UC Riverside

UCR Honors Capstones 2022-2023

Title

Validation Of Selective Detection Task And The Role Of Whisker Related Cortices In Corresponding Sensory-motor Processes

Permalink

https://escholarship.org/uc/item/9rk880jt

Author

Kaur, Emaan   Kaur

Publication Date

2023-06-10

VALIDATION OF SELECTIVE DETECTION TASK AND THE ROLE OF WHISKER

RELATED CORTICES IN CORRESPONDING SENSORY-MOTOR PROCESSES

By
Emaan Kaur
Contributors: Krithiga Aruljothi and Lovleen Swatch
A capstone project submitted for graduation with University Honors
February 16, 2023

University Honors
University of California, Riverside

APPROVED

Dr. Edward Zagha
Department of Psychology

Dr. Richard Cardullo, Howard H Hays Jr. Chair
University Honors

ABSTRACT

Previous studies have demonstrated that primary and secondary motor cortices have a "tutoring" role in learning and executing motor skills, however the process of how the whisker motor cortex (wMC) contributes in learning sensory-motor processes such as sensory selection is not completely understood. To further investigate this, we developed a go/no-go operant whisker detection task in which mice learn to respond following a transient target whisker deflection. We will use signal detection theory to distinguish target from distractor detection. To validate the whisker dependency of this task, we performed a preliminary experiment where there was no manipulation of the mice while performing the said task in complete darkness. After mice reached expert performance, their whiskers were trimmed, after which the task performance declined. This leads us to the conclusion that the task is indeed whisker dependent. There are three possibilities that the wMC may be tutoring the sensory-motor discrimination process: wMC is not contributing to learning the discrimination process, wMC is required for stimulus detection, or wMC is required for stimulus discrimination but not detection. To control for reversible behavioral changes through learning, we will chronically lesion wMC with ibotenic acid and after the mice have learned the task, we will observe changes in the behavioral performance with behavioral measures such as hit rate, false alarm rate, and d' (discriminability index) across learning. Exploring the learning outcomes involved in the selection process can help us further understand impairments in learning trajectories, such as in attention deficit hyperactivity disorder.

ACKNOWLEDGEMENTS

TABLE OF CONTENTS

INTRODUCTION

Stimulus detection is an everyday occurrence. The Triesman attenuation theory (Figure 1) allows for understanding this phenomenon as it explains that both attended and unattended signals enter short-term storage: responses to attended stimuli propagate forward for higher-order processing while responses to unattended stimuli are suppressed by an attenuating filter at some point along the processing stream (Treisman, 1964). This theory was initially formulated in order to understand selection amongst conflicting speech patterns and has been adapted to study sensory selection across multiple sensory modalities and species (Moran and Desimone, 1985; Wiederman and O'Carroll, 2013; Sridharan et al., 2014).

It has previously been proven that the whisker motor cortex is a site of attenuation of distractor sensory signal propagation (Aruljothi 2020), however the process of how the whisker motor cortex (wMC) contributes to the sensory selection process is not completely understood. This area of the cortex has been studied broadly in terms of whisking, including set-point, initiation, and amplitude modulation but it is unknown how the whisker motor cortex "tutors" the discrimination process. Other studies have also been conducted in this topic and demonstrate that wMC is required for learning but not for executing learned motor skills (Kawai, 2015). Researchers have also tested and confirmed the hypothesis that the whisker motor cortex is partially involved in learning to discriminate between target and stimulus which further inhibits distractor sensory-motor propagation in expert mice but is essentially involved in naïve mice (Rizzolatti et al., 1987, Moore and Fallah, 2001; Moore and Armstrong, 2003).

Validating Go/No-go Selective Whisker Detection Task

In order to validate our go/no-go selective whisker detection task and determine if it is whisker dependent, we conducted a preliminary experiment where there was no manipulation to the mice and lights were turned off inside and outside the behavioral training room so the mice were in complete darkness. We also covered the behavior apparatus with a box with black covers in order to eliminate any sensory distractions. Three mice were trained in this environment and whiskers were trimmed under anesthesia after d'≥1 for 3 consecutive days. D' values were high while the whiskers were intact and went down post whiskers trim. Hit rate was also high until whiskers were trimmed and went down post whiskers trim. There are some high rates post whiskers trim which can be explained by the whiskers growing back. False alarm rate had a similar pattern as hit rate where it was high before the whiskers were trimmed and decreased post whisker trim. Due to this, we can conclude that the task is indeed whiskers dependent though mice might be using multiple sensory modalities to perform the task once the stimulus-reward association has been formed. We then developed experiments to understand the role of whisker motor cortex (wMC) in sensory-motor processes of the task. It also was noted that post whiskers trimming, mice might resort to sampling.

Chronic lesioning of a cortical area to understand its role in learning

The motor cortex, in accordance with its ability to amplify and suppress sensory responses, plays a key role in learning sensory-motor processes such as sensory selection. Revealing these changes in context are possible by lesioning and localizing the area of interest either chronically or acutely. Lesions made with conventional techniques such as aspiration, electrolytic, or thermocoagulation have been proven to damage, not just the area of interest but

adjacent areas as well (Gratton 2012) which can lead to changes in behavioral performance (Bell & Bultitude, 2018). To achieve better localization, psychoactive drugs such as Ibotenic acid, an excitotoxin, can be used. In the lesioning experiments described later in this paper, Ibotenic acid (IBO), a glutamate receptor agonist, is used as excitotoxins are structurally similar to glutamate and therefore the most effective compounds to create lesions of neurons without damage to the fibers of passage. This is because the glutamate receptors are present in the soma, and not the axonal portion of neurons, which helps to decrease the strength of synaptic transmission (Jarrard, 1989).

In this study, we train chronically lesioned mice in our task. We use signal detection theory to distinguish target from distractor expectation and observe changes in the behavioral performance with behavioral measures such as hit rate, false alarm rate, and d' (discriminability index) across learning. Exploring the learning outcomes involved in the selection process can help us further understand impairments in learning trajectories, such as in attention deficit hyperactivity disorder.

MATERIALS AND METHODS

Experimental Animals

All experiments occurred at the University of California, Riverside and followed US National Institutes of Health guidelines for animal research, under an animal use protocol approved by the Institutional Animal Care and Use Committee and Office of Research Integrity at the University of California, Riverside. Mice were purchased from Jackson Laboratories (JAX). We used both male and female wildtype mice in these experiments. Mice were housed on a light cycle of 12 hours light/12 hours dark to create an optimal environment and minimize stress as studies have shown that in mice, chronic psychosocial stress leads to depression-relevant behavior, including decreased motivation for reward (Grandjean et al. 2016,) which is something we would like to avoid in our experiments. All training was conducted on mice head-fixed in a behavioral apparatus via a headpost.

Surgical Procedure

For headpost implantation, 2 to 5 months old mice were placed under a combination of isoflurane (1-2%), ketamine (100 mg/kg), and xylazine (10 mg/kg) anesthesia. Once immobile, the mice were laid in a prone position and an isoflurane nose cone supplied by an isoflurane vaporizer was placed on their nose to maintain anesthesia. A 10 mm x 10 mm piece of scalp was then resected to expose the skull and connective tissue was removed from the exposed skull. We selected one group of mice for the Ibotenic Acid (IBO) lesions and one group as a control. Burr hole craniotomies were conducted over wMC (1 mm lateral, 1 mm anterior from bregma) of about ~500 um diameter (Zareian et al., 2021). 200 nL of saline (sham) was injected in the control mice and 200 nL of IBO was injected in the experimental mice bilaterally via Nanoject

III Programmable Nanoliter injector (Drummond Scientific Company) in each of layers 2/3 and 5 of wMC (Hooks et al., 2013). Then, a custom built, lightweight titanium/stainless steel headpost (3 cm in length and 1.5 grams in weight) was implanted onto the skull with cyanoacrylate gap-filling glue to both seal the exposed skull and enhance skull transparency. The headpost has an 8 mm x 8 mm central window for imaging and recording, which was not used during behavioral training. Silicone elastomer (Reynolds Advanced Materials) was additionally applied on the central window of the headpost. After surgery, the mice were placed onto a heating pad to recover. They were administered Meloxicam (0.3 mg/kg) and Enrofloxacin (5 mg/kg) for three days postoperatively. Mice were given at least three days to recover from the surgery before proceeding with water-restriction, habituation, and behavioral training. The mice also received postoperative care to fully recover from the cranial window surgery and headbar attachment.

Go/No-Go Whisker Selective Detection Task

After undergoing surgery, the mice went through a handling phase, habituation phase, and a pre-training phase. Mice were handled for about 5 minutes each day for a period of up to three days to acclimate the mice to the experimenter to prevent the mice from feeling stressed during the handling involved with the experimental setup. By the end of the handling phase, the mice become accustomed to the experimenter, and are ready to move on to the habituation phase.

Habituation is a process where mice are exposed to repeated stimuli so eventually their response to that stimuli is minimized (Leussis 2006). In this case, we wanted to habituate the mice to certain parts of our procedure that could cause stress, such as removing them from their cages or placing them in the behavior apparatus. For three days, about 15 minutes per session,

the mice were placed in the behavior rig for habituation to the soundproof chamber and behavioral apparatus. During these habituation sessions, mice were introduced to the head restraint and behavioral apparatus, including the lickport that dispenses water. Upon starting habituation, water restriction would also begin. The water deprivation during habituation is implemented to motivate mice to lick and seek reward once the training phase begins. Mice were restricted to a minimum of 1 mL of water a day and given food *ad libitum*. Weights of the mice were recorded on a daily basis to maintain at least 85% of their initial post surgery weights. Additional water and/or food was given as needed to maintain this level.

After this, all mice were trained in a Go/No-Go passive whisker selective detection task (Figure 2). The behavioral apparatus used in this task was controlled by Arduino and custom MATLAB (MathWorks) code. Piezo-controlled paddles (Physik Instrumente and Piezo) were placed bilaterally in the whisker fields, with each paddle contacting the whiskers of the mice. The paddle deflections had rising phases that ranged from 0.1 s (for large deflections) to 0.01 s (for small deflections), followed by an immediate falling phase. Stimulus duration and amplitude were varied with training with the goal of maintaining a 75% hit rate. This target hit rate was selected in order to maintain high reward rates while still operating within the dynamic range of each mouse's psychometric curve. Within every session, target and distractor stimulus strengths were calibrated to be identical. Directly below the mouse's snout was a central lick port. Each "hit" trial in which the mouse would lick at the appropriate time was rewarded with ~5 μL of water delivered through the lick port. In this task, mice learned to respond (lick) to small, transient whisker deflections within one whisker field (target) and to ignore identical whisker deflections in the opposite whisker field (distractor) (Figure 2A and 2F). In the task structure, we impose a 200 ms lockout between stimulus onset and response window, and mice learn to

9

withhold responding across this delay. Mice are considered experts in this task once they achieve a separation (d to target) and false alarm rate (response toprime) between hit rate (response distractor) greater than 1 for three consecutive days.

After the mice have established a level of familiarity and comfortability with the experimental setup, they underwent behavioral training which consisted of three stages. Intertrial intervals (ITI) for all stages varied from 5 to 9 s with a negative exponential distribution to minimize potential timing strategies. Additionally, in all stages a "lockout" period of 200 ms separated stimulus onset and the earliest opportunity for reward. The target and distractor whisker fields were assigned at Stage 1 and remained constant throughout training. Stage 1 of behavioral training consisted of classical conditioning in which a unilateral target whisker deflection was paired with a reward (water). The distractor whisker deflection was neither rewarded or punished. Mice were trained in this stage for 1 to 3 days, one session per day. The next stage was operant conditioning, in which the mice were required to contact the lick port within the lick detection window of 1.5 seconds to initiate the water reward, following unilateral target whisker deflection. Mice were trained in this stage for 2–3 days, one session per day. The final stage of training was impulse control. This involves a similar task structure as previously described, however all incorrect responses, such as licking during the ITI, during the lockout period, or following distractor deflections, were punished by re-setting the ITI. This acted as a time out in our task and the response detection window was shortened to 1 second.

Following the full-length intertrial intervals (ITI), trial types were selected randomly from a distribution of 80% distractor and 20% target. For distractor trials, not responding (correct rejection) was rewarded with a shortened ITI and a subsequent target trial. If mice licked to the distractor paddle (false alarm) or did not respond to the target (miss), a subsequent full-length ITI

would occur. Responding to the target stimulus (hit) triggered a reward (water), followed by a full-length ITI.

A single, contiguous behavioral window was considered for analyses, which we interpreted as the engagement period. Hit rate, false alarm rate, spontaneous lick rate, and reaction times were all used to assess task performance. Foremost, we used the sensitivity or d-prime (d') framework from signal detection theory. Traditionally, d' is used as a measure of detection between stimulus present and stimulus absent conditions. Here, we implemented a discriminability d' between target detection and distractor detection, where Z is the inverse of the normal cumulative distribution function. Mice were considered experts in our task once they achieved a d' > 1 for three consecutive days. Spontaneous lick rate was calculated as the response rate during the last 1 s of the full-length ITI.

For the whisker validation task, we performed a preliminary experiment where there was no manipulation of the mice while performing the said task in complete darkness. After mice reached expert performance, their whiskers were trimmed. The data was then analyzed to determine whether or not the mice depend on their whiskers to complete the task.

Data Analysis

All data analyses were performed in MATLAB using custom scripts.

Note on Data Exclusion

During data collection, external factors can influence the animal's performance and behavior that do not reflect the ability of mice to discriminate between the stimuli. These factors/variables include poor health due to extreme weight loss and technical issues related to the behavior setup. Values that were influenced by these variables were excluded.

Histological Analysis and Immunohistochemistry

Mice were anesthetized, perfused with 20 ml PBS and 20ml 4% paraformaldehyde, and tissues were collected in order to confirm the accuracy and effects of the injections. Brains were fixed in 4% paraformaldehyde and coronally cryosectioned using a precision vibrating microtome at 100-120 microns. Brightfield imaging was performed in order to visualize the structural effects of manipulation in the mouse brain.

RESULTS

Selective Detection Task

We used a Go/No-go passive whisker detection task in order to study sensory-motor processes such as sensory selection. In the selective detection task, the target stimuli are rapid deflections of multiple whiskers in one whisker field and the distractor stimuli are identical deflections in the opposing whisker field. In training, the task performance of the mice was quantified by the separation between hit rate and false alarm rate, also known as d' (discriminability context). Mice were deemed to be performing at 'expert' level once they obtained a d' of 1 or more in three consecutive trials.

Validation of Selective Detection Whisker Task

Before conducting the lesioning experiment, it is important to prove the validity of our task. We performed a preliminary experiment where there was no manipulation of the mice while performing the task in complete darkness. We expected to see a decline in performance, indicated by decrease in hit rate, prestimulus spontaneous rate, and target d'.

In this experiment, a behavioral analysis was conducted for a total of 7 mice. 3 were trained with the lights off (no visual masking) and 4 were trained in complete darkness (visual masking). Performance measures for the training sessions used in subsequent analyses are shown in Figures 5-8 [n= 177 sessions, n = 7 [3 masked and 4 unmasked]] and Table 1 with the statistical analyses. Performance measures used for this particular analysis are: Hit rate (%), prestimulus spontaneous rate (%), Target detection d' (a.u.) and Engagement period (seconds).

The unmasked mice are indicated in red on the graphs and the masked mice are indicated in blue. All mice were trained to expert performance (d'>1) and subsequently had their whiskers trimmed. The dashed line on the graphs indicates the day that the whiskers were trimmed.

Table 1. Performance Measures for Validation of Selective Detection Whisker Task

	No visual mask pre whisker trim	No visual mask post whisker trim	Paired sample t-test	Visual mask pre whisker trim	Visual mask post whisker trim	Paired sample t-test
Hit rate (%) (Mean $\pm$ SEM)	57.1 $\pm$ 5.68	52.9 $\pm$ 12.7	p = 0.73 t(df)= 0.382 (2)	42.4 $\pm$ 5.58	18.5 $\pm$ 4.28	p = 0.0035 t(df)= 8.46 (3)
Target detection d' (a.u.) (Mean $\pm$ SEM)	0.66 $\pm$ 0.115	0.394 $\pm$ 0.259	p= 0.19 t(df)= 1.89 (2)	0.581 $\pm$ 0.147	0.0678 $\pm$ 0.117	p= 0.014 t(df)= 5.16 (3)
Prestimulus spontaneous rate (%) (Mean $\pm$ SEM)	33.4 $\pm$ 3.27	40.1 $\pm$ 7.73	p= 0.64 t(df)= -0.539 (2)	20.3 $\pm$ 2.13	16.58 $\pm$ 3.77	p= 0.43 t(df)= 0.899 (3)
Engagement (seconds) (Mean $\pm$ SEM)	3.91e+03 $\pm$ 281	4.22e+03 $\pm$ 401	p= 0.501 t(df)= -0.813 (2)	4.36e+03 $\pm$ 239	4.35e+03 $\pm$ 409	p= 0.95 t(df)= 0.067 (3)

Role of whisker motor cortex (wMC) in learning sensory-motor processes

Chronically lesioning wMC in naïve mice prior to learning might lead to various behavioral changes. We emphasize three possibilities that the wMC may be tutoring the discrimination process: 1) wMC is not contributing to learning the discrimination process or

successful performance of the task. 2) wMC is required for stimulus detection, and 3) wMC is required for stimulus discrimination and not detection.

When wMC is bilaterally lesioned in naïve mice prior to learning, with the assumption that wMC does not contribute to learning the discrimination process or successful performance, we expected to observe a steady increase in d' reflecting the increase to saturation in HR with an initial increase followed by a steady decrease in FAR. We expect all three measures (d', HR, and FAR) to remain at zero if wMC is required for stimulus detection. This indicates the mice will fail to detect either stimulus. If wMC is required for stimulus discrimination, we expect to see HR increase to saturation, but FAR would also increase to saturation through learning. The d' would still be at zero.

In this experiment, a behavioral analysis was conducted for a total of 3 mice, 2 control and 1 experiment. Performance measures for the training sessions used in subsequent analyses are shown in Figures 9-11 [n= 49 sessions for n =2 [control mice] and n=30 sessions for n=1 [experiment mouse]] and Table 2 with the statistical analyses. Performance measures used for this particular analysis are: Hit rate (%), False alarm rate (%), and discrimination d'.

Table 2. Performance Measures for wMC lesioning experiment

	Control mouse 1 (saline injected)	Control mouse 2 (saline injected)	Experiment mouse (Ibotenic acid injected)
Hit rate (%)	Mean $\pm$ SEM = 0.368 $\pm$ 0.06 R^2 = 0.66, Adj R^2 = 0.65 F = 53.4 (27) p = 7.3e-08	Mean $\pm$ SEM = 0.355 $\pm$ 0.055 R^2 = 0.119, Adj R^2 = 0.069 F = 2.42 (18) p = 0.13	Mean $\pm$ SEM = 0.461 $\pm$ 0.064 R^2 = 0.621, Adj R^2 = 0.607 F = 45.8 (28) p = 2.3e-07
False alarm rate (%)	Mean $\pm$ SEM = 0.244 $\pm$ 0.038 R^2 = 0.101, Adj R^2= 0.067 F = 3.03 (27) p = 0.093	Mean $\pm$ SEM = 0.1141 $\pm$ 0.0162 R^2 = 0.050, Adj R^2 = -0.002 F = 0.953 (18) p = 0.34	Mean $\pm$ SEM = 0.2800 $\pm$ 0.0399 R^2 = 0.241, Adj R^2 = 0.214 F = 8.88 (28) p = 0.0059
Discrimination d' (a.u.)	Mean $\pm$ SEM = 0.380 $\pm$ 0.174 R^2 =0.552, Adj R^2 = 0.535 F = 33.3 (27) p = 3.9e-06	Mean $\pm$ SEM = 0.6267 $\pm$ 0.1584 R^2 = 0.148, Adj R^2 = 0.101 F = 3.14 (18) p = 0.093	Mean $\pm$ SEM = 0.4732 $\pm$ 0.1516 R^2 = 0.549, Adj R^2 = 0.533 F = 34.1 (28) p = 2.8e-06

Histological Analysis and Immunohistochemistry

Histology proves that the injection works as cell death was visualized in one mouse (Figure 3). Cell death is indicated by the darker portion on the slice that is circled in the figure. One explanation for cell death not being visualized in all of the lesioned mice is that the volume and/or concentration of Ibotenic (IBO) Acid used was not enough. In future experiments, we can reassess the amount of IBO acid used and possibly increase the amount used.

By using the coordinates from Allen Mouse Brain Atlas as a reference, it is also noted that the lesion was made in M2/ALM and not in M1, our target cortical area. Thus, in this experiment we were unable to correctly observe the whisker motor cortex's contribution in learning sensory-motor processes.

DISCUSSION

We trained mice in a Go/NoGo selective detection task to study the role of whisker cortices in sensory-motor processing in mice. In order to prove the validity of the whisker dependency of this task, we performed a preliminary experiment where there was no manipulation of the mice while performing the said task in complete darkness. After mice reached expert performance, their whiskers were trimmed, after which the task performance declined. We expected, and noticed, an average decrease in hit rate, target detection, and prestimulus spontaneous rate after the whisker trim in the mice trained in the dark. This can allow us to conclude that the mice were not using any other sensory modalities to detect the stimulus. Notably, there is a non-significant increase in average prestimulus spontaneous rate in the mice trained in the light after the whisker trim. This can be attributed to mice that were trained with the lights on using their eyes to watch the paddles in place of using their whiskers. This leads us to the conclusion that the task is indeed whisker dependent.

We then tested the role of the whisker motor cortex (wMC) in sensory-motor processes. Primary and secondary motor cortices have been shown to have a "tutoring" role in learning and executing motor skills. To control for reversible behavioral changes through learning, we chronically lesioned whisker motor cortex before the mice have learned the task and observed changes in the behavioral performance with behavioral measures such as Hit rate (HR), False alarm rate (FAR) and d' (discriminability index) across learning.

When wMC is bilaterally lesioned in naïve mice prior to learning, we expect one of three possibilities in this experiment regarding whether wMC is required for executing the learned discrimination process: 1) wMC is not required for execution, 2) wMC is fully required for execution, and 3) wMC is partially required for execution (Figure 4). If wMC is not required for

executing the discrimination process, we would expect that suppressing wMC would lead to no change in mice's behavioral performance from the expert level; d' and HR remain high while FAR remains low. On the other hand, if wMC is fully required for executing the discrimination process, suppressing wMC should lead to high response rates (both HR and FAR) driving the d' to zero.

In our experiment, we observed no overall difference between the control and lesion mice. All mice obtained a d'>1 with high hit rates and false alarm rates. This leads us to believe that wMC makes no contribution to learning and performance, however this conclusion was proven to be misleading after performing histology. Histology was conducted to confirm our injection site but it instead revealed that we injected in the incorrect motor cortical area. Rather than injecting in M1, the area responsible for sensory-motor processing, we injected in M2/ALM which is the motor area that is responsible for licking.

Histology proves that the injection works as cell death can be visualized, however it is important to be more cognizant of the area we are lesioning and confirming coordinates of the brain. This experiment is still in its preliminary phase as this was our first batch of mice lesioned with an increased concentration and volume of IBO acid that yielded visualized cell death. From a behavioral standpoint, in addition to doing the correct lesion, we must train more mice with this increased concentration and volume of IBO acid to come to a concrete conclusion.

In the future, we aim to do a post-learning lesioning experiment once the role of wMC in learning sensory motor processes is established. We would perform the same experiment in learned mice to study the tutoring role of wMC in sensory motor processes and observe the changes in behavior to determine the extent of involvement of wMC in executing learned functions.

Figure 1. Treisman Attenuation Model. Suggests that both attended and unattended signals enter an early sensory store. At some point in the processing stream, an attenuating filter suppresses unattended signals while allowing attended signals to propagate forward for higher order processing. Figure adapted from Aruljothi et al., 2020.
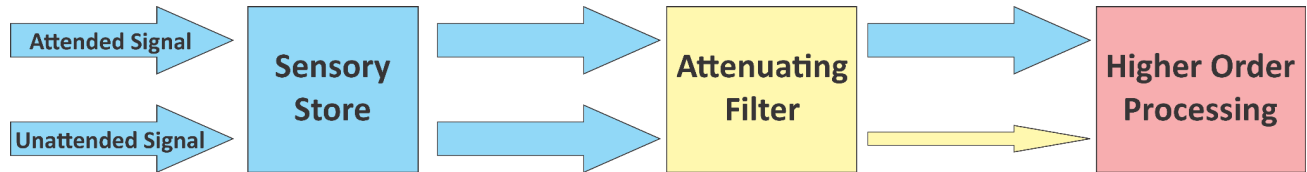

Figure 2. Selective Detection Task. Behavior paradigm and selective detection measures. A. Behavioral setup. Mice are head-fixed to the behavioral rig with piezo-controlled paddles within their whisker fields bilaterally. Each paddle is assigned as target (purple) or distractor (green). Mice receive rewards from a central lick port. B. Task structure. Each trial consists of an intertrial interval, a stimulus and 200-ms lockout, and a 1-s response window. Trial type can be target, distractor or catch (no stimulus). C. Calculation of discriminability d'. Indicated by the separation between hit rate and false alarm rate. D. Performance trajectories for all mice (n = 43 mice) and box and whiskers summary plot. Mice were considered experts once they achieved a d'>1 for three consecutive days. E. Comparison of d' for novice mice and expert mice. F. Performance measures for the sessions. G. Example session data showing reaction time distributions for target and distractor trials. Figure adapted from Aruljothi et al., 2020.
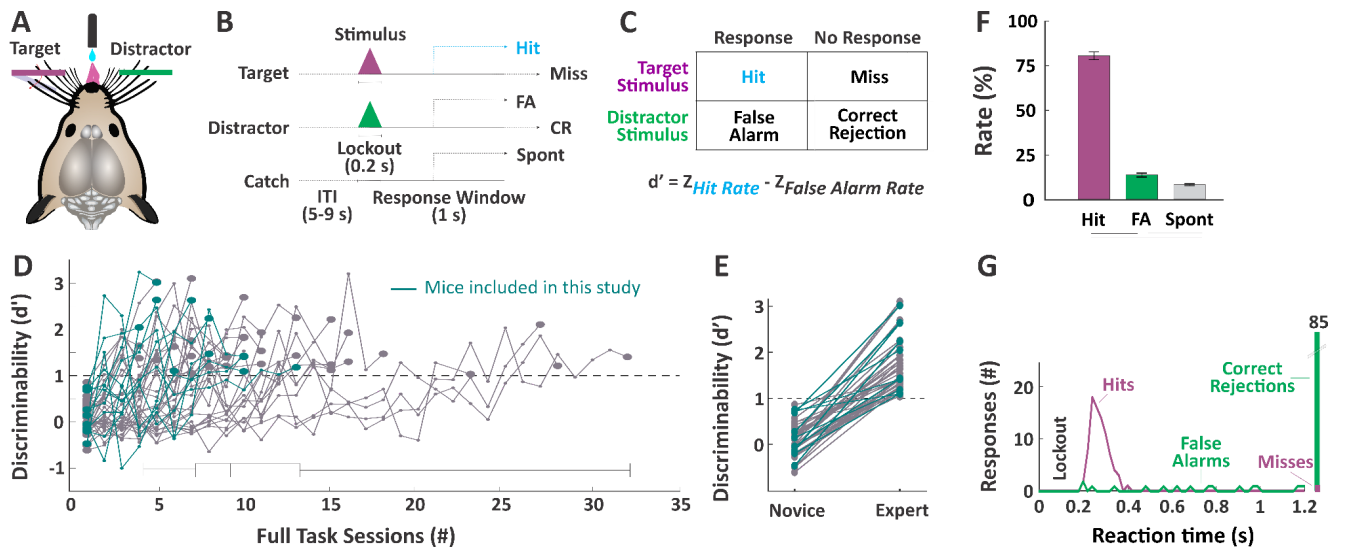
A Target | Distractor

B
Stimulus
Target — ▲ → Hit
· Miss
Distractor — ▲ · FA
· CR
Lockout (0.2 s) · Spont
Catch
ITI (5-9 s) | Response Window (1 s)

C
	Response	No Response
Target Stimulus	Hit	Miss
Distractor Stimulus	False Alarm	Correct Rejection

$d' = Z_{Hit\ Rate} - Z_{False\ Alarm\ Rate}$

F
Rate (%) — Hit, FA, Spont

D
Discriminability (d')
— Mice included in this study
Full Task Sessions (#)

E
Discriminability (d')
Novice | Expert

G
Responses (#)
Lockout
Hits
Correct Rejections
False Alarms
Misses
85
Reaction time (s)

Figure 3. Ibotenic Acid Lesion. Red box indicates site of lesion and cell death in M2. Green box indicates M1, target cortical area for lesioning.
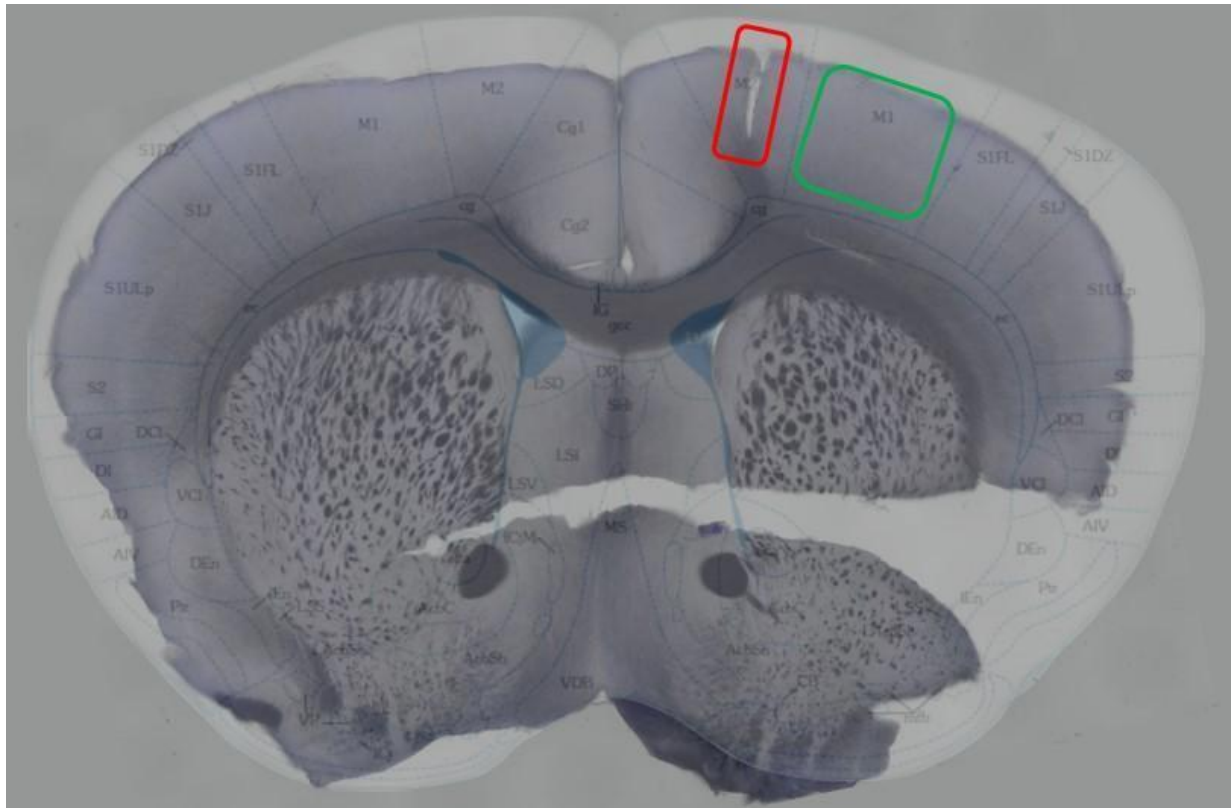
Figure 4. wMC lesion hypotheses. Green indicates H_0: wMC makes no contribution to learning and performance. Blue indicates H_1: wMC is required for stimulus detection. Red indicates H_2: wMC is required for stimulus discrimination.
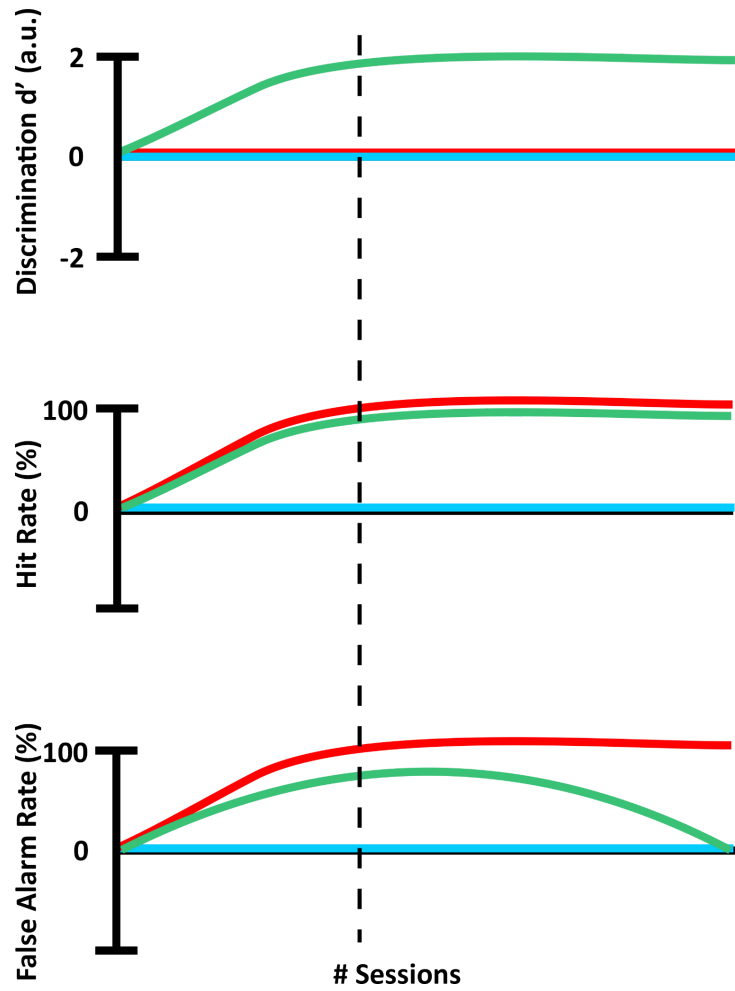
Figure 5. Hit Rates for Mice with and without visual masking. *(A)* Hit rates (in %) across sessions for mice with visual masking (blue traces, n=4 mice) and without visual masking (red traces, n=3 mice). The dashed line represents the day of whisker trim for both sets of mice. *(B)* Average hit rates for the two sets of mice separated into bars of pre and post whisker trim. Though both sets of mice showed a decrease in average hit rates post whisker trim, only mice with visual masking showed significant decrease (as indicated by the *).

A)
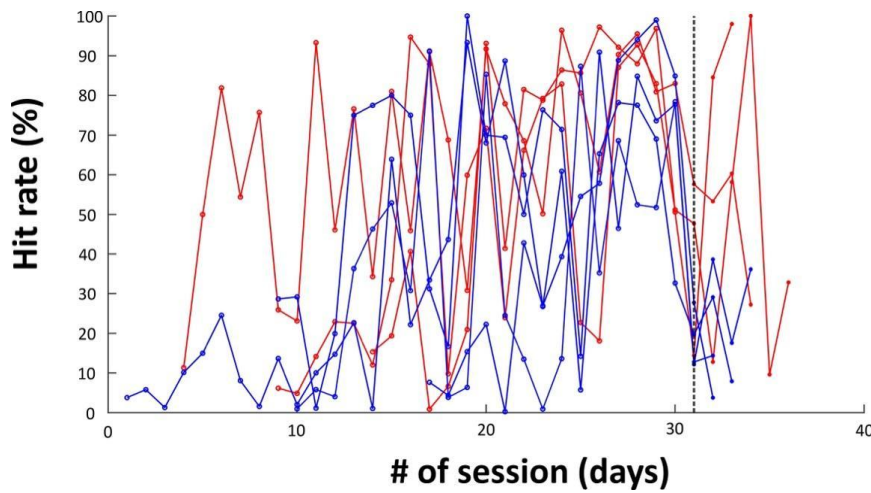
B)
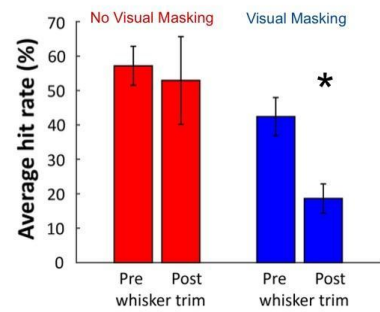
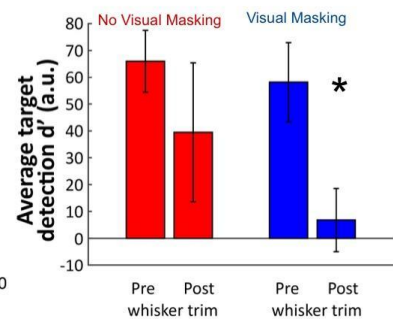**Figure 6. Target Detection d' 'for Mice with and without visual masking.** *(A)* Target Detection d'(in %) across sessions for mice with visual masking (blue traces, n=4 mice) and without visual masking (red traces, n=3 mice). The dashed line represents the day of whisker trim for both sets of mice. *(B)* Average target Detection d' for the two sets of mice separated into bars of pre and post whisker trim. Though both sets of mice showed a decrease in average target detection d' plot whisker trim, only mice with visual masking showed significant decrease(as indicated by the *).

A)
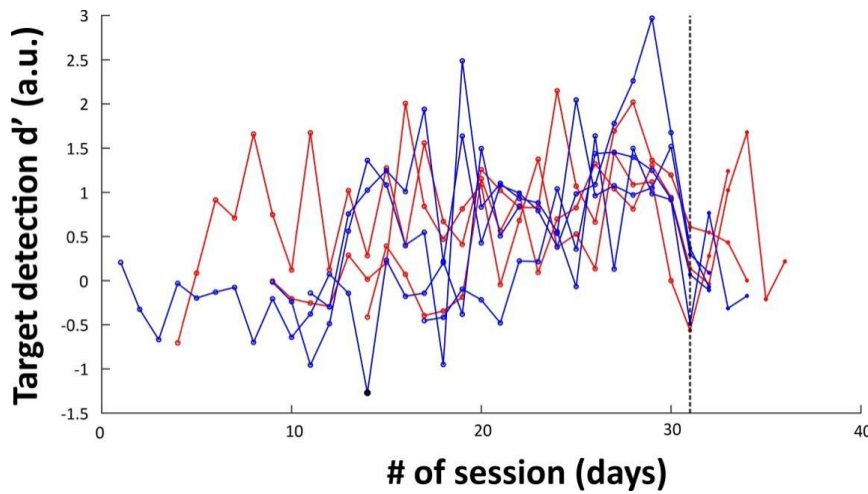
B)

Figure 6. Prestimulus Spontaneous Rate for Mice with and without visual masking. *(A)* Prestimulus Spontaneous Rate (in %) across sessions for mice with visual masking (blue traces, n=4 mice) and without visual masking (red traces, n=3 mice). The dashed line represents the day of whisker trim for both sets of mice. *(B)* Average prestimulus spontaneous rate for the two sets of mice separated into bars of pre and post whisker trim.
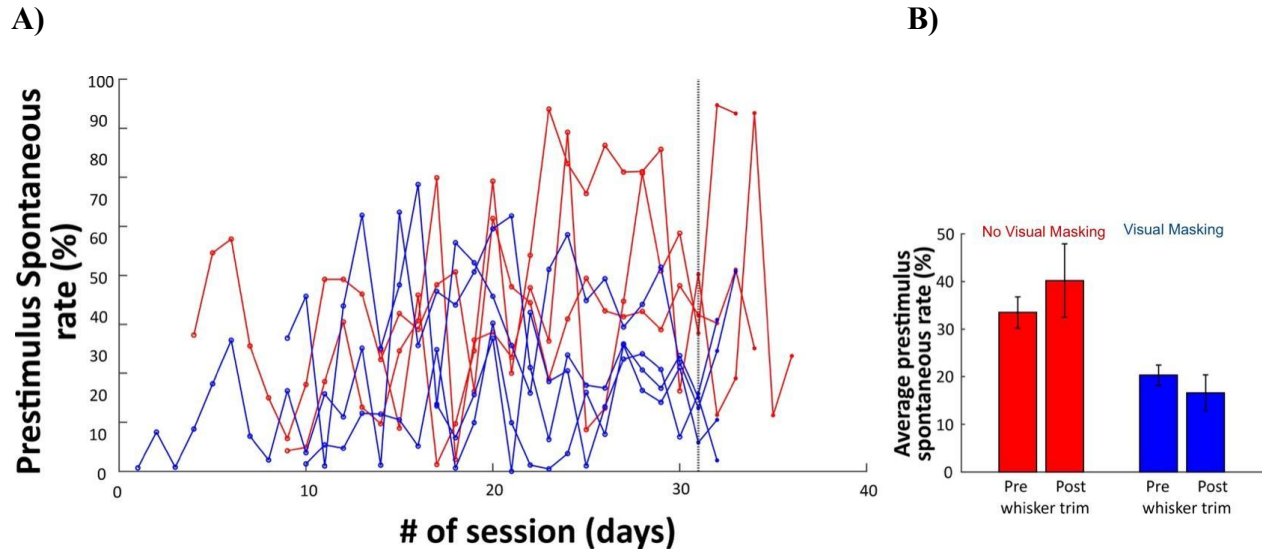
A)

B)

Figure 8. Engagement Period. Time in seconds of how long mice were engaged in the task.
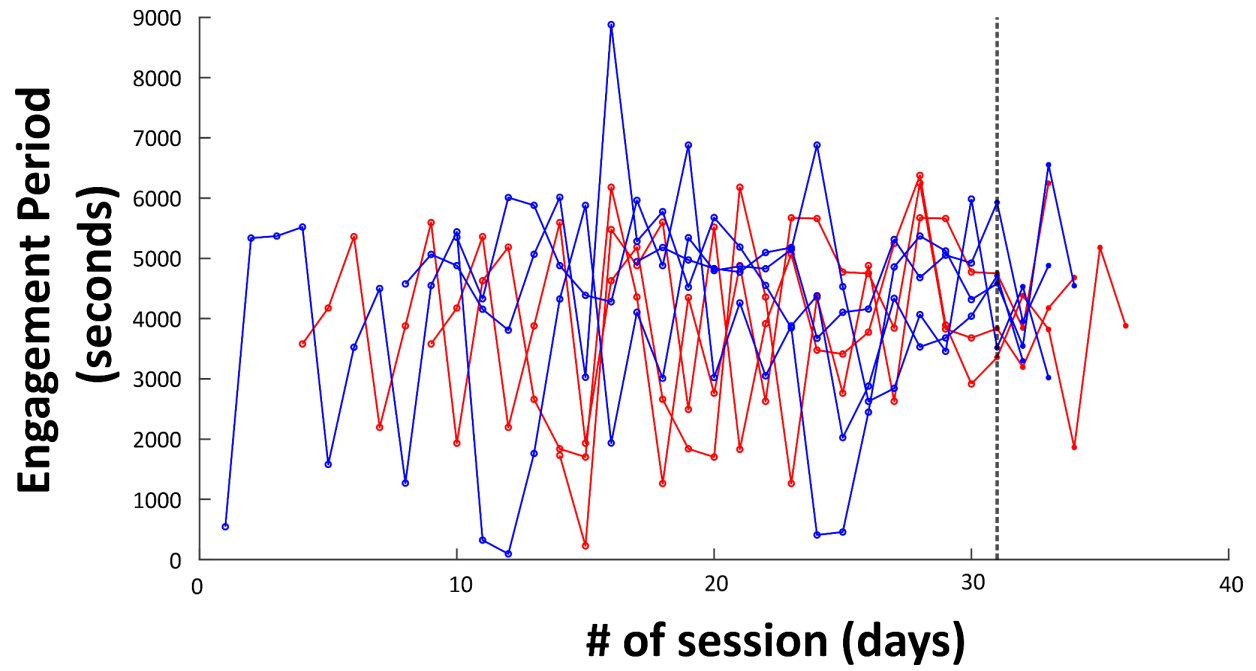
Figure 9. Hit Rate for Mice injected with Saline (control) and Ibotenic Acid (experiment) in wMC. Hit rates (in %) across sessions for mice with saline injected (blue traces, n=2 mice) and ibotenic acid injected (red traces, n=1 mouse) in whisker motor cortex. Dashed lines are regression fit lines for corresponding mice.
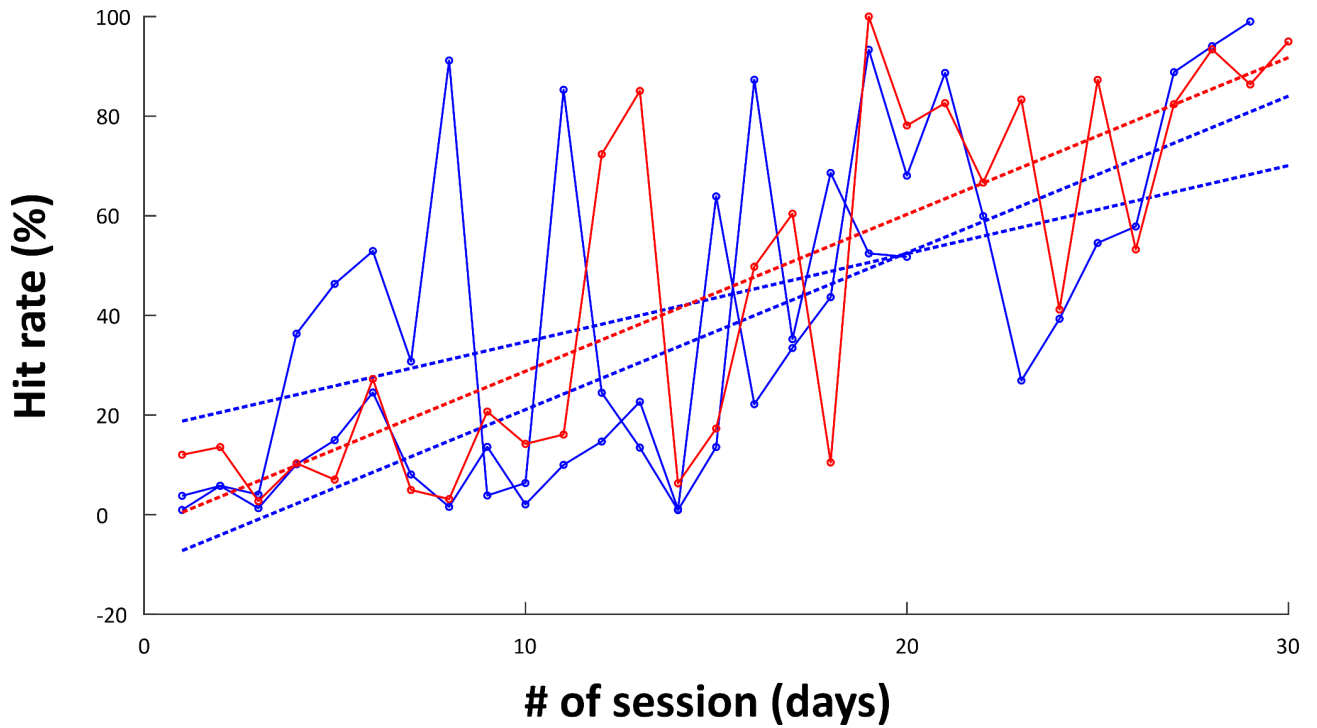
Figure 10. False Alarm Rate for Mice injected with Saline (control) and Ibotenic Acid (experiment) in wMC. False alarm rate (in %) across sessions for mice with saline injected (blue traces, n=2 mice) and ibotenic acid injected (red traces, n=1 mouse) in whisker motor cortex. Dashed lines are regression fit lines for corresponding mice.
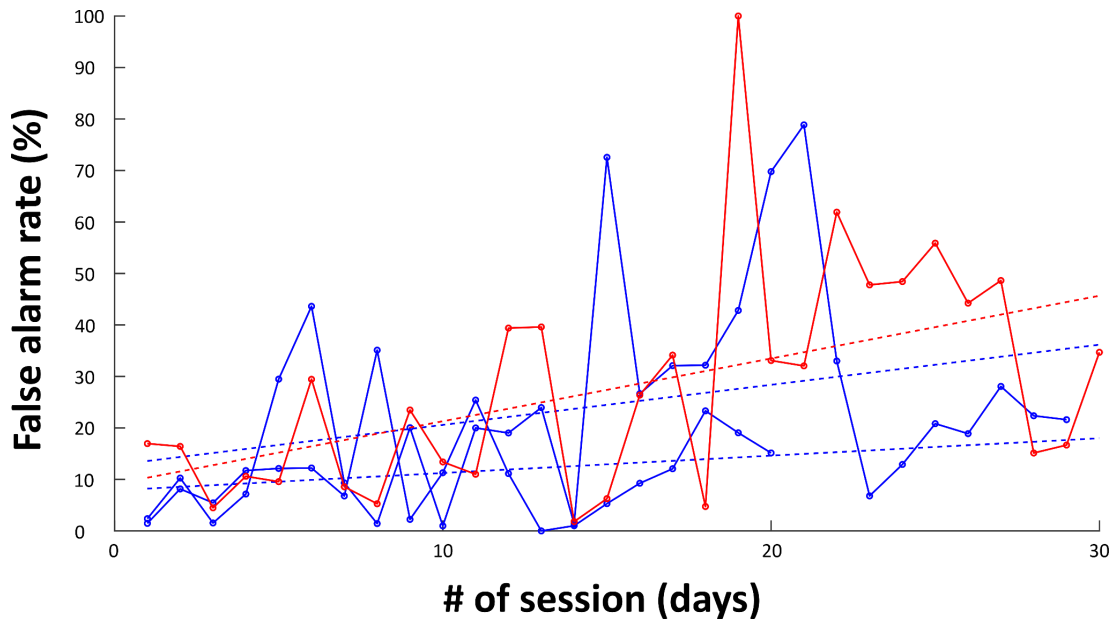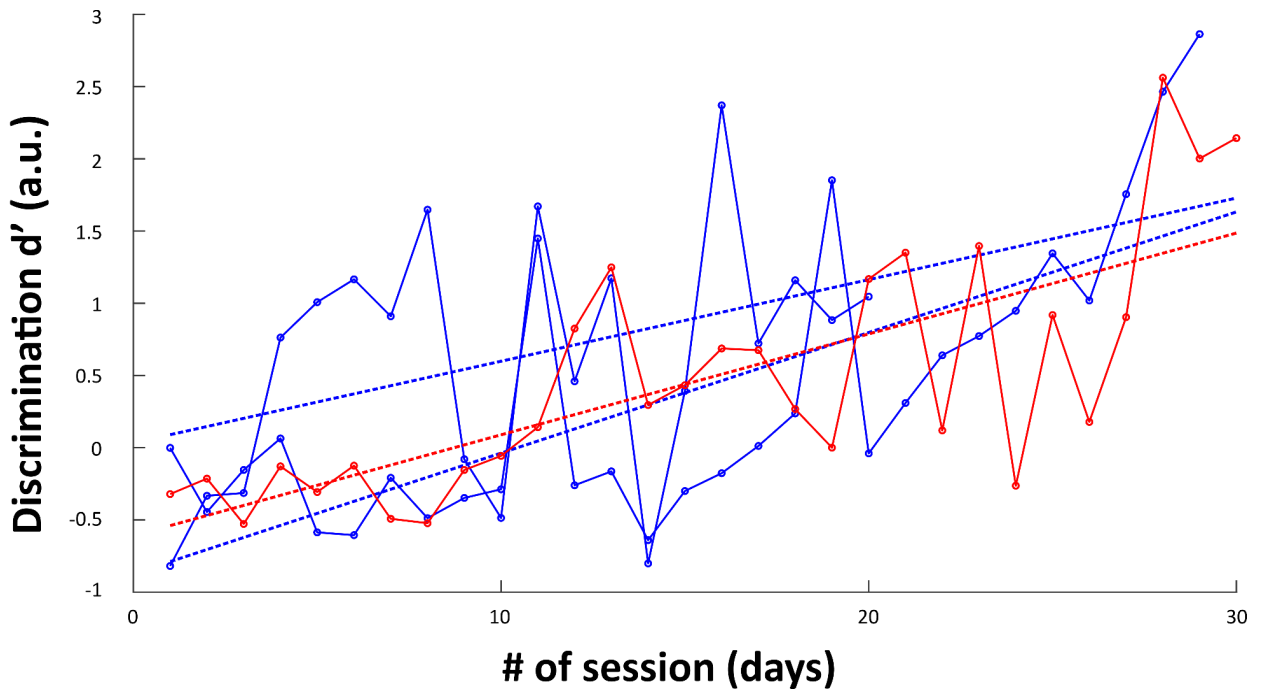
Figure 11. Discriminability d' for Mice injected with Saline (control) and Ibotenic Acid (experiment) in wMC. Discriminability d' across sessions for mice with saline injected (blue traces, n=2 mice) and ibotenic acid injected (red traces, n=1 mouse) in whisker motor cortex. Dashed lines are regression fit lines for corresponding mice.

REFERENCES

Aruljothi, Krithiga, et al. "Functional Localization of an Attenuating Filter within Cortex for a
  Selective Detection Task in Mice." *The Journal of Neuroscience*, vol. 40, no. 28, 2020,
  pp. 5443–5454., https://doi.org/10.1523/jneurosci.2993-19.2020.

Bell, Andrew H., and Janet H. Bultitude. "Methods Matter: A Primer on Permanent and
  Reversible Interference Techniques in Animals for Investigators of Human
  Neuropsychology." *Neuropsychologia*, vol. 115, 2018, pp. 211–219.,
  https://doi.org/10.1016/j.neuropsychologia.2017.09.019.

Grandjean, Joanes, et al. "Chronic Psychosocial Stress in Mice Leads to Changes in Brain
  Functional Connectivity and Metabolite Levels Comparable to Human Depression."
  NeuroImage, vol. 142, 2016, pp. 544–552.,
  https://doi.org/10.1016/j.neuroimage.2016.08.013.

Gratton, Caterina, et al. "Focal Brain Lesions to Critical Locations Cause Widespread Disruption
  of the Modular Organization of the Brain." *Journal of Cognitive Neuroscience*, vol. 24,
  no. 6, 2012, pp. 1275–1285., https://doi.org/10.1162/jocn_a_00222.

Hooks, Bryan M., et al. "Organization of Cortical and Thalamic Input to Pyramidal Neurons in
  Mouse Motor Cortex." *The Journal of Neuroscience*, vol. 33, no. 2, 2013, pp. 748–760.,
  https://doi.org/10.1523/jneurosci.4338-12.2013.

Jarrard, Leonard E. "On the Use of Ibotenic Acid to Lesion Selectively Different Components of
  the Hippocampal Formation." *Journal of Neuroscience Methods*, vol. 29, no. 3, 1989, pp.
  251–259., https://doi.org/10.1016/0165-0270(89)90149-0.

Kawai, Risa, et al. "Motor Cortex Is Required for Learning but Not for Executing a Motor Skill."
  Neuron, vol. 86, no. 3, 2015, pp. 800–812., https://doi.org/10.1016/j.neuron.2015.03.024.

Leussis, Melanie P., and Stephen C. Heinrichs. "Routine Tail Suspension Husbandry Facilitates
Onset of Seizure Susceptibility in El Mice." *Epilepsia*, vol. 47, no. 4, 2006, pp. 801–804.,
https://doi.org/10.1111/j.1528-1167.2006.00525.x.

Moore, Tirin, and Katherine M. Armstrong. "Selective Gating of Visual Signals by
Microstimulation of Frontal Cortex." *Nature*, vol. 421, no. 6921, 2003, pp. 370–373.,
https://doi.org/10.1038/nature01341.

Moore, Tirin, and Mazyar Fallah. "Control of Eye Movements and Spatial Attention."
Proceedings of the National Academy of Sciences, vol. 98, no. 3, 2001, pp. 1273–1276.,
https://doi.org/10.1073/pnas.98.3.1273.

Paxinos, George, and Franklin Keith B J. *The Mouse Brain in Stereotaxic Coordinates*.
Academic Press, 2019.

Rizzolatti, Giacomo, et al. "Reorienting Attention across the Horizontal and Vertical Meridians:
Evidence in Favor of a Premotor Theory of Attention." *Neuropsychologia*, vol. 25, no. 1,
1987, pp. 31–40., https://doi.org/10.1016/0028-3932(87)90041-8.

Zareian, Behzad, et al. "Cortical Localization of the Sensory-Motor Transformation in a Whisker
Detection Task in Mice." 2020, https://doi.org/10.1101/2020.07.08.194555.

Zareian, Behzad, et al. "Dorsolateral Striatum Is a Bottleneck for Responding to Task-Relevant
Stimuli in a Learned Whisker Detection Task in Mice." *The Journal of Neuroscience*,
2023, https://doi.org/10.1523/jneurosci.1506-22.2023.