual representation of the response rates, their equations, and other behavioral variables studied throughout the study **C.** Application of Signal Detection Theory to Our Task to Define Recorded Behaviors and Timing Layout of Task (Marrero et al., 2023)

Chapter 2: Identification of Response Selection Behaviors in Mice Learning and Mastering a Selective Detection Task

Introduction

As mentioned in chapter 1, the traditional way of measuring strength of response selection and/or response inhibition being exhibited by participants completing goal-directed behavioral tasks is through analysis of behavioral responses. Hit Rate is used to measure response selection. False Alarm Rate is used to measure response inhibition. In our Go/No-Go task, we first seek to identify any behavioral trends that could inform us regarding which cognitive strategy is being utilized and/or learned. The specific behavioral variables analyzed to help us address this include hit rate, false alarm rate, and discrimination. We test three alternative hypotheses to determine whether mice are learning response selection, response inhibition, and/or both to complete the task. One alternative hypothesis predicts that changes in Discrimination d' reflect increases in response selection, as reflected by increases in Hit Rates. Another alternative hypothesis predicts that changes in Discrimination d' reflect increases in response selection, as reflected by decreases in False Alarm Rates. The final alternative hypothesis predicts changes in Discrimination d' reflect increases in response selection and response inhibition, as reflected by simultaneous increases in Hit Rates and decreases in False Alarm Rates. Response selection will be defined by significant hit rate increases across sessions and a significant positive correlation between hit rate and discrimination. Response inhibition will be defined by significant false alarm rate decreases across sessions and a significant negative correlation between hit rate and discrimination. If response inhibition and response selection are both occurring, we would expect to see both requirements previously outlined for response selection and response inhibition occurring simultaneously.

Methods

In this chapter, we used the following tests to analyze changes in Hit Rate, False Alarm Rate, and Discrimination across all session days: Linear Regression, Pearson Correlation Coefficient, and One Sample t-tests. Linear regression analyses were used to determine slopes of response rates (Hit Rate and False Alarm Rate) and Discrimination across sessions per mouse (Figures 1A, 1B, 1C); the slopes of individual linear regressions for each response rate type were averaged to determine mean linear slopes for the response rates. If the mean linear slope for a response rate or Discrimination across mice was significantly positive, the trend of the measure was identified as 'increasing'. In contrast, if the mean linear slope for a response rate or Discrimination across mice was significantly negative, the measure was identified as 'decreasing'. Pearson correlation coefficient tests were used to determine levels of association between response rates and Discrimination across all session days. Reported correlations are calculated from the mean correlation using the individual correlations from each mouse. All mean values reported as the mean ± standard error of the mean (SEM). All reported values are also round to three significant figures.

Results

Hit Rate, False Alarm Rate, and Discrimination Across All Session Days

In this study we present longitudinal data from 6 mice. We first investigated changes in Discrimination (separation of hit rate and false alarm rate) across training sessions. We expected that Discrimination would significantly increase across training session days. An increase in discrimination across training sessions indicated a learning direction from naïve to expert status (Figure 2C, one sample t-test μmDiscrimination=0.128±0.0103, $p<0.0005$, $n=6$ mice). Changes in Hit Rates and False Alarm Rates were assessed to determine which of them were improving across training days. Improvements in Hit Rate and False Alarm Rate were determined by the slopes of their linear fits across sessions. We expected that Hit Rates would show significant increases while False Alarm Rates would decrease. Hit rates significantly increased across sessions (Figure 2A, one sample t-test μmHitRate=0.0346±0.00290, $p<0.00005$, $n=6$ mice). We then determined the average False Alarm Rate (FAR) amongst all mice across session days. Unexpectedly, False Alarm Rates also significantly increased across sessions (Figure 2B, one sample t-test μmFalseAlarmRate=0.0103±0.00386, $p<0.05$, $n=6$ mice).

Discrimination Correlations With Hit Rate and False Alarm Rate

We first investigated the correlation between Discrimination and Hit Rate across all sessions. As Hit Rate improves, we would expect Discrimination to improve and be positively and strongly correlated with Hit Rate. To measure the correlational relationship between Discrimination and Hit Rate across all mice, we first determined the mean

Discrimination and Hit Rate correlation coefficient using all the behavioral data from the six mice (individual data for each mouse not shown). We found that the correlation between Discrimination and Hit Rate was positive and significant (Table 1, one sample t-test μmDiscrimmination&HR corr =0.895±0.0195, p<0.0000005, n=6 mice). To measure the correlational relationship between Discrimination and False Alarm Rate across all mice, we determined the mean Discrimination and False Alarm Rate correlation coefficient using all the behavioral data from the six mice (individual data for each mouse not shown). We found that the correlation between Discrimination and False Alarm Rate was not significant (Table 1, one sample t-test μmDiscrimination&FAR corr =0.307±0.150, p=0.0962, n=6 mice). Our data is consistent with response selection behavioral performance.

Discussion

Mice Exhibit a Response Selection Strategy Across All Session Days

In this chapter, we have identified changes in response rate exhibited by mice learning and mastering a Go/No-Go whisker-based selective detection task. When reviewing mouse performance holistically (using their behavioral data from all session days they completed), mice demonstrated a significant improvement in their Hit Rates across learning (Figure 2A, 2D). Mice also showed that False Alarm Rate increased across learning but not in a significant manner (Figure 2B, 2D). When looking at changes in Discrimination across session days, Discrimination significantly increases (Figure 2C, 2D) which meets our expectation and matches observed Discrimination increases in other studies utilizing the same task (Aruljothi et al., 2020).

The changes in Hit Rate and False Alarm Rate best resemble a cognitive strategy of response selection. Response selection, in the context of goal-directed behaviors and tasks, involves the selection and execution of an appropriate response in reaction to the presentation of a task related stimulus (Goghari & MacDonald, 2009). The significant increases in Hit Rate suggests that mice are choosing to selectively respond to target trials. This increase of selectivity may be the result of the mice learning to associate responding to target trials with receiving water rewards. Furthermore, the insignificant increases of False Alarm Rate across learning suggests that the mice are selectively choosing to not respond to distractor trials. The insignificant increases in False Alarm Rate may be the result of the mice establishing a preference regarding which trial they will respond to (preferring target trials over distractor trials). It is also worth noting that the significant increases of False Alarm Rate across learning suggest that response inhibition is not the primary strategy being used by mice. If response inhibition was the strategy being used, we would expect to observe a significant decrease in False Alarm Rate; response inhibition involves the suppression of inappropriately executed actions that interfere with the execution of goal-driven behaviors (Mostofsky & Simmonds, 2008).

When looking at the correlation between response rates (Hit Rate and False Alarm Rate) with Discrimination, the correlation between Hit Rate and Discrimination is positive and significant (Figure 2E, Table 1). We also see that the correlation between False Alarm Rate and Discrimination is positive but not significant (Figure 2E, Table 1). It is expected that there would be some form of significant correlation between response rates and Discrimination given that the calculation of Discrimination is directly calculated by the difference between the normative inverse of Hit Rate and False Alarm Rate (see Materials and Methods). It is worth noting that in the case of False Alarm Rate, despite False Alarm Rate significantly increasing, it still was not statistically significant with respect to being correlated with and driving Discrimination. In summary, we suggest that our mice demonstrate a cognitive behavioral strategy of response selection across learning and mastery of the task.

Figures

Figure 2A: HR v.s. Session Days (6 Mice)

one sample t-test μmHitRate=0.0346±0.00290, p<0.00005, n=6 mice

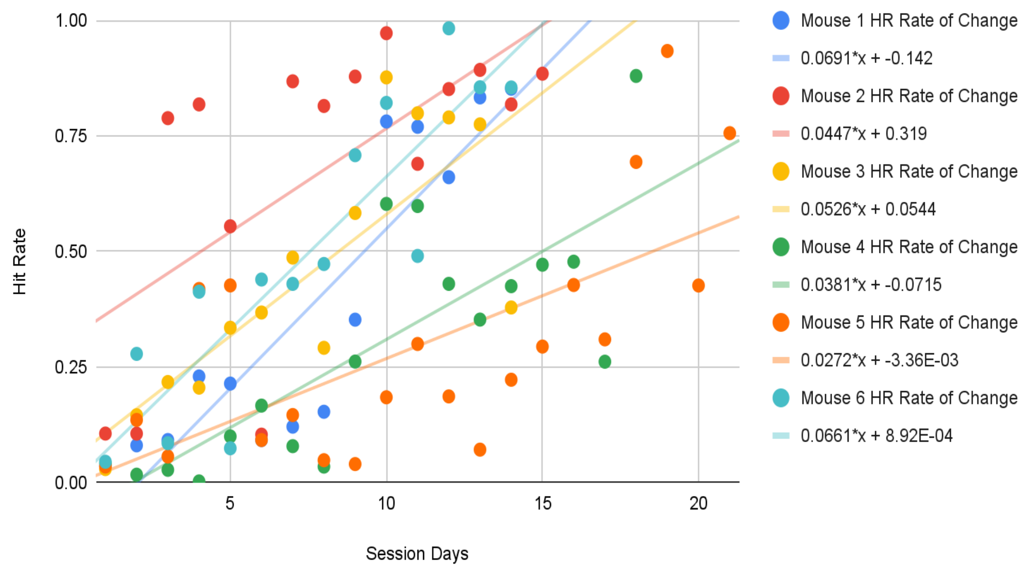


Figure 2B: FAR v.s. Session Days (6 Mice)

one sample t-test μmFalseAlarmRate=0.0103±0.00386, p<0.05, n=6 mice

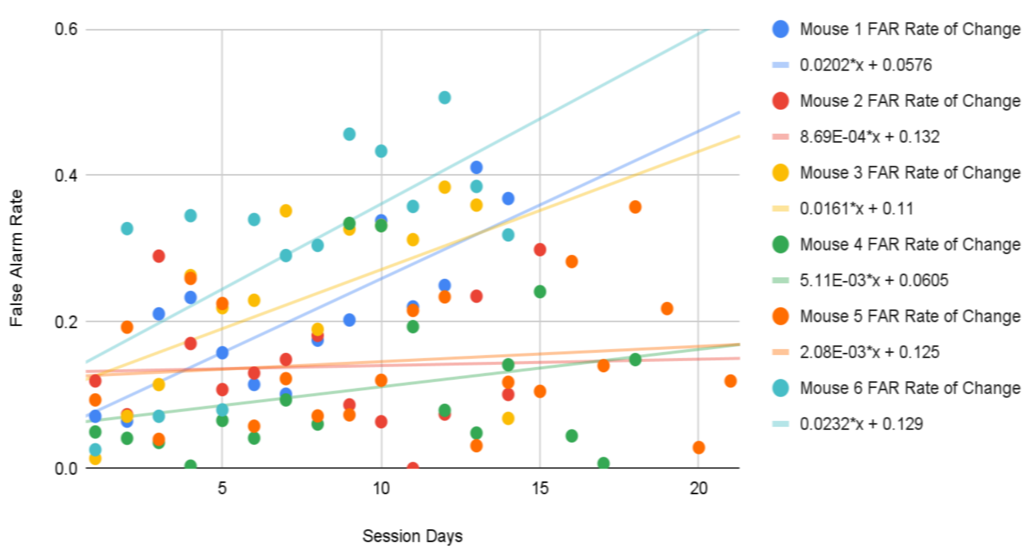


Figure 2C: Discrimination d' v.s. Session Days

one sample t-test μmDiscrimination=0.128±0.0103, p<0.0005, n=6 mice

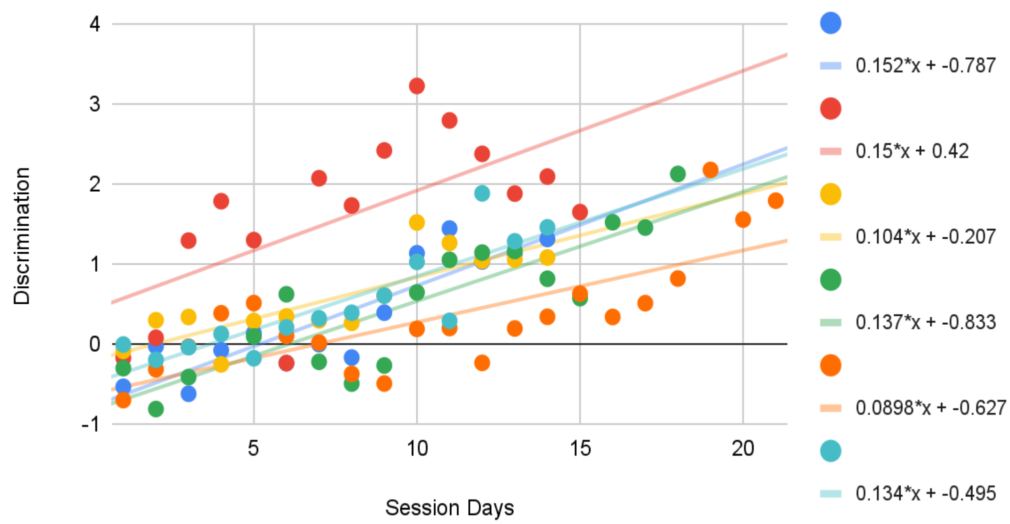


Figure 2E: Correlation Between Disc d' and Response Rates

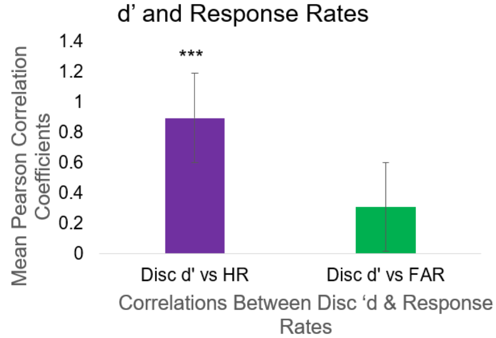
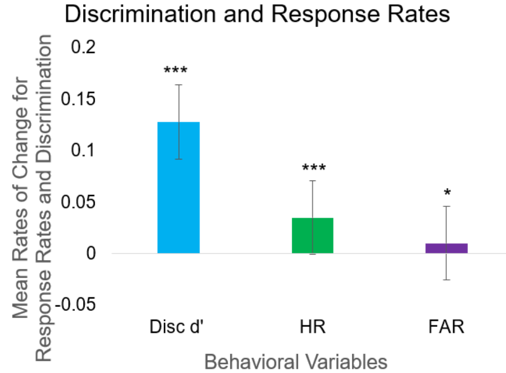


Figure 2D: Mean Rate of Change for Discrimination and Response Rates



* p<0.05, ** p<0.01, *** p<0.0001

Figure 2: A. Average Rate of Change of Hit Rates for Six Mice. The y-axis is the recorded hit rates. The x-axis is session days. Each set of colored dots represents the daily Hit Rates for a single mouse. The slope of each line represents the rate of change for the Hit Rates of a single mouse. **B.** Average Rate of Change of False Alarm Rates for Six Mice. The y-axis is the recorded false alarm rates. The x-axis is session days. Each set of colored dots represents the daily False Alarm Rates for a single mouse. The slope of each line represents the rate of change for the False Alarms Rate of a single mouse. **C.** Average Rate of Discrimination for Six Mice. The y-axis is the recorded discrimination. The x-axis is session days. Each set of colored dots represents the daily Discriminations for a single mouse. The slope of each line represents the rate of change for the Discriminations of a single mouse. **D.** Mean Rate of Change for Discrimination and Response Rates Across Six Mice. The y-axis is the mean rate of change for Discrimination d', Hit Rate, and False Alarm Rate. The x-axis categorically lists out the behavioral measures being analyzed (Discrimination d', Hit Rate, and False Alarm Rate). Asterisks above any column representing the mean rate of change value for a behavioral measure indicates significance (one sample t-test). **E.** Correlation Between Discrimination d' and Response Rates. The y-axis is the mean pearson correlation coefficient value for Discrimination d'vs Hit Rate and for Discrimination d'vs False Alarm Rate. The x-axis categorically lists out the correlations of behavioral measures being analyzed (Discrimination d' vs Hit Rate and Discrimination d' vs False Alarm Rate). Asterisks above any column representing the mean pearson correlation coefficient between two behavioral measures indicates significance (one sample t-test).

Table 1: Discrimination Correlations With Hit Rate and False Alarm Rate.

	Disc & HR	Disc & FAR
Mean Correlation R Value	0.895	0.307
One Sample t-test P-Value	0	0.0962

Table 1: Discrimination Correlations With Hit Rate and False Alarm Rate. The middle column has the mean correlation R value for Disc & HR. The middle column also contains the p-value that originated from doing a one sample t test for the mean Disc & HR. The right column has the mean correlation R value for Discrimination & FAR. The right column also contains the p-value that originated from doing a one sample t test for the mean Disc & FAR.

Chapter 3: Characteristics of Response Selection Behaviors

Introduction

As mentioned in chapter 1, there is little research that has been done to characterize the behavioral measures that are used to identify response selection and response inhibition in mouse models. In this chapter, we analyze the changes in and relationships between behavioral mechanisms (Target Detection, Distractor Detection, Pretrial Spontaneous Rate) and response selection behaviors (response rates) across all session days. We expect that as mice learn to associate which trials and behaviors grant them rewards, they will prioritize licking to the target stimuli and reducing all other behavioral outcomes. To elaborate, we expect that mice will show increases in target detection (stimulus-detection behavioral mechanism) and decreases in pretrial spontaneous rate (impulsive behavioral mechanism). Additionally, we expect that target detection will be positively and significantly correlated with Hit Rate. These expectations allow us to test three alternative hypotheses regarding which behavioral mechanisms (detection of stimuli and impulsivity) drive the learning of response selection. Our first alternative hypothesis is that the learning of response selection will be driven by improvements in detection of the target stimuli, as evidenced by a positive and significant correlation between Hit Rate and Target Detection. Our second alternative hypothesis is that the learning of response selection will be driven by increases in impulsivity, as evidenced by a positive and significant correlation between Hit Rate and Pretrial Spontaneous Rate. Our final alternative hypothesis is that the learning of response selection will be driven by both improvements in detection of the target stimuli and increases in impulsivity, as evidenced by positive and significant correlations between Hit Rate and both Pretrial Spontaneous Rate and Target Detection. These hypotheses are also tested for False Alarm Rate as well.

Methods

In this chapter, we used the following tests to analyze the relationships and changes in Target Detection, Distractor Detection, Pretrial Spontaneous Rate, False Alarm Rate, and Hit Rate across all session days: Linear Regression, Pearson Correlation Coefficient, and One Sample t-tests. Linear regression analyses were used to determine slopes of behavioral mechanisms (Target Detection, Distractor Detection, and Pretrial Spontaneous Rate) across sessions per mouse (Figures 3,4); the slopes of individual linear regressions for each behavioral mechanism were averaged to determine mean linear slopes for the behavioral mechanism. If the mean linear slope for a behavioral mechanism across mice was significantly positive, the behavioral variable was identified as ‘increasing’. In contrast, if the mean linear slope for a behavioral mechanism across mice was significantly negative, the behavioral variable was identified as ‘decreasing’. Pearson correlation coefficient tests were used to determine levels of association between various behavioral variables during all session days. Reported correlations are calculated from the mean correlation using the individual correlations from each mouse. All mean values reported as the mean ± standard error of the mean (SEM).

Results

The behaviors of Hit Rate and False Alarm Rate are proportional driven based on changes to the following behavioral mechanisms: Target Detection (T DP), Distractor Detection (D DP), and Pretrial Spontaneous Rate (PSR) (Materials & Methods). We expect that T DP will significantly increase, D DP will not significantly increase, and PSR will significantly decrease. Regarding correlation expectations, we expect that T DP will be positively and significantly correlated with Hit Rate. We also expect that D DP will be positively but not significantly correlated with False Alarm Rate. Additionally, we also expect that PSR will be negatively and significantly correlated with observed increases in Hit Rate and False Alarm Rate given that the mice are expected to learn that spontaneous behaviors result in the delaying of both target and distractor trials. These expectations are guided by the principle that mice are anticipated to learn that only licking in response to the detection of the target stimuli provides them with a water reward. The mice are expected to learn that any other behavior will result in them receiving a timeout and no water rewards.

Characteristics of Response Selection Behaviors: Hit Rate

We first assessed changes in Target Detection (T DP) across session days. T DP is the measure of the amount of Hit Rates that are actually caused by the mice detecting the target stimuli (Materials & Methods). Target Detection significantly increased across sessions (Figure 3A, 3C, one sample t-test $\mu mTargetDetection=0.126 \pm 0.00901$, $p<0.0000005$, n=6 mice). We then investigated changes in Pretrial Spontaneous Rate

(PSR) across session days. PSR is the rate of licks detected one second prior to the onset of either a target or distractor stimuli (Materials & Methods). PSR did significantly increase from a non-zero value across session days (Figure 3B, 3C, one sample t-test $\mu mPSR=0.00993\pm0.00438$, $p<0.05$, n=6 mice).

Hit Rate Correlations With Related Behavioral Mechanisms

We next investigated the correlational relationship between T DP and Hit Rate and the correlational relationship between PSR and Hit Rate across all session days. We tested the hypothesis that, given that mice are expected to learn that properly responding to the target stimulus results in a water reward, observed increases in Target Detection will proportionally drive observed increases in Hit Rate. We also tested the hypothesis that, given that mice are expected to learn that spontaneous behaviors delay the onset of trails, observed increases in Pretrial Spontaneous Rate will not proportionally drive observed increases in Hit Rate. The null hypothesis is that changes in Target Detection and/or Pretrial Spontaneous Rate do not proportionally drive observed increases in Hit Rate across learning.

To measure the correlational relationship between Hit Rate and Target Detection across all mice, we first determined the mean Target Detection and Hit Rate correlation coefficient using behavioral data from all session days (individual data for each mouse not shown). We found that the correlation between Target Detection and Hit Rate significantly positive across all session days (one sample t-test μmHR&T DP corr $=0.871\pm0.0311$, $p<0.0005$, n=6 mice).

To measure the correlational relationship between Hit Rate and PSR across all mice, we then determined the mean Hit Rate and PSR correlation coefficient using behavioral data from all session days (individual data for each mouse not shown). We found that the correlation between PSR and Hit Rate was significantly positive across all session days (one sample t-test μmHR&PSR corr $=0.567\pm0.0906$, $p<0.005$, n=6 mice).

Characteristics of Response Selection Behaviors: False Alarm Rate

We assessed changes in Distractor Detection (D DP) across session days. D DP is the measure of the amount of False Alarm Rates that are actually caused by the mice detecting the distractor stimuli (Materials and Methods). Distractor Detection did not increase significantly across sessions (Figure 4A, one sample t-test μmDistractorDetection$=0.00732\pm0.00630$, $p=0.298$, n=6 mice).

False Alarm Rate Correlations With Related Behavioral Mechanisms

We next investigated the correlational relationship between D DP and False Alarm Rate and the correlational relationship between PSR and False Alarm Rate across all session days. We tested the hypothesis that, given that the observed increases in Distractor Detection are not significant, Distractor Detection will not be significantly correlated with False Alarm Rate across learning. We also tested the hypothesis that, given that the observed increase in Pretrial Spontaneous Rate is significant, Pretrial Spontaneous Rate will be significantly correlated with False Alarm Rate across learning. The null hypothesis is that changes in Distractor Detection and/or Pretrial Spontaneous Rate do not drive decreases in False Alarm Rate across learning.

To measure the correlational relationship between False Alarm Rate and Distractor Detection across all mice, we first determined the mean False Alarm Rate and Distractor Detection correlation coefficient using behavioral data from all session days (individual data for each mouse not shown). We found that the correlation between Distractor Detection and False Alarm Rate was not significant across sessions (Figure 4B, one sample t-test μmFAR&D DP corr =0.258±0.112, p=0.0704, n=6 mice).

To measure the correlational relationship between False Alarm Rate and PSR across all mice, we first determined the mean False Alarm Rate and PSR correlation coefficient using behavioral data from all session days (individual data for each mouse not shown). We found that the correlation between PSR and False Alarm Rate was positive and significant across sessions (one sample t-test μmFAR&PSR corr =0.875±0.0203, p<0.0000005, n=6 mice).

Discussion

Detection and Impulsivity Proportionally Drive Observed Response Selection Response Rates

In this chapter, we have identified changes in three behavioral mechanisms that drive and impact observed changes in response rates. When looking at how Target Detection changes across learning, we see that Target Detection significantly increases over time (Figure 3A). When looking at how Distractor Detection changes across learning, we see that Distractor Detection rate of change is not significantly different from zero (Figure 4A). When looking at how Pretrial Spontaneous Rate changes across learning, see that Pretrial Spontaneous Rate significantly increases over time (Figure 3B).

When focusing on changes in detection, the significant increase in target detection across sessions suggests that the mice are responding specifically when they detect/sense the target stimulus. The increase in Hit Rate observed in chapter 2 is being driven as a result of the mice responding specifically when they detect/sense the target stimulus (Figure 4B). When looking at how distractor detection changes overtime, we see that the rate of change for distractor detection is not significant and is not significantly different from zero. This suggests that the mice are not learning to respond to distractor trials solely because they detected the moving distractor stimuli. When looking at how Pretrial Spontaneous Rate changes the cross sessions, we see that Pretrial Spontaneous Rate increases significantly across session days. Given these changes and considering that the Pretrial Spontaneous Rate precedes both target and distractor trials, this suggests that reduction in impulsivity is not required for mice to become experts at the task. Additionally, one might suggest that the impulsivity is beneficial and essential for the increases in Hit Rate necessary for mice to achieve mastery status.

It is currently unclear as to why mice in our study seemingly choose to change their response in ways that utilize both significant persistent impulsive strategies and fluctuating detection strategies. The mice used in this study were not genetically or surgically altered to mimic conditions such as ADHD. These circumstances bring forth the question as to why the mice don't seemingly demonstrate a willingness nor tendency to decrease reward-reducing behaviors (False Alarm Rate). One might expect that mice would want to learn to maximize the number of rewards they receive by reducing generally any behaviors that disrupt goal-directed behaviors. If mice did adopt such as a strategy across learning and mastery, behavioral variables such as Pretrial Spontaneous Rate, Distractor Detection, and False Alarm Rate, would significantly decrease over time potentially while goal-directed behaviors that result in rewards would increase (Hit Rate and Target Detection would increase). Considerations that can be made include the possibility that mice completing our task might be under some form of anxiety and/or stress that is beyond our measurable capabilities. Another consideration that can be made include psychological factors; mice were water restricted as described in the methods of chapter 1. If the mice are desperate enough to the point where they are willing to engage in any behaviors that could potentially result in them getting water rewards (e.g. a mouse might decide to lick spontaneously or to everything with the hopes that some of their licks are bound to result in the delivery of a reward), this could potentially explain why spontaneous behaviors persist despite evidence that shows the mice are learning to discriminate between target and distractor stimuli/trials (Goltstein et al., 2018). To evaluate whether psychological conditions cause variances in behaviors, we could train non-water restricted mice to complete our task and record their behaviors. We would predict that if the psychological condition of water-restriction is responsible for failure of impulsive behaviors to decrease, non-water restricted mice would show improvements in Discrimination and Hit Rates and potentially show decreases in Pretrial Spontaneous Rates.

Figures

Figure 3A: T DP v.s. Session Days (6 Mice)

one sample t-test μmTargetDetection=0.126±0.00901, p<0.0000005, n=6 mice

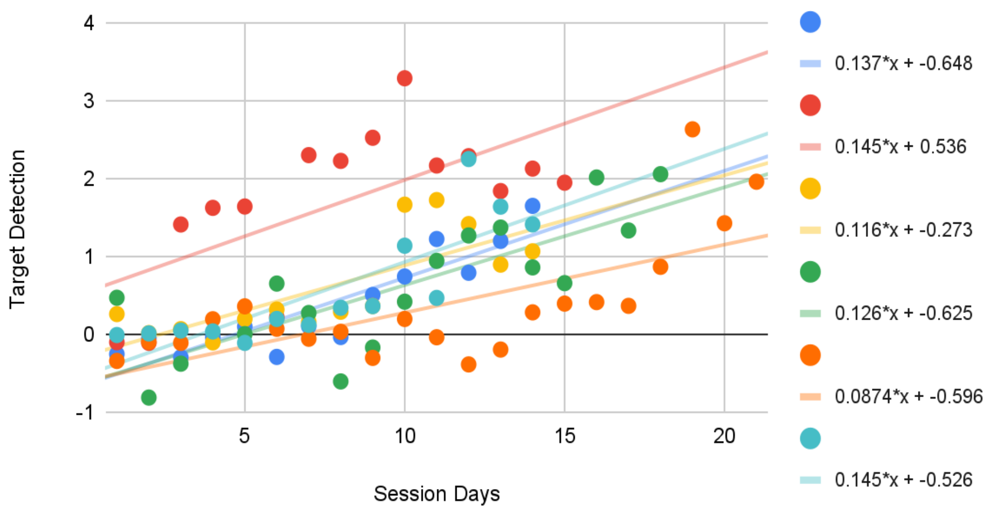
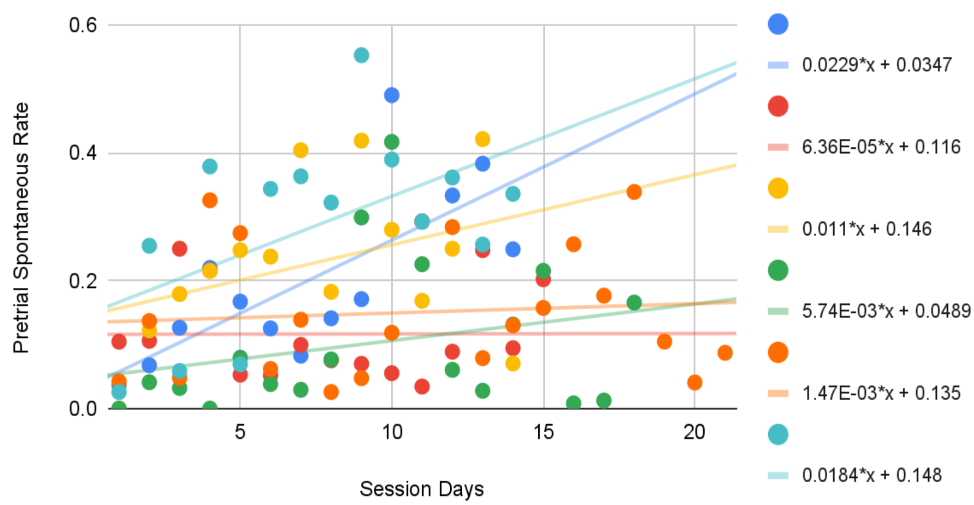


Figure 3B: PSR v.s. Session Days (6 Mice)

one sample t-test μmPSR=0.00993±0.004378, p<0.05, n=6 mice



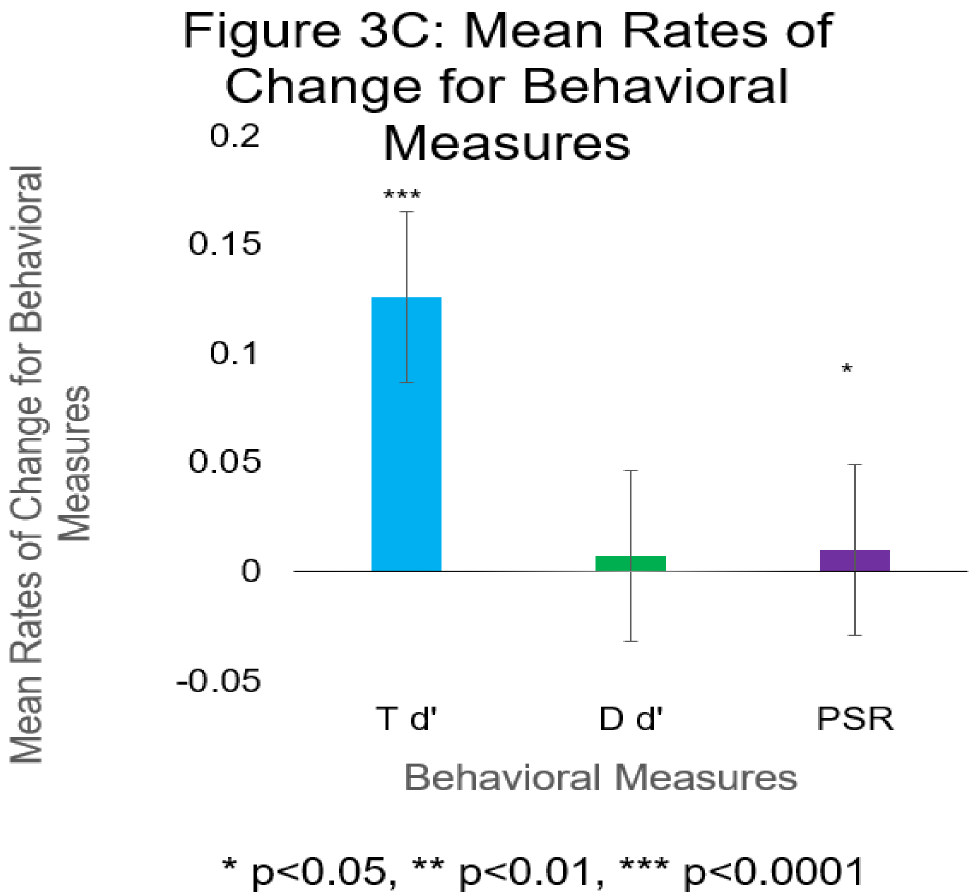


Figure 3: A. Average Rate of Change of Target Detection for Six Mice. The y-axis is the recorded target detections. The x-axis is session days. Each set of colored dots represents the daily target detections for a single mouse. The slope of each line represents the rate of change for the target detections of a single mouse. **B.** Average Rate of Change of Pretrial Spontaneous Rates for Six Mice. The y-axis is the recorded pretrial spontaneous rates. The x-axis is session days. Each set of colored dots represents the daily Pretrial Spontaneous Rates for a single mouse. The slope of each line represents the rate of change for the pretrial spontaneous rates of a single mouse. **C.** Mean Rates of Change for Behavioral Measures. The y-axis is the mean rate of change for Target Detection, Distractor Detection, and Pretrial Spontaneous Rate. The x-axis categorically lists out the behavioral measures being analyzed (Target Detection, Distractor Detection, and Pretrial Spontaneous Rate). Asterisks above any column representing the mean rate of change value for a behavioral measure indicates significance (one sample t-test).

Table 2: Hit Rate Correlations With Target Detection and Pretrial Spontaneous Rate.

	HR & T DP	HR & PSR
Mean R Value	0.871	0.567
One Sample T - Test P-Value	0.000001	0.002

Table 2: Hit Rate Correlations With Target Detection and Pretrial Spontaneous Rate. The middle column has the mean correlation R value for HR & T DP. The middle column also contains the p-value that originated from doing a one sample t test for the mean HR & T DP. The right column has the mean correlation R value for HR & PSR. The right column also contains the p-value that originated from doing a one sample t test for the mean HR & PSR.

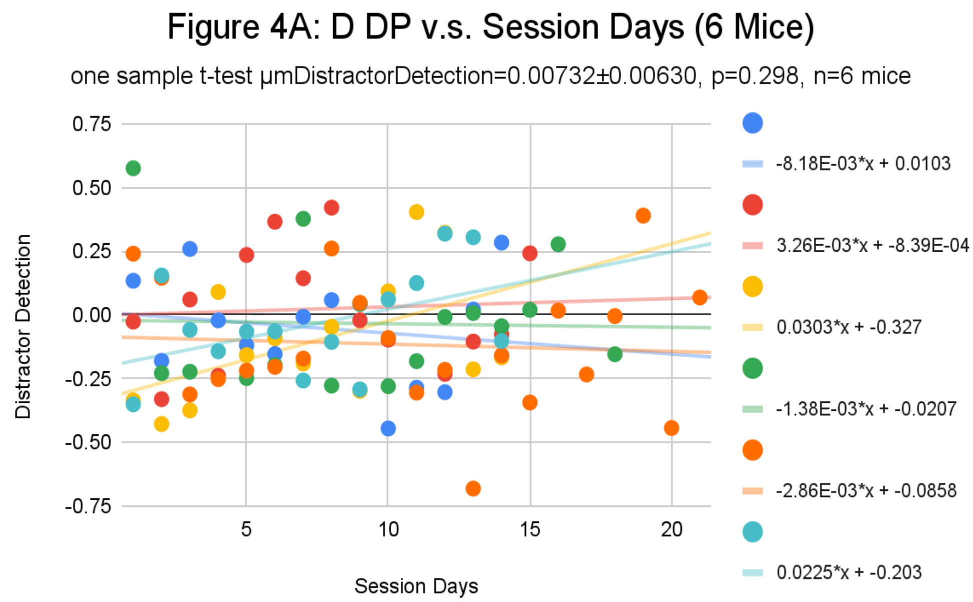


Figure 4A: D DP v.s. Session Days (6 Mice)
one sample t-test µmDistractorDetection=0.00732±0.00630, p=0.298, n=6 mice
Distractor Detection
0.75
0.50
0.25
0.00
-0.25
-0.50
-0.75
5
10
15
20
Session Days
-8.18E-03*x + 0.0103
3.26E-03*x + -8.39E-04
0.0303*x + -0.327
-1.38E-03*x + -0.0207
-2.86E-03*x + -0.0858
0.0225*x + -0.203

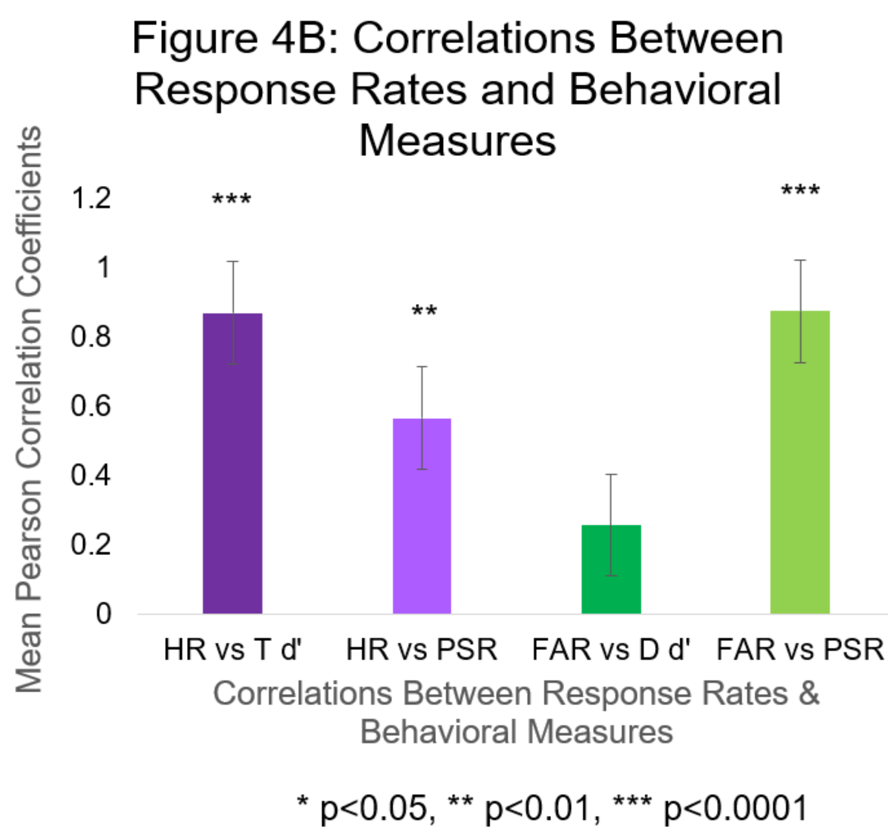


Figure 4B: Correlations Between Response Rates and Behavioral Measures
Mean Pearson Correlation Coefficients
1.2
1
0.8
0.6
0.4
0.2
0
***
**
***
HR vs T d'
HR vs PSR
FAR vs D d'
FAR vs PSR
Correlations Between Response Rates & Behavioral Measures
* p<0.05, ** p<0.01, *** p<0.0001

Figure 4: A. Average Rate of Change of Distractor Detection for Six Mice. The y-axis is the recorded distractor detections. The x-axis is session days. Each set of colored dots represents the daily distractor detections for a single mouse. The slope of each line represents the rate of change for the distractor detections of a single mouse. **B.** Correlations Between Response Rates and Behavioral Measures. The y-axis is the mean Pearson correlation coefficient value for Hit Rate vs Target Detection, Hit Rate vs Pretrial Spontaneous Rate, False Alarm Rate vs Distractor Detection, and False Alarm Rate vs Pretrial Spontaneous Rate. The x-axis categorically lists out the correlations of behavioral measures being analyzed (Hit Rate vs Target Detection, Hit Rate vs Pretrial Spontaneous Rate, False Alarm Rate vs Distractor Detection, and False Alarm Rate vs Pretrial Spontaneous Rate). Asterisks above any column representing the mean Pearson correlation coefficient between two behavioral measures indicates significance (one sample t-test).

Table 3: False Alarm Rate Correlations With Distractor Detection and Pretrial Spontaneous Rate

	FAR & D DP	FAR & PSR
Mean R Value	0.258	0.875
One Sample T - Test P-Value	0.070	0.0000001

Table 3: False Alarm Rate Correlations With Distractor Detection and Pretrial Spontaneous Rate. The middle column has the mean correlation R value for FAR & D DP. The middle column also contains the p-value that originated from doing a one sample t test for the mean FAR & D DP. The right column has the mean correlation R value for FAR & PSR. The right column also contains the p-value that originated from doing a one sample t test for the mean FAR & PSR.

Chapter 4: Response Selection Behaviors During Naïve and Expert Periods

Introduction

As mentioned in chapter 2, we were able to determine that across all session days, mice exhibited response selection as their main cognitive strategy based on analyses of their Hit Rates and False Alarm Rates. However, these findings only apply to behavior across all session days. They do not provide insight into how response rates change (which can tell us whether response selection or response selection is being learned) during the naïve periods and expert periods specifically. One might wonder whether response rates significantly increase during the naïve periods but not during the expert period (implying that response selection is learned during the naïve periods) and vice versa. The null hypothesis tested in this chapter is that changes in response rates and their correlations with Discrimination during the naïve and expert periods will not significantly reflect the learning of either response selection and/or response inhibition. An alternative hypothesis is that changes in response rates and their correlations with Discrimination during the naïve periods will reveal that response selection first appears during the naïve days (learning days). Another alternative hypothesis is that changes in response rates and their correlations with Discrimination during the expert periods will reveal that response selection first appears during the expert days (mastery days).

Methods

In this chapter, we used the following tests to analyze changes in Hit Rate, False Alarm Rate, and Discrimination across the naïve and expert session periods: Linear Regression, Pearson Correlation Coefficient, One Sample t-tests, Paired t-tests, and a two-way ANOVA. Linear regression analyses were used to determine slopes of response rates (Hit Rate and False Alarm Rate) and Discrimination across sessions per mouse; the slopes of individual linear regressions for each response rate type were averaged to determine mean linear slopes for the response rates. If the mean linear slope for a response rate or Discrimination across mice was significantly positive, the trend of the measure was identified as 'increasing'. In contrast, if the mean linear slope for a response rate or Discrimination across mice was significantly negative, the measure was identified as 'decreasing'. Pearson correlation coefficient tests were used to determine levels of association between response rates and Discrimination across all session days. Paired t-tests were used to determine whether the mean naïve and expert response rates differed significantly from each other. Paired t-tests were also used to determine whether the mean naïve and expert response rates correlations with Discrimination differed significantly from each other. A two-way ANOVA with replication was used to see if there is any interaction between response behavior type (Hit Rate and False Alarm Rate) and performance status (naïve and expert periods). Reported correlations are calculated from the mean correlation using the individual correlations from each mouse. All mean values reported as the mean ± standard error of the mean (SEM).

Results

The data presented in chapter 2 is consistent with response selection behavioral performance being exhibited by the mice. The data presented in chapter 3 provides information regarding which behavioral mechanisms driving observed changes in Hit Rate and False Alarm Rate. The analyses and findings presented in chapters 2 and 3, however, can only be utilized when studying mice behaviors across all session days completed. As previously stated in Materials and Methods, for any mouse that was included in this study, they experienced a period of naïve performance followed by a period of expert performance. As mentioned in the Materials and Methods, a mouse has achieved expert status when they achieve three consecutive days of a Discrimination value of 1 or greater. During all the session days that precede a mouse's expert period, their performance is their naive. In this chapter, we utilize the same statistical tests and analyses used in chapter 2 to examine behaviors (Hit Rate and False Alarm Rate) and behavioral correlations separately during the naïve and expert periods. Additionally, with the use of paired t-tests and subsequent analyses, we study how the behaviors and behavioral correlations change (transition) across the naïve and expert periods.

Hit Rate: Naïve Days v.s. Expert Days

We first assessed changes in Hit Rate (HR) during the naïve periods of all mice (changes during all days preceding three consecutive days of having a Discrimination value greater than one). Naïve Hit Rates significantly increased across naïve sessions days (Figure 5A, Table 4, one sample t-test $\mu_{mnaiveHitRate}=0.0483\pm0.0102$, $p<0.05$, $n=6$ mice).

We then assessed changes in Hit Rate (HR) during the expert periods of all mice (changes during three consecutive days when the mice had a Discrimination DP greater than one). Hit Rates did not significantly increase and rather decreased across sessions (Figure 5B, Table 4, one sample t-test μmexpertHitRate=-0.0233±0.0581, p=0.706, n=6 mice).

False Alarm Rate: Naïve Days v.s. Expert Days

We then assessed changes in False Alarm Rate (FAR) during the naïve periods of all mice (changes during all days preceding three consecutive days of having a Discrimination value greater than one). Naïve False Alarm Rates did not significantly increase across expert session days (Figure 6A, 7A, Table 4, one sample t-test μmnaiveFalseAlarmRate=0.0135±0.00546, p=0.0562, n=6 mice).

We then assessed changes in False Alarm Rate (FAR) during the expert periods of all mice (changes during three consecutive days when the mice had a Discrimination DP greater than one). Expert False Alarm Rates non-significantly decreased across expert session days (Figure 6B, 7A, Table 4, one sample t-test μmexpertFalseAlarmRate=-0.0587±0.0281, p=0.0910, n=6 mice).

Differences in Hit Rate and False Alarm Rate Across Naïve and Expert Periods

We compared and analyzed changes of Hit Rate during the naïve and expert periods using a paired t-test. The same statistical test and analyses were performed on changes of

False Alarm Rate during the naïve and expert periods as well (Table 4). The null hypothesis is that changes in behaviors (Hit Rate and False Alarm Rate) during the naïve and expert periods do not significantly differ from each other. An alternative hypothesis is that changes in behaviors (Hit Rate and False Alarm Rate) during the naïve and expert periods do significantly differ from each other.

The results of the paired t-test for Hit Rate show that changes in naïve Hit Rate and changes in expert Hit Rate do not differ significantly (Table 4, paired t-test μmNaiveHR&ExpertHR, p=0.286, n=6 mice). Additionally, the results of the paired t-test for False Alarm Rate show that changes in naïve False Alarm Rate and changes in expert False Alarm Rate do not differ significantly (Table 4, paired t-test μmNaiveFAR&ExpertFAR, p=0.0691, n=6 mice).

False Alarm Rate, Hit Rate, and Discrimination Correlations Across Naïve Days

We then investigated the correlational relationship between Discrimination and Hit Rate and the correlation relationship between Discrimination and False Alarm Rate across during naïve session days. To measure these relationships, we first determined the mean naïve Discrimination and Hit Rate correlation coefficient using behavioral data from just naïve session days (individual naïve data for each mouse not shown). We found that the naïve Discrimination and Hit Rate correlation was positive and significant (Table 5, one sample t-test μmnaiveDiscrimmination&HR corr =0.870±0.0291, p<0.0005, n=6 mice). To measure the correlational relationship between naïve Discrimination and False Alarm

Rate across all mice, we determined the mean naïve Discrimination and False Alarm Rate correlation coefficient using behavioral data from just naïve session days (individual naïve data for each mouse not shown). We found that the correlation between naïve Discrimination and naïve False Alarm Rate was positive and significant (Table 5, one sample t-test $\mu_{mnaiveDiscrimination\&FAR\ corr} = 0.410 \pm 0.0818$, $p<0.05$, $n=6$ mice).

False Alarm Rate, Hit Rate, and Discrimination Correlations Across Expert Days

We then investigated the correlational relationship between Discrimination and Hit Rate and the correlation relationship between Discrimination and False Alarm Rate across during expert session days. To measure these relationships, we first determined the mean expert Discrimination and Hit Rate correlation coefficient using behavioral data from just expert session days (individual naïve data for each mouse not shown). We found that Discrimination and Hit Rate was not significantly correlated during expert session days (Table 5, one sample t-test $\mu_{mexpertDiscrimination\&HR\ corr} = 0.593 \pm 0.312$, $p<0.116$, $n=6$ mice). To measure the relationship between expert Discrimination and expert False Alarm Rate across all mice, we determined the mean expert Discrimination and False Alarm Rate correlation coefficient using behavioral data from just expert session days (individual data for each mouse not shown). We found that Discrimination and False Alarm Rate was not significantly correlated during expert session days (Table 5, one sample t-test $\mu_{mexpertDiscrimination\&FAR\ corr} = 0.0663 \pm 0.391$, $p=0.872$, $n=6$ mice).

Differences in Hit Rate v.s. Discrimination and False Alarm Rate v.s. Discrimination Across Naïve and Expert Days

We then investigated whether the correlations between Discrimination and behaviors (Hit Rate and False Alarm Rate) change, fluctuate, or remain similar across the naïve and expert periods. A paired t-test was used to compare the mean naïve HR&Discrimination correlation coefficient and the mean expert HR&Discrimination correlation coefficient (Table 5). A further paired t-test was used to compare the mean naïve FAR&Discrimination correlation coefficient with the mean expert FAR&Discrimination correlation coefficient (Table 5). The results of the paired t-test comparing the correlation between naïve Discrimination and Naïve Hit Rate to the correlation between expert Discrimination and expert Hit Rate show that the pair of mean correlation values do not differ significantly (Table 5, paired t-test μmNaiveHRv.s.DiscriminationCorr v.s. μmExpertHRv.s.DiscriminationCorr, p=0.426, n=6 mice). Additionally, the results of the paired t test comparing the correlation between naïve Discrimination and naïve False Alarm Rate to the correlation between expert Discrimination and expert False Alarm Rate show that the pair of mean correlation values do not differ significantly (Table 5, paired t-test, μmFARv.s.DiscCorr v.s. μmExpertFARv.s.DiscCorr, p=0.423, n=6 mice).

Two Way ANOVA With Replication for Correlation Between Discrimination and Response Rates

We investigate whether the changes in the correlation between Discrimination and Response Behaviors was dependent on the specific response behavior being correlated

(Hit Rate and False Alarm Rate) or the performance status of the mouse (naïve status and expert status). To set up the two-way ANOVA, we set the dependent variable to be correlation values between Discrimination and Response Behavior. One of the independent variables was Response Behavior Type (Hit Rate and False Alarm). The other independent variable was performance status type (naïve status and expert status). A null hypothesis proposed is that there exists no relationship between the independent variables and between each individual variable with the dependent variable.

The results of the two-way ANOVA show that response behavior type does not have a significant effect on the correlation between Discrimination and Response Behavior (two-way $ANOVA_{Resp|Disc\&BehaviorCorr}$, $p=0.0663$). The results also show that performance status type does not have a significant effect on the correlation between Discrimination and Response Behavior (two-way $ANOVA_{PerformanceStatus|Disc\&BehaviorCorr}$, $p=0.237$). Lastly, the results show us there is no significant interaction between both response behavior type and performance status type (two-way $ANOVA_{PerformanceStatus|Resp}$, $p=0.896$).

Discussion

Average of Response Rates During the Naïve and Expert Periods

In this chapter, we have first shown how Hit Rate and False Alarm Rate differ across the naïve and expert periods. When looking at the average Hit Rate during the naïve and expert days, the average naïve Hit Rate was significantly increasing. We also noticed that the average expert Hit Rate was decreasing although not significantly. When looking at the average False Alarm Rate during the naïve and expert days, the average naïve False Alarm Rate was increasing although not significantly. We also noticed that the average expert False Alarm Rate was decreasing although not significantly. When looking at the various differences between response rates between the naïve and expert periods, we see that expert Hit Rate was not significantly different from the naïve Hit Rate. We also see that the expert False Alarm Rate is not significantly different from the naïve False Alarm Rate. These initial findings, which were generated using paired t-tests, combined with the findings that the naïve Hit Rates were significantly increasing, tells us that Hit Rate, the response rate most important for mice to improve upon to receive rewards, experiences significant changes. This is to be expected. The paired t-tests comparing the naïve and expert False Alarm Rates tell us that the mice are not showing improvements in False Alarm Rate, which is desired. However, seeing that expert False Alarm Rate did not significantly change from naïve False Alarm Rate informs us that the mice are not learning to withhold licking behavior during False Alarm trials. Despite these revealing findings regarding False Alarm Rate during the naïve and expert periods, it is important to remember that all mice included in this study reached expert status. This suggests that improvements in withholding are not necessary for mice to learn and become masters at the task. This suggestion is supported by analyses conducted to study changes in response rates over time during the naïve and expert periods.

Comparisons of Changes of Response Rates During the Naïve and Expert Periods

Linear regression analysis shows how Hit Rate and False Alarm Rate changes between naïve session days and expert session days in mice. Naïve Hit Rate significantly increased across naïve session days (Figure 5A, 7A, Table 4). Naïve False Alarm Rate was not significant from zero (Figure 6A, 7A, Table 4). Expert Hit Rate was not significant from zero (Figure 5B, 7A, Table 4). Expert False Alarm Rate was not significant from zero (Figure 6B, 7A, Table 4).

When looking at just naïve response rates, the naïve response rate data is similar to observed changes in response rates across all session days (Figures 2A, 2B, 5A, 6A). The changes in naïve Hit Rate and False Alarm Rate best resemble a cognitive strategy of response selection. The significant increase in naïve Hit Rate suggests that mice are learning to shift more of their responses to target trials. Furthermore, the insignificant increases of naïve False Alarm Rate across learning suggests that the mice are not learning to suppress licking following onset of distractor stimuli. These findings suggest that mice included in this study are learning response selection as a strategy to become experts at the task and to maximize rewards. When looking at just expert response rates, the expert response rate data differs relative to observed response rates across all session days (Figures 2A, 2B, 5B, 6B; Table 4). We see that Discrimination does not change significantly across expert days (these days when the mice have reached expert status). This suggests that once mice have reached expert status, they do not seek to continue making improvements in Discrimination led by changes in expert Hit Rate and False

Alarm Rate. This is also evident by expert Hit Rate and False Alarm Rate not significantly changing or being significantly different from zero (Figures 5B, 6B). These findings suggest that the learning of response selection as a cognitive strategy over the course of session days becomes the strategy that mice use to complete the task once they are experts at the task. This is supported by the fact that the expert Hit Rates and False Alarm Rates are not significantly increasing from zero.

Comparison of Correlations Between Discrimination & Response Rates During Naïve and Expert Periods

In this chapter, we have shown how Discrimination & Response Rate Behaviors differ between the naïve and expert periods. Naïve Hit Rate & Discrimination correlation was positive and significant across naïve session days (Table 5). Naïve False Alarm Rate & Discrimination correlation was positive and significant across naïve session days (Figure 7B, Table 5). Expert Hit Rate & Discrimination correlation was positive and significant across expert session days (Figure 7B, Table 5). Expert False Alarm Rate & Discrimination correlation was not significant across expert session days (Figure 7B, Table 5). With the usage of paired t-tests, correlation differences between the naïve and expert periods were not statistically significant from each other (Figure 7B, Table 5). Despite the results of paired t-tests showing no significant differences, it is important to highlight that in the context of Hit Rate & Discrimination correlations, despite the apparent loss of correlational strength observed, the expert Hit Rate & Discrimination correlations remain significant. In contrast, in the context of False Alarm Rate &

Discrimination correlations, expert False Alarm Rate & Discrimination correlations are insignificant despite the results of the paired t-test indicating that the mean naïve and expert False Alarm Rate & Discrimination correlations are not significantly different from each other.

Discrimination Correlates With Response Rates: Impact of Response Rate and Behavioral Status

Our two-way ANOVA with replication reveals that there is no significant difference in the means of Discrimination & Response Rate correlations (the dependent variable) when grouping the dependent variable based on response rate type (one of the two independent factors used in the test). It is also revealed that there is no significant difference in the means of Discrimination & Response Rate correlations when grouping the dependent variable based on performance status (one of the two independent factors used in the test). There is also no significant interaction between both independent variables.

Limitations

One limitation that we acknowledge is that only the naïve periods studied fluctuate in duration across all mice. The variance in naïve period lengths could potentially be masking significant changes in False Alarm Rate and Hit Rate that occur during subsets of times within the naïve periods. Another limitation that could partially explain these results is the small sample size used for analyses; six mice were trained and had their behaviors analyzed. A larger sample size could present us with more behavioral data that could either reinforce or refute current findings presented in this study (e.g. if we reviewed a sample size of 30 mice, perhaps the data collectively will reveal that False Alarm Rate during the expert period is significantly correlated with changes in expert Discrimination).

Figures

Figure 5A: HR v.s. Naive Session Days

one sample t-test μmnaiveHitRate=0.0483±0.0102, p<0.05, n=6 mice

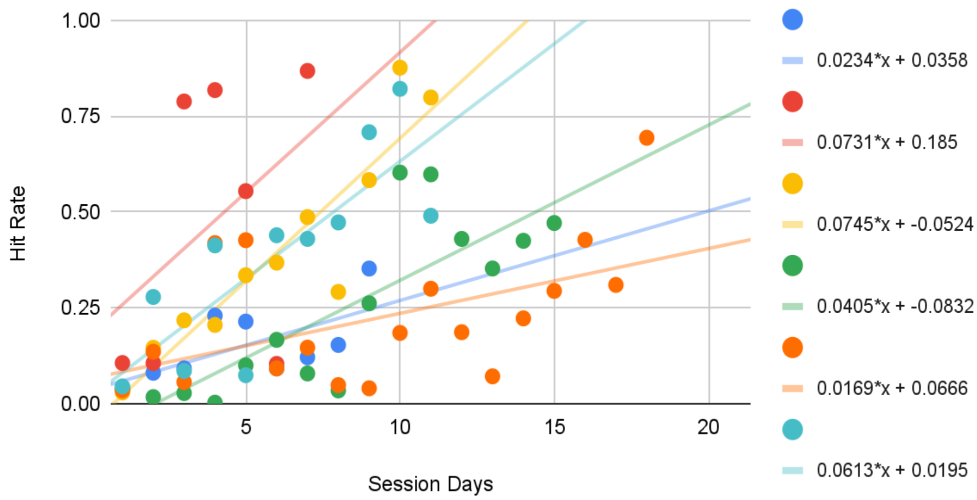


Figure 5B: HR v.s. Expert Session Days

one sample t-test μmexpertHitRate=-0.0233±0.0581, p=0.706, n=6 mice

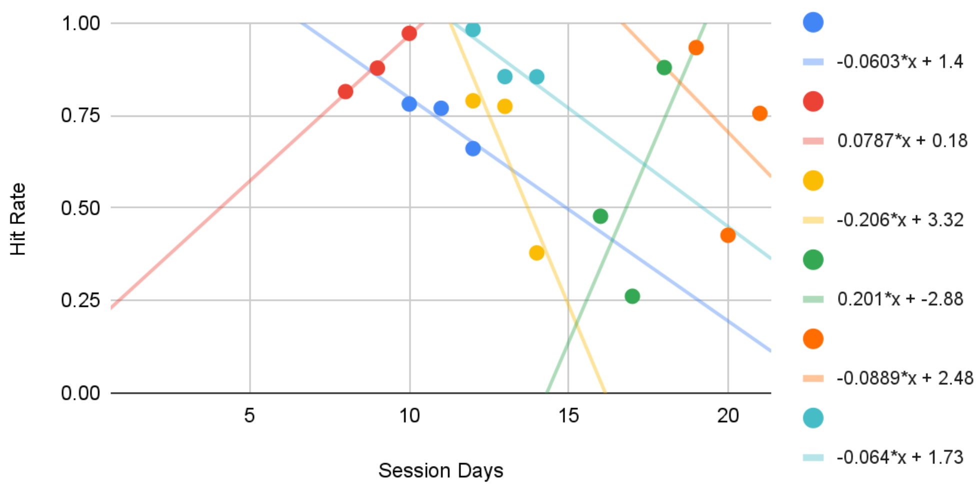


Figure 5: A. Average Rate of Change of Naïve Hit Rates for Six Mice. The y-axis is the recorded naïve hit rates. The x-axis is session days. Each set of colored dots represents the daily naïve Hit Rates for a single mouse. The slope of each line represents the rate of change for the naïve Hit Rates of a single mouse. **B.** Average Rate of Change of Expert Hit Rates for Six Mice. The y-axis is the recorded expert hit rates. The x-axis is session days. Each set of colored dots represents the daily expert Hit Rates for a single mouse. The slope of each line represents the rate of change for the expert Hit Rates of a single mouse.

Figure 6A: FAR v.s. Naive Session Days

one sample t-test μmnaiveFalseAlarmRate=0.0135±0.00546, p=0.0562, n=6 mice

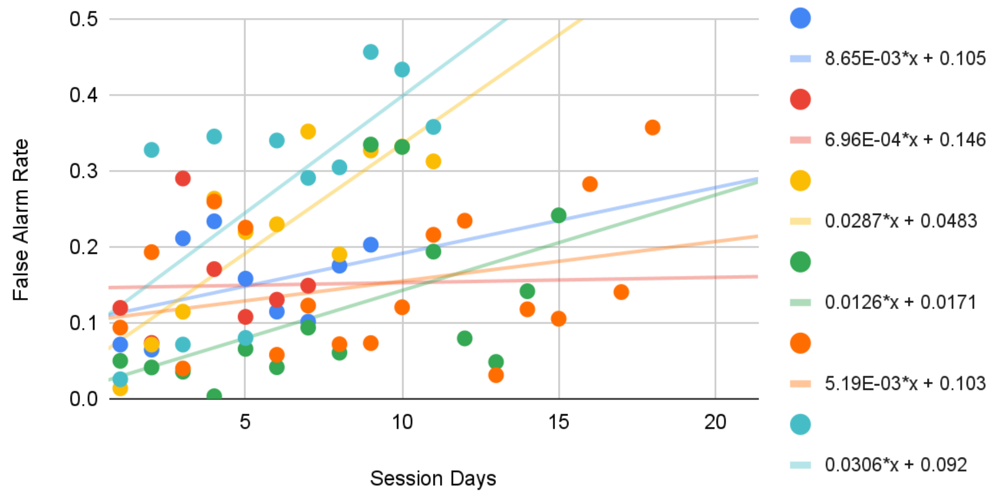


Figure 6B: FAR v.s. Expert Session Days

one sample t-test μmexpertFalseAlarmRate=-0.0587±0.0281, p=0.0910, n=6 mice

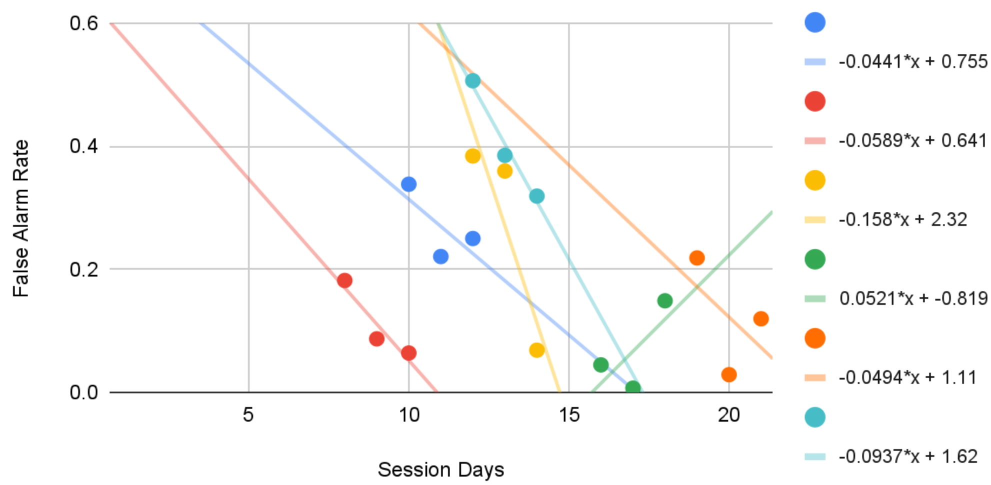


Figure 6: A. Average Rate of Change of Naïve False Alarm Rates for Six Mice. The y-axis is the recorded naïve false alarm rates. The x-axis is session days. Each set of colored dots represents the daily naïve False Alarm Rates for a single mouse. The slope of each line represents the rate of change for the naïve False Alarm Rates of a single mouse. **B.** Average Rate of Change of Expert False Alarm Rates for Six Mice. The y-axis is the recorded expert false alarm rates. The x-axis is session days. Each set of colored dots represents the daily expert False Alarm Rates for a single mouse. The slope of each line represents the rate of change for the expert False Alarm Rates of a single mouse.

Table 4: Comparison of Naïve and Expert Performance Measures for Selective Detection Whisker Task

	HR	FAR
Naïve Mean Rate of Change	0.048	0.0135
One Sample T Test P-Value	0.005	0.06
Expert Mean Rate of Change	-0.023	-0.059
One Sample T Test P-Value	0.706	0.091
Paired T-Test Between Naïve and Expert Response Rates	0.2860	0.0691

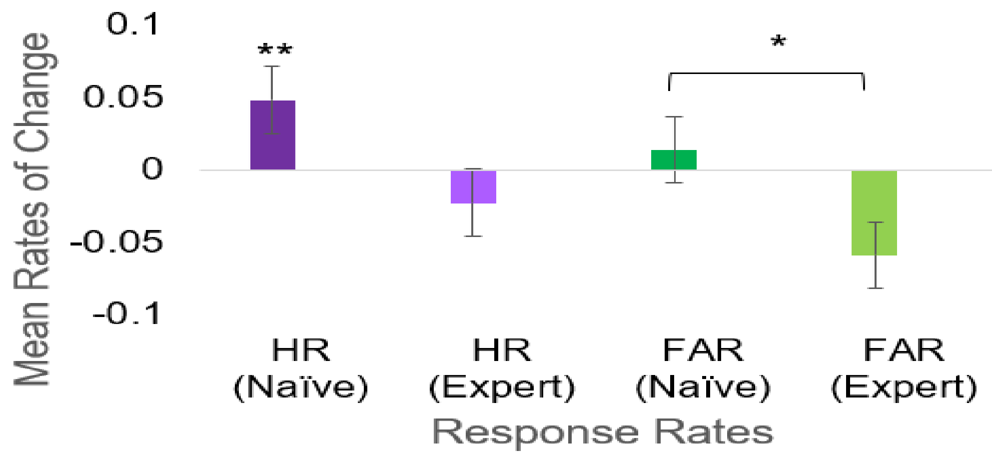
Table 4: Comparison of Naïve and Expert Performance Measures for Selective Detection Whisker Task. The middle column, going from top to bottom, has the following information: behavior type (HR), mean naïve HR rate of change, p-value originating from one sample t test for mean naïve HR rate of change value, mean expert HR rate of change, p-value originating from one sample t test for mean expert HR rate of change value, and p-value originating from paired t test comparing mean naïve HR rate of change value and mean expert HR rate of change value. The right column, going from top to bottom, has the following information: behavior type (FAR), mean naïve FAR rate of change, p-value originating from one sample t test for mean naïve FAR rate of change value, mean expert FAR rate of change, p-value originating from one sample t test for mean expert FAR rate of change value, and p-value originating from paired t test comparing mean naïve FAR rate of change value and mean expert FAR rate of change value.

Table 5: Comparison of Naïve and Expert Performance Correlations for Selective Detection Whisker Task

	Disc & HR	Disc & FAR
Naïve Mean Correlation Value	0.870	0.410
One Sample T Test P-Value	0.0000008	0.004
Expert Mean Correlation Value	0.593	0.066
One Sample T Test P-Value	0.116	0.872
Paired T-Test Between Naïve and Expert Discrimination Correlations	0.426	0.422

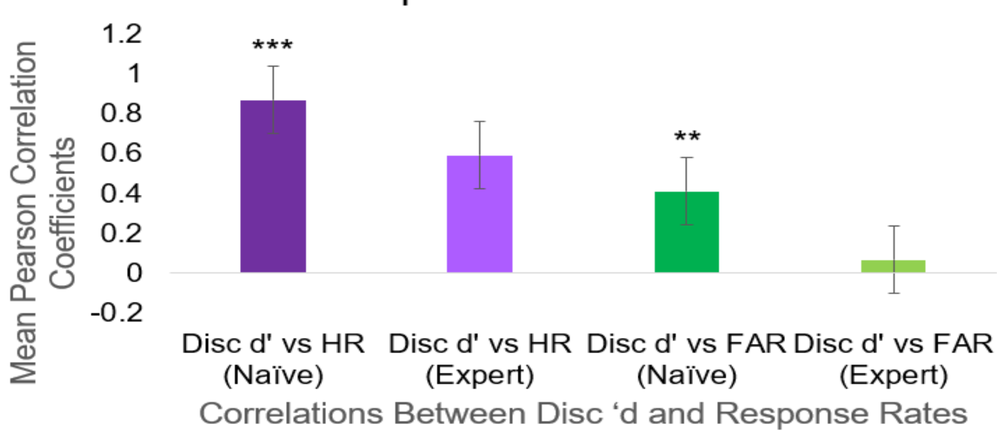
Table 5: Discrimination Correlations With Hit Rate and False Alarm Rate. The middle column contains the mean Pearson correlation coefficient for naïve Disc & HR and its p-value (one sample t test for the mean naïve Disc & HR). The middle column also contains the mean Pearson correlation coefficient for expert Disc & HR and its p-value (one sample t test for the mean expert Disc & HR). Lastly, in the middle column, the result of a paired test between the naïve and expert mean Pearson correlation values for Disc & HR is provided. The right column contains the mean Pearson correlation coefficient for naïve Disc & FAR and its p-value (one sample t test for the mean naïve Disc & FAR). The right column also contains the mean Pearson correlation coefficient for expert Disc & FAR and its p-value (one sample t test for the mean expert Disc & FAR). Lastly, in the right column, the result of a paired test between the naïve and expert mean Pearson correlation values for Disc & FAR is provided.

Figure 7A: Mean Rate of Change of Response Rates During Naïve and Expert Periods



* p<0.05, ** p<0.01, *** p<0.0001

Figure 7B: Correlations Between Disc d’ and Response Rates During Naïve and Expert Periods



* p<0.05, ** p<0.01, *** p<0.0001

Figure 7: A. Mean Rate of Change of Response Rates During Naïve and Expert Periods. The y-axis is the mean rate of change for naïve Hit Rate, expert Hit Rate, naïve False Alarm Rate, and expert False Alarm Rate. The x-axis categorically lists out the behavioral measures being analyzed (naïve Hit Rate, expert Hit Rate, naïve False Alarm Rate, and expert False Alarm Rate). Asterisks above any column representing the mean rate of change value for a behavioral measure indicates significance (one sample t-test). **B.** Correlations Between Discrimination d' and Response Rates During the Naïve and Expert Periods. The y-axis is the mean Pearson correlation coefficient value for naïve Discrimination d' vs naïve Hit Rate, expert Discrimination d' vs expert Hit Rate, naïve Discrimination d' vs naïve False Alarm Rate, and expert Discrimination d' vs expert False Alarm Rate. The x-axis categorically lists out the correlations of behavioral measures being analyzed (naïve Discrimination d' vs naïve Hit Rate, expert Discrimination d' vs expert Hit Rate, naïve Discrimination d' vs naïve False Alarm Rate, and expert Discrimination d' vs expert False Alarm Rate). Asterisks above any column representing the mean Pearson correlation coefficient between two behavioral measures indicates significance (one sample t-test).

Chapter 5: Characterization of Response Selection Behaviors During the Naïve and Expert Periods

Introduction

Building off of the findings from chapter 4, we next sought to determine any significant relationships between behavioral measures and response rates during the naïve and expert periods. In this chapter, we analyze the relationships and changes in behavioral mechanisms (Target Detection, Distractor Detection, Pretrial Spontaneous Rate) and response rates (False Alarm Rate and Hit Rate) during the naïve and expert periods with comparison analyses. We expect that all three behavioral mechanisms (target detection, false alarm rate, and pretrial spontaneous rate) will be significantly correlated with naïve behaviors during the naïve period (the mice will lick in an uncontrollable manner initially). We also expect expert mice will show significantly elevated target detection (stimulus-detection behavioral mechanism) and subdued pretrial spontaneous rate (spontaneous behavioral mechanism). Given these expectations, we test the hypothesis that naïve and expert period correlations between behavioral mechanisms and response rates will significantly differ from each other.

Methods

In this chapter, we used the following tests to analyze the relationships and changes in Target Detection, Distractor Detection, Pretrial Spontaneous Rate, False Alarm Rate, and Hit Rate across all session days: Linear Regression, Pearson Correlation Coefficient, and

One Sample t-tests. Linear regression analyses were used to determine slopes of behavioral mechanisms (Target Detection, Distractor Detection, and Pretrial Spontaneous Rate) across sessions per mouse (Figures 3,4); the slopes of individual linear regressions for each behavioral mechanism were averaged to determine mean linear slopes for the behavioral mechanism. If the mean linear slope for a behavioral mechanism across mice was significantly positive, the behavioral variable was identified as 'increasing'. In contrast, if the mean linear slope for a behavioral mechanism across mice was significantly negative, the behavioral variable was identified as 'decreasing'. Pearson correlation coefficient tests were used to determine levels of association between various behavioral variables during all session days. Reported correlations are calculated from the mean correlation using the individual correlations from each mouse. All mean values reported as the mean ± standard error of the mean (SEM).

Results

This chapter examines the nature of behavioral mechanisms during the naïve and expert periods, how they are correlated with naïve and expert response behaviors (Hit Rate and False Alarm Rate), and how the naïve and expert correlations differ. We study the nature of the behavioral mechanisms and their respective correlations with behaviors using one sample t tests. We use paired t-tests to study how correlations between response behaviors and behavioral mechanisms differ and change across the naïve and expert periods.

Naïve Detection and Pretrial Spontaneous Rate During Naïve Session Days

We first assessed changes in naïve Target Detection (T DP) using behavioral data from naïve session days. Naïve Target Detection significantly increased across naïve session days (Table 6, one sample t-test $\mu mNaiveTargetDetection=0.117\pm0.0375$, $p<0.05$, n=6 mice). We then assessed changes in naïve Distractor Detection (D DP) using behavioral data from naïve session days. Naïve Distractor Detection did not significantly increase across naïve session days (Table 6, one sample t-test $\mu mNaiveDistractorDetection=0.0188\pm0.0146$, $p=0.253$, n=6 mice). We then investigated changes in naïve Pretrial Spontaneous Rate (PSR) using behavioral data from naïve session days. Naïve PSR did not significantly increase across naïve session days (Table 6, one sample t-test $\mu mNaivePSR=0.0119\pm0.00594$, $p=0.101$, n=6 mice).

Naïve Target Detection and Pretrial Spontaneous Rate Correlations With Naïve Hit Rates

We investigated the correlational relationship between naïve T DP & naïve Hit Rate and the correlational relationship between naïve PSR & naïve Hit Rate across naïve session days. We hypothesized that, given that observed increases in naïve T DP are significant, naïve T DP will be positively and significantly correlated with naïve Hit Rate. We also hypothesized that, given that observed increases in naïve PSR are not significant, naïve PSR will not be significantly correlated with naïve Hit Rate.

To measure the correlational relationship between naïve Hit Rate and naïve Target Detection, we first determined the mean naïve Hit Rate and naïve Target Detection correlation coefficient using behavioral data from naïve session days (individual data for each mouse not shown). We found that the correlation between naïve Target Detection and naïve Hit Rate was positive and significant (Table 7, one sample t-test $\mu_{mNaiveHR\&NaiveT\ DP\ corr} = 0.835 \pm 0.0351$, $p < 0.00005$, n=6 mice). To measure the correlational relationship between naïve Hit Rate and naïve PSR, we determined the mean naïve PSR and naïve Hit Rate correlation coefficient using behavioral data from naïve session days (individual data for each mouse not shown). We found that the correlation between naïve PSR and naïve Hit Rate was positively significant (Table 7, one sample t-test $\mu_{mNaiveHR\&NaivePSR\ corr} = 0.734 \pm 0.0598$, $p < 0.0005$, n=6 mice).

Naïve Distractor Detection and Pretrial Spontaneous Rate Correlations With Naïve False Alarm Rates

We investigated the correlational relationship between naïve D DP and naïve False Alarm Rate and the correlational relationship between naïve PSR and naïve False Alarm Rate across naïve session days. We hypothesized that, given that observed increases in naïve D DP are not significant, naïve D DP will not be significantly correlated with naïve False Alarm Rate. We also hypothesized that, given that observed increases in naïve PSR are not significant, naïve PSR will not be significantly correlated with naïve False Alarm Rate.

To measure the correlational relationship between naïve False Alarm Rate and naïve Distractor Detection, we first determined the mean naïve False Alarm Rate and naïve Distractor Detection correlation coefficient using behavioral data from naïve session days (individual data for each mouse not shown). We found that the correlation between naïve Distractor Detection and naïve False Alarm Rate was positive and significant (Table 7, one sample t-test μmNaiveFAR&μmNaiveD DP corr =0.244±0.0950, p<0.05, n=6 mice). To measure the correlational relationship between naïve False Alarm Rate and naïve PSR, we determined the mean naïve False Alarm Rate and naïve PSR correlation coefficient using behavioral data from naïve session days (individual data for each mouse not shown). We found that the correlation between naïve PSR and naïve False Alarm Rate was positive and significant (Table 7, one sample t-test μmNaiveFAR&μmNaivePSR corr =0.892±0.0255, p<0.000005, n=6 mice).

Expert Detection and Pretrial Spontaneous Rate During Expert Days

We first assessed changes in expert Target Detection (T DP) using behavioral data from expert session days. Expert Target Detection did not significantly decrease across expert session days (Table 6, one sample t-test μmexpertTargetDetection=-0.0592±0.139, p=0.688, n=6 mice). We then assessed changes in expert Distractor Detection (D DP) using behavioral data from expert session days. Expert Distractor Detection did not significantly increase across expert session days (Table 6, one sample t-test μmexpertDistractorDetection=0.136±0.147, p=0.398, n=6 mice). We then investigated changes in expert Pretrial Spontaneous Rate (PSR) using behavioral data from expert session days. Expert PSR did not significantly decrease across expert session days (Table 6, one sample t-test $\mu_{mexpertPSR}$=-0.0202±0.0247, p=0.452, n=6 mice).

Expert Target Detection and Pretrial Spontaneous Rate Correlations With Expert Hit Rates

We investigated the correlational relationship between expert T DP and expert Hit Rate and the correlational relationship between expert PSR and expert Hit Rate across expert session days. We tested three alternative hypotheses. Our first alternative hypothesis is that Hit Rate during the expert periods will be driven by improvements in detection of the target stimuli, as evidenced by a positive and significant correlation between Hit Rate and Target Detection. Our second alternative hypothesis is that Hit Rate during the expert periods will be driven by increases in impulsivity, as evidenced by a positive and significant correlation between Hit Rate and Pretrial Spontaneous Rate. Our final alternative hypothesis is that Hit Rate during the expert periods will be driven by both improvements in detection of the target stimuli and increases in impulsivity, as evidenced by positive and significant correlations between Hit Rate and both Pretrial Spontaneous Rate and Target Detection.

To measure the correlational relationship between expert Hit Rate and expert Target Detection, we first determined the mean expert Hit Rate and expert Target Detection correlation coefficient using behavioral data from expert session days (individual data for each mouse not shown). We found that the correlation between expert Target Detection and expert Hit Rate was positive and significant (Table 7, one sample t-test μmexpertHR&T DP corr $=0.716\pm0.141$, $p<0.005$, n=6 mice). To measure the relationship between expert Hit Rate and expert PSR across all mice, we determined the mean expert PSR and expert Hit Rate correlation coefficient using behavioral data from expert session days (individual data for each mouse not shown). We found that the correlation between expert PSR and expert Hit Rate was not significant (Table 7, one sample t-test μmexpertHR&expertPSR corr $=0.480\pm0.307$, $p=0.178$, n=6 mice).

Expert Distractor Detection and Pretrial Spontaneous Rate Correlations With Expert False Alarm Rates

We investigated the correlational relationship between expert D DP and expert False Alarm Rate and the correlational relationship between expert PSR and expert False Alarm Rate across expert session days. We tested three alternative hypotheses. Our first alternative hypothesis is that False Alarm Rate during the expert periods will be driven by changes in detection of the distractor stimuli, as evidenced by a significant correlation between False Alarm Rate and Distractor Detection. Our second alternative hypothesis is that False Alarm Rate during the expert periods will be driven by changes in impulsivity, as evidenced by a significant correlation between False Alarm Rate and Pretrial Spontaneous Rate. Our final alternative hypothesis is that False Alarm Rate during the expert periods will be driven by both changes in detection of the distractor stimuli and changes in impulsivity, as evidenced by significant correlations between False Alarm Rate and both Pretrial Spontaneous Rate and Distractor Detection.

To measure the correlational relationship between expert False Alarm Rate and expert Distractor Detection, we first determined the mean expert False Alarm Rate and expert Distractor Detection correlation coefficient using behavioral data from expert session days (individual data for each mouse not shown). We found that the correlation between expert Distractor Detection and expert False Alarm Rate was positive and significant (Table 7, one sample t-test μmexpertFAR&D DP corr =0.213±0.389, p=0.608, n=6 mice). To measure the correlational relationship between expert False Alarm Rate and expert PSR, we determined the mean expert False Alarm Rate and expert PSR correlation coefficient using behavioral data from expert session days (individual data for each mouse not shown). We found that the correlation between expert PSR and expert False Alarm Rate was positive and significant (Table 7, one sample t-test μmexpertFAR&PSR corr =0.830±0.0918, p<0.0005, n=6 mice).

Differences in Target Detection, Distractor Detection, and Pretrial Spontaneous Rate Across Naïve and Expert Periods

We compared and analyzed changes of Target Detection, Distractor Detection, and Pretrial Spontaneous Rate during the naïve and expert periods using a paired t-test. The null hypothesis is that changes in measures of detection (Target Detection and Distractor Detection) and measures of impulsivity (Pretrial Spontaneous Rate) during the naïve and expert periods do not significantly differ from each other. An alternative hypothesis is that changes in measures of detection (Target Detection and Distractor Detection) and measures of impulsivity (Pretrial Spontaneous Rate) during the naïve and expert periods do significantly differ from each other.

The results of the paired t-test for Target Detection show that changes in naïve Target Detection and changes in expert Target Detection do not differ significantly (Table 6, paired t-test μmNaiveT DP&ExpertT DP, p=0.171, n=6 mice). Additionally, the results of the paired t-test for Distractor Detection show that changes in naïve Distractor Detection and changes in expert Distractor Detection do not differ significantly (Table 6, paired t-test μmNaiveD DP&ExpertD DP, p=0.458, n=6 mice). Lastly, the results of the paired t-test for Pretrial Spontaneous Rate show that changes in naïve Pretrial Spontaneous Rate and changes in expert Pretrial Spontaneous Rate do not differ significantly (Table 6, paired t-test μmNaivePSR&ExpertPSR, p=0.273, n=6 mice).

Differences in Correlations Between Hit Rate & Target Detection, Hit Rate & Pretrial Spontaneous Rate, False Alarm Rate & Distractor Detection, & False Alarm Rate & Pretrial Spontaneous Rate Across Naïve and Expert Days

We then investigated whether the correlations between response rates (Hit Rate and False Alarm Rate) and behavioral mechanisms (Target Detection, Distractor Detection, and Pretrial Spontaneous Rate) significantly fluctuate or remain similar across the naïve and expert periods. A paired t-test was used to compare the mean naïve HR&T DP correlation coefficient and the mean expert HR&T DP correlation coefficient (Table 7). A further paired t-test was used to compare the mean naïve HR&PSR correlation coefficient with the mean expert HR&PSR correlation coefficient (Table 7). An additional paired t-test was used to compare the mean naïve FAR&D DP correlation coefficient with the mean expert FAR&D DP correlation coefficient (Table 7). A final paired t-test was used to compare the mean naïve FAR&PSR correlation coefficient with the mean expert FAR&PSR correlation coefficient (Table 7).

The results of the paired t-test comparing the correlation between naïve Target Detection and naïve Hit Rate to the correlation between expert Target Detection and expert Hit Rate show that the pair of mean correlation values do not differ significantly (Figure 8A, Table 7, paired t-test μmNaiveHR&T DPCorr v.s. μmExpertHR&T DPCorr, p=0.447, n=6 mice). The results of the paired t-test comparing the correlation between naïve Pretrial Spontaneous Rate and Naïve Hit Rate to the correlation between expert Pretrial Spontaneous Rate and expert Hit Rate show that the pair of mean correlation values do not differ significantly (Figure 8A, Table 7, paired t-test μmNaiveHR&PSRCorr v.s. μmExpertHR&PSRCorr, p=0.409, n=6 mice). The results of the paired t-test comparing the correlation between naïve Distractor Detection and Naïve False Alarm Rate to the correlation between expert Distractor Detection and expert False Alarm Rate show that the pair of mean correlation values do not differ significantly (Figure 8B, Table 7, paired t-test μmNaiveFAR&D DPCorr v.s. μmExpertFAR&D DPCorr, p=0.938, n=6 mice). The results of the paired t-test comparing the correlation between naïve Pretrial Spontaneous rate and Naïve False Alarm Rate to the correlation between expert Pretrial Spontaneous rate and expert False Alarm Rate show that the pair of mean correlation values do not differ significantly (Figure 8B, Table 7, paired t-test μmNaiveFAR&PSRCorr v.s. μmExpertFAR&PSRCorr, $p=0.565$, $n=6$ mice).

Discussion

Linear regression analysis allowed us to calculate the mean rate of change for Target Detection, Distractor Detection, and Pretrial Spontaneous Rates during the naïve session days and expert session days in mice. Naïve Target Detection significantly increased across naïve session days (Table 6). Naïve Distractor Detection and Naïve Pretrial Spontaneous Rate did not significantly increase across the naïve periods (Table 6). Expert Target Detection, expert Distractor Detection, and expert Pretrial Spontaneous Rate did not significantly increase across the expert periods (Table 6). These initial findings suggest the ability of the mice to detect target stimuli is improving during learning (during the naïve periods). It is important to address how these findings regarding changes of behavioral mechanisms impact changes in response rates during the naïve and expert periods.

In this chapter, we have shown the correlational relationships between detection, behavioral mechanisms and impulsive/sampling behavioral mechanisms with response rates. Correlational analysis shows that during the naïve periods, Hit Rate is positively and significantly correlated with target detection, and pretrial spontaneous rate. Correlational analysis also reveals that during the naïve periods, False Alarm Rate is positively and significantly correlated with distractor detection and pretrial spontaneous

Rate. These findings offer an insight into the mechanisms that drive the learning of response selection. We can conclude that detection of stimuli as well as impulsive behaviors are significant with respect to influencing observed changes in response rates and control changes in Discrimination (Table 6,7). One possible explanation for these observed correlations could be that the mice initially learn to respond to both target and distractor stimuli (which could explain the significant correlations between response rates and detection behavioral mechanisms) while also combining a strategy of licking indiscriminately (which could explain the significant correlations between response rates and the impulsive behavioral mechanism).

The correlation analysis shows that during the expert periods, the correlations between the response rates and the behavioral mechanisms change significantly. During the expert periods, we see that hit rate is positively and significantly correlated with target detection; hit rate during the expert period is not significantly correlated with pretrial spontaneous rate. We also see that during the expert period, False Alarm Rate is positively and significantly correlated with pretrial spontaneous rate; False Alarm Rate during the expert period is not significantly correlated with Distractor Detection.

Paired t-test analysis shows that correlations between response rates and behavioral mechanisms do not significantly differ between the naïve and expert periods. Considering these findings, combined with information regarding significance of specific correlations during the naïve and expert periods, we make summarize and make the following conclusions:

1. During the naïve periods, both detection and impulsivity behavioral mechanisms are significant contributors in driving increases in Discrimination.
2. During the expert periods, target detection specifically and significantly drives changes in expert Hit Rate while Pretrial Spontaneous Rate specifically and significantly drives expert changes in False Alarm Rate.
3. Looking at the correlations between naïve and expert periods, we see that in the case of the correlation between Hit Rate and target detection and the correlation between False Alarm Rate and Pretrial Spontaneous Rate, their correlation strength decreases but not enough to a value that is insignificant.
4. In the case of the correlational differences between Hit Rate and Pretrial Spontaneous Rate and the correlation between False Alarm Rate and Distractor Detection across the naïve and expert periods, the correlations weaken going from the naïve to the expert period, so much so that they lose their significance.

Figures

Table 6: Comparison of Naïve and Expert Detection and Spontaneous Behavioral Mechanisms

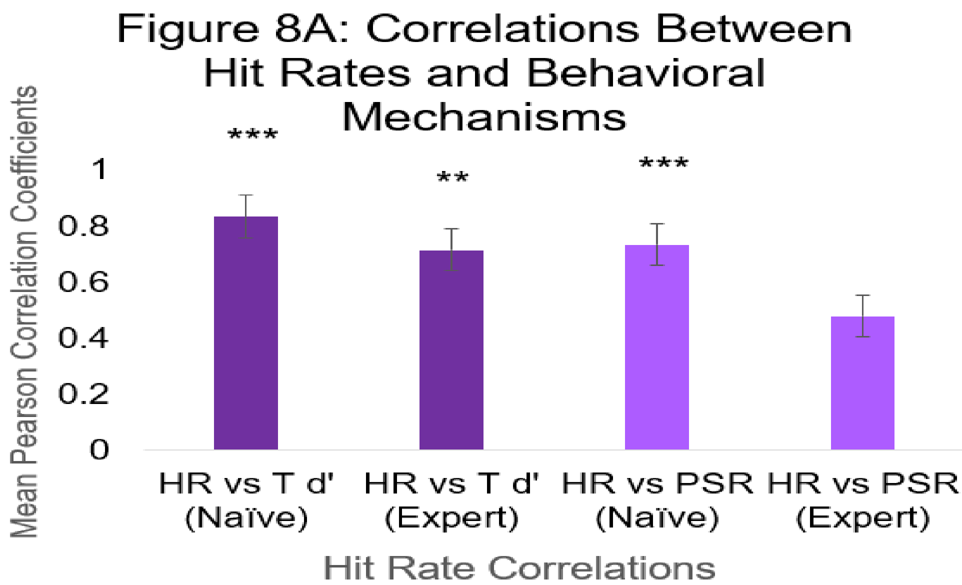
	Target Detection	Distractor Detection	Pretrial Spontaneous Rate
Naïve Mean	0.117	0.0188	0.0119
One Sample T-Test P-Value for Naïve Mean	0.0264	0.253	0.101
Expert Mean	-0.0592	0.136	-0.0202
One Sample T-Test P-Value for Expert Mean	0.688	0.398	0.452
Paired Sample T-Test (Naïve & Expert)	0.171	0.458	0.273

Table 6: Comparison of Naïve and Expert Detection and Spontaneous Behavioral Mechanisms

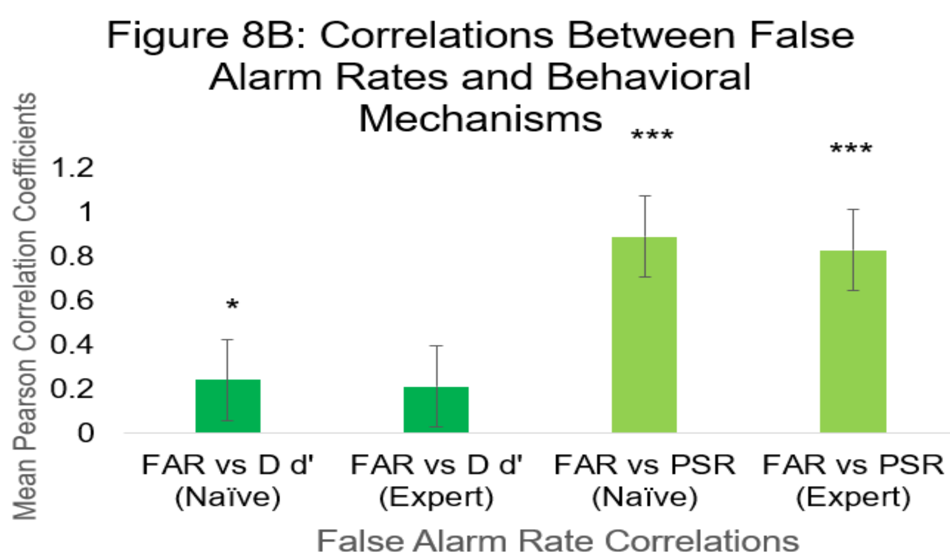
Table 7: Comparison of Naïve and Expert Performance Correlations for Selective Detection Whisker Task

	HR & T DP	HR & PSR	FAR & D DP	FAR & PSR
Naïve Mean Correlation Value	0.835	0.734	0.244	0.892
One Sample T-Test P-Value for Naïve Mean Correlation Value	0.000002	0.00006	0.049	0.0000004
Expert Mean Correlation Value	0.716	0.480	0.213	0.830
One Sample T-Test P-Value for Expert Mean Correlation Value	0.004	0.178	0.608	0.0003
Paired T-Test P Value (Naïve & Expert)	0.445	0.409	0.938	0.565

Table 7: Comparisons of Naïve and Expert Response Rates and Behavioral Mechanism Correlations.



* p<0.05, ** p<0.01, *** p<0.0001



* p<0.05, ** p<0.01, *** p<0.0001

Figure 8: A. Correlations Between Hit Rates and Behavioral Mechanisms. The y-axis is the mean Pearson correlation coefficient value for naïve Hit Rate vs naïve Target Detection, expert Hit Rate vs expert Target Detection, naïve Hit Rate vs naïve Pretrial Spontaneous Rate, expert Hit Rate vs expert Pretrial Spontaneous Rate. The x-axis categorically lists out the correlations of behavioral measures being analyzed (naïve Hit Rate vs naïve Target Detection, expert Hit Rate vs expert Target Detection, naïve Hit Rate vs naïve Pretrial Spontaneous Rate, expert Hit Rate vs expert Pretrial Spontaneous Rate). Asterisks above any column representing the mean Pearson correlation coefficient between two behavioral measures indicates significance (one sample t-test). **B.** Correlations Between False Alarm Rates and Behavioral Mechanisms. The y-axis is the mean Pearson correlation coefficient value for naïve False Alarm Rate vs naïve Distractor Detection, expert False Alarm Rate vs expert Distractor Detection, naïve False Alarm Rate vs naïve Pretrial Spontaneous Rate, expert False Alarm Rate vs expert Pretrial Spontaneous Rate. The x-axis categorically lists out the correlations of behavioral measures being analyzed (naïve Hit Rate vs naïve Target Detection, expert Hit Rate vs expert Target Detection, naïve Hit Rate vs naïve Pretrial Spontaneous Rate, expert Hit Rate vs expert Pretrial Spontaneous Rate). Asterisks above any column representing the mean Pearson correlation coefficient between two behavioral measures indicates significance (one sample t-test).

Chapter 6: Target Reaction Times During All Session Days, Naïve Days, and Expert Days

Introduction

As mentioned in chapter 1, one traditional way of measuring strength of response selection is through analysis of reaction times. Shorter reaction times are associated with mastery of response selection as a cognitive strategy. Previous research has yet to study whether reaction times improve simultaneously or separately with the learning of response selection. In this chapter, we will look at target reaction times during three periods of time: across all session days, during the naïve periods, and during the expert periods. We also analyze the correlations between target reaction time and discrimination during the three periods of time mentioned in the previous sentence. The null hypothesis we establish and test is that as Discrimination changes with learning of the task (the learning of response selection), target reaction time will not improve simultaneously and subsequently not reflect a response selection cognitive approach. An alternative hypothesis predicts that as Discrimination changes with learning of the task (the learning of response selection), changes in target reaction time will improve simultaneously and reflect a response selection cognitive approach. Additionally, for analyses comparing correlations between target reaction time and discrimination during the naïve and expert periods, we establish and test the null hypothesis that target reaction time and their correlations with Discrimination during the naïve and expert periods will not significantly differ. An alternative hypothesis is that changes in target reaction times and their correlations with Discrimination during the naïve periods will reveal that improvements in target reaction time coincide with the learning of response selection during the naïve days (learning days). An alternative hypothesis is that changes in target reaction times and their correlations with Discrimination during the expert periods will reveal that improvements in target reaction time do not coincide with the learning of response selection during the expert days (mastery days). Generally, if target reaction time improves with the learning response selection simultaneously, we expect to see target reaction time be negatively and significantly correlated with Discrimination.

Methods

In this chapter, we used the following tests to analyze changes in target reaction time and Discrimination across all session days, during the naïve periods, and during the expert periods: Linear Regression, Pearson Correlation Coefficient, One Sample t-tests, and Paired t-tests. Linear regression analyses were used to determine slopes of target reaction time and Discrimination across sessions per mouse; the slopes of individual linear regressions for each response rate type were averaged to determine mean linear slopes for the target reaction times. If the mean linear slope for a target reaction time or Discrimination across mice was significantly positive, the trend of the behavioral variable was identified as 'increasing'. In contrast, if the mean linear slope for a target reaction time or Discrimination across mice was significantly negative, the behavioral variable was identified as 'decreasing'. Pearson correlation coefficient tests were used to determine levels of association between target reaction times and Discrimination across all session periods analyzed. Paired t-tests were used to determine whether the mean naïve and expert target reaction times differed significantly from each other. Paired t-tests were also used to determine whether the mean naïve and expert target reaction time correlations with Discrimination differed significantly from each other. Reported correlations are calculated from the mean correlation using the individual correlations from each mouse. All mean values reported as the mean ± standard error of the mean (SEM).

Results

In this final chapter, we study how target reaction time improves across learning, during the naïve periods, and during the expert periods. We expect that across learning, Target Reaction Time will show improvements as the mice learn to lick closer to the earlier portion of the lick period (time range of licking is 200 ms to 1200 ms). We also expect that Target Reaction Time will significantly decrease during the naïve periods and the expert periods. Lastly, we study to see how the correlation between Discrimination and Target Reaction Time changes across the naïve and expert periods.

Characterization of Target Reaction Time During all Session days, Naïve days, and Expert days

We then investigated whether Target Reaction Time significantly changed across all session days, during the naïve days, and during the expert days. We found that target reaction time significantly decreased across all session days (Figure 9A, 9D, one sample t-test μmT RT =-0.0272±0.00480, p<0.005, n=6 mice). We also found that Target Reaction Time significantly decreased during the naïve session days (Figure 9B, 9D, one sample t-test μmNaiveT RT =-0.0278±0.00906, p<0.05, n=6 mice). We also found that Target Reaction Time did not significantly decrease across expert session days (Figure 9C, 9D, one sample t-test μmExpertT RT =-0.0378±0.0202, p=0.121, n=6 mice).

Correlations Between Target Reaction Time and Discrimination During all Session days, Naïve days, and Expert days

We also looked at correlations between reaction times and Discrimination across all session days, across naïve days, and across their first three expert days. We found that Target Reaction Time and Discrimination were significantly and negatively correlated across all session days (Figure 9E, one sample t-test μmDiscrimination&TRT corr =-0.728±0.0588, p<0.0001, n=6 mice). We also found that Target Reaction Time and Discrimination were significantly and negatively correlated during the naïve session days (Figure 9E, Table 8, one sample t-test μmnaiveDiscrimination&TRT corr =-0.546±0.120, p<0.05, n=6 mice). We also found that Target Reaction Time and Discrimination were not significantly correlated during the expert session days (Figure 9E, Table 8, one sample t-test μmexpertDiscrimination&TRT corr =-0.0144±0.345, p=0.968 n=6 mice).

We lastly studied how the correlation between Discrimination and Target Reaction Time differed and changed between the naïve session days and the expert session days. Using a paired t-test, we compared the mean naïve Discrimination and Target Reaction Time correlation coefficient with the mean expert Discrimination and Target Reaction Time. The results of the paired t-test show that the mean naïve Discrimination and Target Reaction Time correlation coefficient and the mean expert Discrimination and Target Reaction Time are not significantly different from each other (Table 8, paired t-test µmNaiveDiscrimination&T RTCorr v.s. µmExpertDiscrimination&T RTCorr, $p=0.938$, $n=6$ mice).

Discussion

Observed Target Reaction Times and their significant changes across all session days and during the naïve session days/periods suggests that improvements in reaction times can coincide with improvements in Discrimination; target reaction times significantly decrease across all session days and during the naïve session days/periods. During the expert session days/periods, target reaction time decreases but not significantly. This approach and analyses are an upgrade to traditional analyses using reaction times as a means to measure response selection specifically. To test whether improvements in target reaction time actually is dependent on learning of response selection as a cognitive strategy, we carried our Pearson correlation coefficient tests between Discrimination and Target Reaction Times during naïve periods, expert periods, and across all session days.

Target Reaction Time and Discrimination were negatively and significantly correlated across all session days and during the naïve session days/periods (Table 8). Target Reaction Time and Discrimination were not significantly correlated during the expert session days/periods. These changes in target reaction time are consistent with previous studies looking into order of learning during Go/No-go tasks. Previous research has found that improvements in reaction times generally precede improvements in Discrimination (Marrero et al., 2023). This localization of significant decreases in target reaction time during the naïve period provides new direction with regards to how current research studying response selection is carried out. Most research utilizing reaction times as a means to measure response selection (where shorter reaction times equates to significant usage of response selection), averages the reaction times recorded for all trials presented during any task. This fails to account for how reaction times change across learning and more generally leaves out any information regarding trends in reaction time that can exist during specific time frames.

Figures

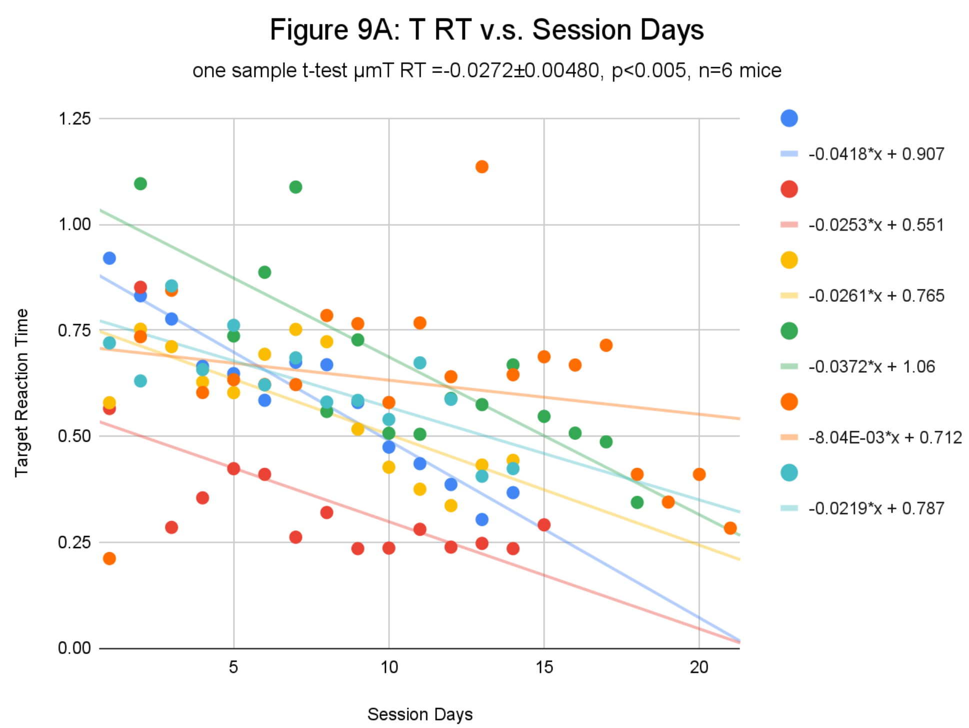


Figure 9A: T RT v.s. Session Days
one sample t-test μmT RT =-0.0272±0.00480, p<0.005, n=6 mice
Target Reaction Time
1.25
1.00
0.75
0.50
0.25
0.00
5
10
15
20
Session Days
-0.0418*x + 0.907
-0.0253*x + 0.551
-0.0261*x + 0.765
-0.0372*x + 1.06
-8.04E-03*x + 0.712
-0.0219*x + 0.787

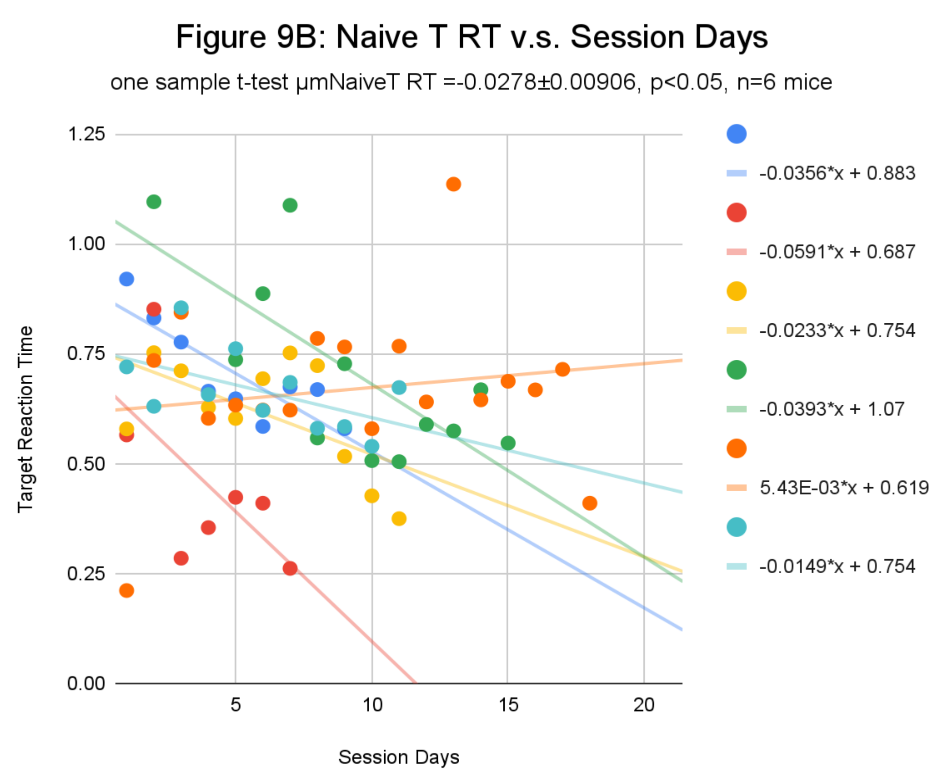


Figure 9B: Naive T RT v.s. Session Days
one sample t-test μmNaiveT RT =-0.0278±0.00906, p<0.05, n=6 mice
Target Reaction Time
1.25
1.00
0.75
0.50
0.25
0.00
5
10
15
20
Session Days
-0.0356*x + 0.883
-0.0591*x + 0.687
-0.0233*x + 0.754
-0.0393*x + 1.07
5.43E-03*x + 0.619
-0.0149*x + 0.754

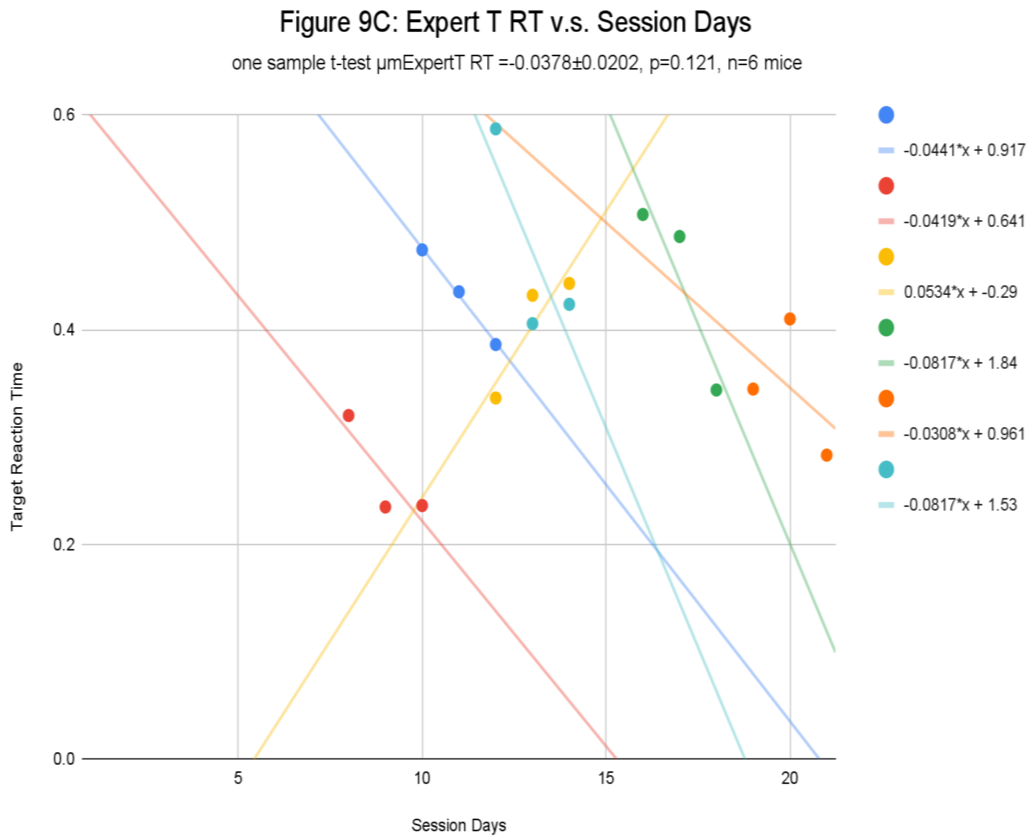


Figure 9C: Expert T RT v.s. Session Days
one sample t-test μmExpertT RT =-0.0378±0.0202, p=0.121, n=6 mice
Target Reaction Time
Session Days
0.6
0.4
0.2
0.0
5
10
15
20
-0.0441*x + 0.917
-0.0419*x + 0.641
0.0534*x + -0.29
-0.0817*x + 1.84
-0.0308*x + 0.961
-0.0817*x + 1.53

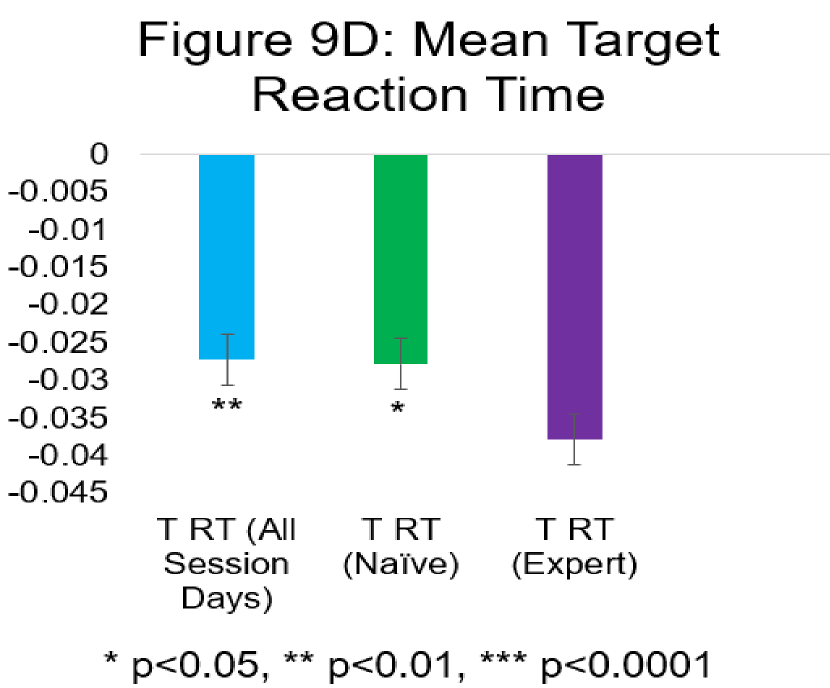
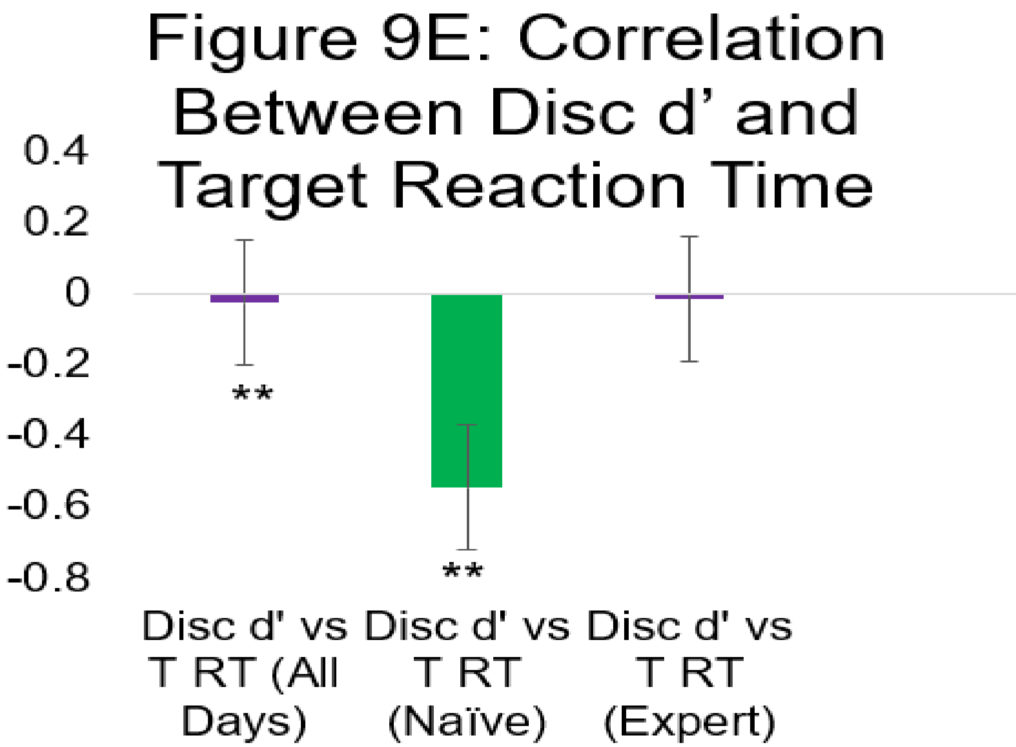


Figure 9D: Mean Target Reaction Time
0
-0.005
-0.01
-0.015
-0.02
-0.025
-0.03
-0.035
-0.04
-0.045
**
*
T RT (All Session Days)
T RT (Naïve)
T RT (Expert)
* p<0.05, ** p<0.01, *** p<0.0001



* p<0.05, ** p<0.01, *** p<0.0001

Figure 9: A. Average Rate of Change of Target Reaction Time for Six Mice. The y-axis is the recorded target reaction times. The x-axis is session days. Each set of colored dots represents the daily target reaction times for a single mouse. The slope of each line represents the rate of change for the target reaction times of a single mouse. **B.** Average Rate of Change of naïve Target Reaction Time for Six Mice. The y-axis is the recorded naïve target reaction times. The x-axis is naïve session days. Each set of colored dots represents the daily naïve target reaction times for a single mouse. The slope of each line represents the rate of change for the naïve target reaction times of a single mouse. **C.** Average Rate of Change of expert Target Reaction Time for Six Mice. The y-axis is the recorded expert target reaction times. The x-axis is expert session days. Each set of colored dots represents the daily expert target reaction times for a single mouse. The slope of each line represents the rate of change for the expert target reaction times of a single mouse. **D.** Mean Target Reaction Time. The y-axis is the mean rate of change for Target Reaction Time across all session days, Target Reaction Time during the naïve periods, and Target Reaction Time during the expert periods. The x-axis categorically lists out the behavioral measures being analyzed (Target Reaction Time across all session days, Target Reaction Time during the naïve periods, and Target Reaction Time during the expert periods). Asterisks above any column representing the mean rate of change value for a behavioral measure indicates significance (one sample t-test). **E.** Correlation Between Discrimination d' and Target Reaction Time. The y-axis is the mean Pearson correlation coefficient value for Discrimination d' vs Target Reaction Time across all session days, naïve Discrimination d' vs naïve Target Reaction Time, and expert Discrimination d' vs expert Target Reaction Time. The x-axis categorically lists out the correlations of behavioral measures being analyzed (Discrimination d' vs Target Reaction Time across all session days, naïve Discrimination d' vs naïve Target Reaction Time, and expert Discrimination d' vs expert Target Reaction Time). Asterisks above any column representing the mean Pearson correlation coefficient between two behavioral measures indicates significance (one sample t-test).

Table 8: Comparison of Naïve and Expert Correlations Between Discrimination and Target Reaction Time

	Disc & T RT
Naïve Mean Correlation Value	-0.546
One Sample t-test P-Value for Naïve Mean Correlation Value	0.006
Expert Mean Correlation Value	-0.0144
One Sample t-test P-Value for Expert Mean Correlation Value	0.968
Paired t-test (between Naïve and Expert Mean Correlations)	0.239

Table 8: Comparison of Naïve and Expert Correlations Between Discrimination and Target Reaction Time. The right column, going from top to bottom, has the following information: correlation (Discrimination & Target Reaction Time), mean naïve Disc & T RT correlation value, p-value originating from one sample t test for mean naïve Disc & T RT correlation value, mean expert Disc & T RT correlation value, p-value originating from one sample t test for mean expert Disc & T RT correlation value, and p-value originating from paired t test comparing mean naïve Disc & T RT correlation value and mean expert Disc & T RT correlation value.

Chapter 7: Conclusions and Future Direction

Throughout the previous chapters, we have studied and reviewed response selection with respect to how it is presented in the behavior of our mice. We have been able to identify response selection as being the cognitive strategy used by our mice. We have been able to show that response selection is characterized by observed increases in Hit Rates. We have also shown that response inhibition is not the strategy being utilized as evidenced by observed increases in False Alarm Rates. We have been able to determine which behavioral mechanisms drive these observed increases in response rates with Hit Rate being driven by changes in target-detection and impulsivity and False Alarm Rate being driven by changes in impulsivity. Furthermore, we have been able to show that response selection is learned early before the mice become masters at the task. We have been able to show that response selection behaviors are driven by both stimulus detection and impulsivity during the naïve periods. Subsequently, we have been able to show that during the expert periods, Hit Rate is only driven by detection and False Alarm Rate is driven by only impulsivity. Lastly, we have been able to show that target reaction times improve simultaneously with the learning of response selection. These findings relating to response selection were determined using only behavioral data. However, it is important for us to remember that all behaviors exhibited by our mice are generated because of neuronal activity in various different regions of the brain.

Cortical Regions and Neural Activity Studies

The brain is divided up into various different regions and each region generally is associated with some type of process. The regions control functions such as movement, thought, learning, cognition, memory, senses, and many other body-related functions (Batista-García-Ramó & Fernández-Verdecia, 2018). Previous studies had studied how neural activity fluctuates in subjects concurrently executing behaviors (Aruljothi et al., 2020). As a means to further better understand response selection and how it is executed in subjects completing behavioral tasks, we suggest and recommend that neural studies be conducted on mice completing our task with particular focus on the area of the brain called the cerebral cortex.

The cerebral cortex is a region in mammalian brains containing many different subregions such as the neocortex and dorsolateral striatum areas. These areas are known to control specific bodily functions and cognitive processes such as decision making (Zareian et al., 2023). Within the neocortex, there are neocortical areas called the primary motor cortex and somatosensory cortex. Primary motor cortex controls motor behaviors by sending signals to muscles that are needed to execute a specific behavior or behaviors (Teka et al., 2017). Somatosensory cortex is responsible for processing sensory inputs and then relay those inputs as sensorimotor signals to other parts of the brain such as the motor cortex and the dorsolateral striatum. When the somatosensory cortex sends sensory input information to the motor cortex, the motor cortex can then send signals to various muscles and other anatomical structures that control movement (Borich et al., 2015, Teka et al., 2017). Previous studies have shown that whisker stimulus responses can be directed from the somatosensory cortex and into the dorsolateral striatum. Furthermore, some studies have found that suppressing the activity of the dorsolateral striatum in mice completing a two paddle whisker detection task impedes the ability of mice to respond to task-relevant stimuli (Zareian et al., 2023). New and previous knowledge regarding how all these areas work together to control sensorimotor transformations has led researchers to highlight the importance of studying neural activity occurring in these areas when mice are completing Go/No-Go tasks (Aruljothi et al., 2020; Marrero et al., 2022). Recent studies have utilized neural activity recording techniques such as widefield calcium imaging to study neural activity occurring in these areas (primary motor cortex, primary somatosensory cortex, dorsolateral striatum) when mice are completing our two paddle whisker detection task (Aruljothi et al., 2020).

Widefield calcium imaging is a relatively new but effective tool in studying how different brain regions become active or suppressed when subjects are experiencing sensation, carrying out motor movements, and/or other brain-dependent functions (Aruljothi et al., 2022; Nietz et al., 2022). Widefield calcium imaging utilizes specialized emission-fluorescence detecting cameras that can detect changes in calcium levels in the organs of subjects that have genetically encoded calcium indicators (Nietz et al., 2022). In the context of studying neural activity, mice that have their skulls exposed and are genetically modified to express genetically encoded calcium indicators can use the previously mentioned specialized cameras to study changes in calcium levels in the brain

(Aruljothi et al., 2022; Nietz et al., 2022). Fluctuations in calcium levels in the brain are interpreted to determine which brain areas become activated or suppressed during the detection of stimuli and the execution of motor functions.

Neural and Behavioral Correlates

Considering the technology we have access to that can study neural activity (e.g. widefield calcium imaging), the final step that can be taken to thoroughly describe and characterize response selection and response inhibition as cognitive strategies is to correlate neural data with behavioral data. For example, if widefield calcium imaging is used on mice completing our task, assuming that the behaviors of the mice are also being recorded, we can determine which brain regions (e.g. primary motor cortex, primary somatosensory cortex, dorsolateral striatum) are active or suppressed when the mice are detecting the paddles and when they are executing licking behaviors (Aruljothi et al., 2020; Nienborg & Cumming, 2010). We can also determine if different brain regions work together in processes such as signal propagation (e.g. when a mouse detects a paddle, do we see the detection of paddle get encoded in primary somatosensory cortex and then relayed to dorsolateral striatum or primary motor cortex to induce licking). With the support of neural data from neural detecting techniques combined with behavioral data, we can then begin to ask new questions that relate response selection and response inhibition (e.g. how does neural activity in specific brain regions change with the learning and mastery of response selection and response inhibition). Furthermore, studying correlations between behavior and neural activity can serve as a means to better understand response selection and response inhibition in populations with behavioral disorders such as ADHD (Wilens & Spencer, 2010). Overall, we suggest and recommend that the combination of studying neural activity with behaviors can provide additional insights regarding the learning of response selection and response inhibition as cognitive strategies.

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