USING A MOUSE MODEL TO UNDERSTAND AUDITORY LEARNING

by

GABRIEL TOEA

A THESIS

Presented to the Department of Biology
and the Robert D. Clark Honors College
in partial fulfillment of the requirements for the degree of
Bachelor of Science

April 2024

An Abstract of the Thesis of

Gabriel Toea for the degree of Bachelor of Science
in the Department of Biology to be taken June 2024

Title: Using a Mouse Model to Understand Auditory Learning

Approved: *Santiago Jaramillo Ph.D.*
Primary Thesis Advisor

This project's purpose was to characterize the length of time required for a cohort of mice to learn a frequency or amplitude modulated sound discrimination task and to understand if mice could learn to alternate between these two tasks every other day. To answer these questions, a cohort of nine mice were trained to learn a two-choice frequency discrimination task while another cohort of nine mice were trained to learn a two-choice amplitude modulated sound discrimination task followed by a two-choice frequency discrimination task. Results from these experiments highlight mice can learn both the frequency and amplitude modulated sound discrimination tasks. On average, it took 18 days for a cohort of mice to learn the frequency discrimination task, while it took 39 days for a cohort of mice to learn the amplitude modulated discrimination task. Excluding the days required for behavioral shaping, the mice learning the frequency discrimination task took 8 days to pass the final training stage, while mice learning the amplitude modulated discrimination task took 32 days to pass the final stage of training. For the cohort that learned the frequency discrimination task after the amplitude modulated discrimination task, mice on average took 6 days to pass the final training stage. This was a two-day reduction compared to the cohort that only learned the frequency discrimination task, suggesting that mice can quickly learn other sound discrimination tasks.

Acknowledgements

I would like to thank Professor Santiago Jaramillo and Professor Casey Shoop for serving on my thesis committee and helping me through the thesis defense process. I would like to thank Professor Jaramillo for mentoring me these past three years. His support helped me become a better researcher and scientific communicator and I have learned a lot about the scientific process through the work I did in his lab.

Additionally, I would like to thank Dr. Jenny Mohn for helping with the data analysis portion of my project and for helping me troubleshoot issues that came up during the animal training process. I would also like to thank Wendy Gillespie for helping me get the animals I needed to perform my project and Ciarra Thomas and Komal Kaur for helping me train them. This project would not have been possible without your help.

Table of Contents

List of Figures

Introduction

Background Information

The study of auditory neuroscience is important for understanding how neuron populations change during learning in the auditory system. Traditionally, this type of research relied on pure tones, which are simple sounds composed of a single sinusoidal wave, to investigate auditory learning. However, utilizing pure tones to study auditory learning is often limiting because organisms are rarely exposed to these types of sounds organically. Instead, current research efforts have focused on utilizing complex sounds to study how learning alters the auditory system. Complex sounds can be thought of as auditory stimuli composed of multiple frequencies or tones (Figure 1).

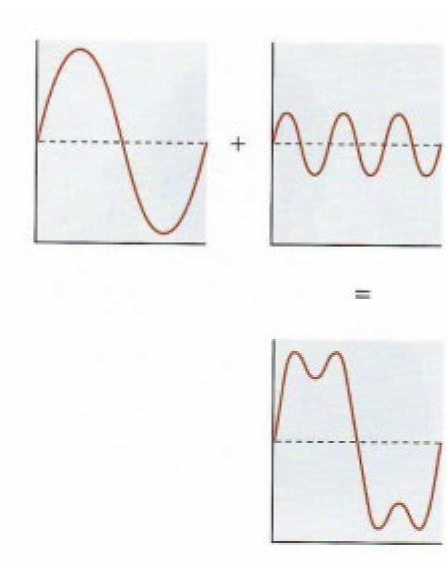

Figure 1. Creation of a complex waveform is produced by combining two or more tones

Figure was adapted from the Sound and Perception Textbook Fourth Edition (2020).

Through this research, we can hopefully gain a better understanding of the neural mechanisms driving language learning, which will lead to the development of better and more comprehensive language learning strategies.

Prior Research into Auditory Learning

Prior research has elucidated some aspects of language learning in the auditory system. Numerous studies have examined how sensory cortical neurons encode sensory information through selectively tuned responses to the acoustic frequency or loudness of sounds in the primary auditory cortex (Town et al., 2018). For example, research from primates revealed that auditory learning alters the way that certain neuron populations respond to trained frequency sounds in the auditory cortex (Recanzone et al., 1993). Additional mouse lesion studies demonstrated that the auditory cortex is heavily involved in the discrimination of complex sounds but is not required for simpler auditory tasks like frequency discrimination (Porter et al., 2011). This finding was further corroborated by optogenetic suppression studies which found that optogenetic suppression of the auditory cortex impacts auditory discrimination of complex sounds (O'Sullivan et al., 2020). Meanwhile, more recent studies have also found that certain neuron populations can be trained to respond to specific complex sounds (Wang et al., 2020).

Research efforts from the Jaramillo lab have also found that, on average, mice can learn to correctly discriminate between /ba/ and /da/ human speech sounds in 48 days. Despite the ability for these mice to learn this task, it takes them an incredibly long time to learn. This poses several issues because it is harder to track a group of neurons using our electrophysiology recording techniques over a longer training time. If we decrease the time it takes the mice to learn a complex auditory sound, it enables us to gather more data and decrease potential problems with the functioning of the electrophysiology equipment.

My research project was designed to help solve this training issue by creating a more efficient mouse training protocol and by categorizing the time it took a mouse to learn either a frequency or amplitude modulated (AM) sound discrimination task. We wanted to use these two tasks because they might take a shorter amount of time for the mice to learn them, and the target sounds for these tasks still carried relevant features for speech sounds. We also wanted to test if learning a more complex sound discrimination task impacted the training time of mice to learn a simpler discrimination task afterwards.

To test these objectives, we set out to train a cohort of nine animals on a frequency discrimination task and then categorize the time it took these animals to successfully learn the task. We then trained an additional cohort of nine animals to learn the AM discrimination task first and then trained these animals on the frequency discrimination task. Given that auditory learning alters the neurons in the auditory system, we expected that learning the AM task first would impact learning time for the frequency discrimination task.

Learning Theory

The main theory that underlies this research posits that an organisms' nervous system must change when it undergoes categorization learning. This transformation occurs so that future stimuli can be assigned faster to their appropriate learning categories. As an organism learns to categorize different sounds, the neural representation of the stimuli from each category change so that the categories are as separable as possible and the boundaries for the sound category are established which makes future samples easier to assign to the correct category (Figure 2).

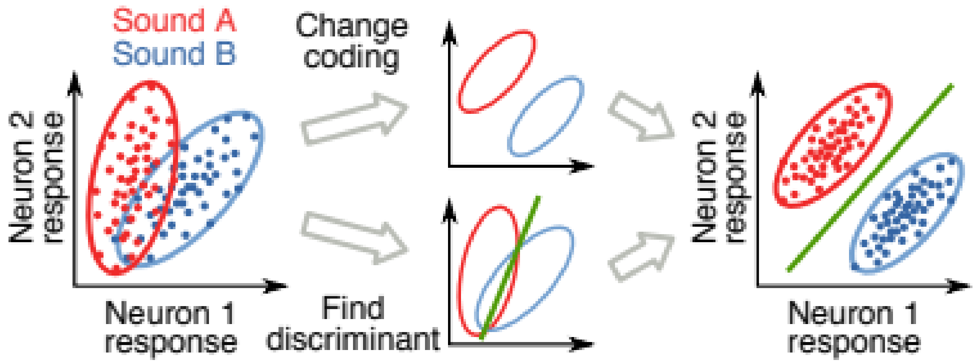

Figure 2. Illustration of Categorization Learning

Figure is adapted from the Jaramillo Lab

Mouse Model

This project utilizes C57BL/6J mice that are commonly used across research laboratories. Mice are a good model organism to use for auditory research because their auditory systems have several similarities to the human auditory system, making it possible to apply the knowledge gained from mouse experiments to humans at large (Ehret et al., 2002). Additionally, using mice enables invasive monitoring and imaging techniques that are not possible on human subjects. These imaging instruments are critical for understanding how cellular response changes to language learning and are the principal reason why mice are preferred to other organisms.

Experimental Methods

Auditory Stimuli

The first part of the project required the mice to learn a frequency discrimination task. The two target sounds for this task were composed of a high and low frequency chord. A chord is a sound with a combination of 3 or more sinusoidal wave components. The sounds were generated by the rig computer, and rig testing ensured they were presented correctly before the start of every training session. The high frequency chord was set at 16000 Hz while the low frequency chord was set at 3000 Hz. The target sounds were presented for 0.1 seconds during each trial period. Sound intensity was randomized throughout the training process to control for the possibility that the original sound intensity for the two sounds were not equal.

The second part of the project required the mice to first learn an AM sound discrimination task before learning the frequency discrimination task. The target sounds for this training task differed based on their modulation rate. The AM rate is based on the amplitude change of the sound over time. The fast modulation rate was set at 32 Hz, while the slow modulation rate was set at 8 Hz. The base sound that was amplitude modulated was white noise that had a high frequency of 16000 Hz and a low frequency of 5000 Hz. The target sounds were presented for 0.5 seconds during each trial period. Sound intensity was also randomized throughout the training process for the AM sounds.

Training Protocol for Freely Moving Mice

The mice for this project were trained in a freely moving experimental setup. In the freely moving setup, mice are free to move around a box that contains three water ports with lick sensors. The training protocol's main goals are to get the animal to initiate trials and to learn the sound discrimination task correctly.

For the animal to learn the task, they must first learn how to initiate a trail in the rig setup. A single trial is comprised of three core parts, the presentation of the sound stimulus, followed by a fixed period where the mouse must make a choice in response to the stimulus, and then a period for the mouse to receive their water award if they made the correct choice.

Before the mouse starts their training period, they are first put on water regulation the day before they start training. This makes the mouse more motivated to learn the task the following day and makes the water reward more enticing for the animal.

To initiate trails, the mouse would poke their head into the center port of the rig. Once the mouse initiates a trial, one of the two target sounds will play, and the mouse must decide whether to go to the left or the right port. Each target sound corresponds to either the left or the right side. If the mouse chooses the side that corresponds with the correct sound, they get a water reward. If they incorrectly identify the sound, they get no reward. Mouse mastery of the sound discrimination task is measured as a percentage of correct trials that the mouse performs within one session, with 70 percent correct being the benchmark for task mastery. For this project, mice are supposed to go to the right port for the fast AM rate or high frequency sound and to the left port for the slow AM rate or the low frequency sound (Figure 3).

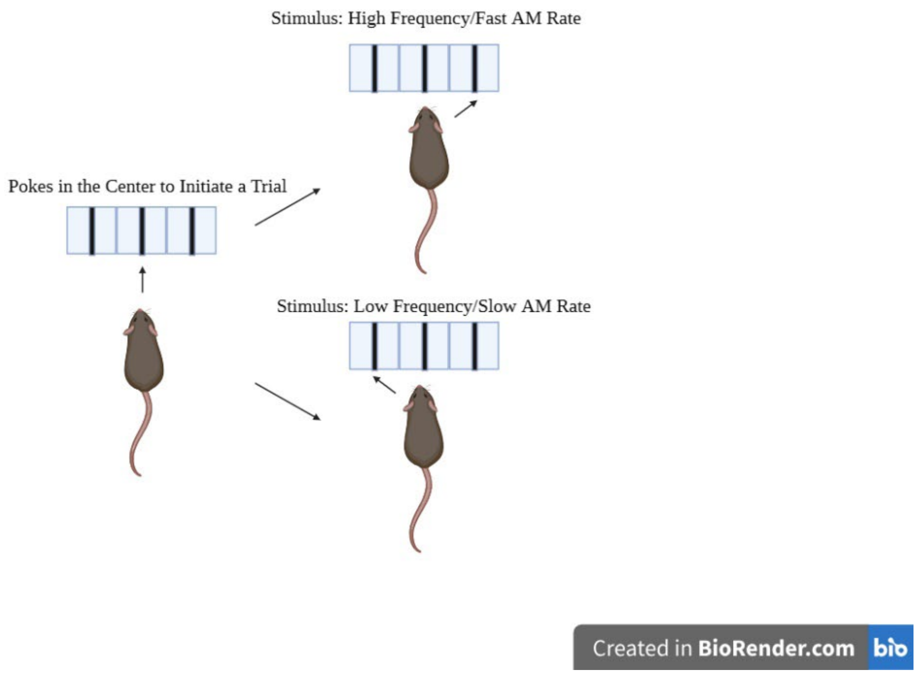

Figure 3. Freely moving mouse training setup

Figure was created by Gabriel Toea in Bio render

Description of Training Stages for Freely Moving Mice

To get the mice to correctly perform a trial, they were run through a four-stage training protocol that got them acclimated to the rig environment. The first three stages were necessary for the mouse to learn the basic process of initiating trials for the task, while the last stage required the mouse to perform the discrimination task. For all stages the mice were trained for one hour every single day.

Stage 0 required the mice to poke their heads into any of the three ports to get a water reward. Completion of 100 successful trials was the criteria to move onto Stage 1.

Stage 1 required the mice to poke their heads into the center port to initiate a trial and were then required to go to either the left or right ports to receive a water reward. After the mice initiated 200 successful trails, they were moved onto Stage 2.

Stage 2 required the mice to initiate a trial in the center port and keep their head there for a longer amount of time before hearing the sound. They could still go to either port to receive a reward at this stage. Once the animals completed 300 successful trials, they moved onto Stage 3 of the training process.

Stage 3 of training required the animals to successfully discriminate between the two target sounds. In this stage mice initiated the trial by poking in the center port. After hearing the sound, they were required to go to the correct corresponding port. Mice were penalized for incorrectly identifying a sound by not receiving a water reward. Mice successfully passed this training stage by initiating more than three hundred trials and getting 70 percent correct of the initiated trials for both sounds in one training session. To move onto the psychometric stage, animals needed to pass the 70 percent threshold for two consecutive days.

The animals that passed Stage 3 were moved to the psychometric training stage. The psychometric stage of the training required the animals to discern sounds between the two target sounds. For the AM discrimination task this would mean that on any given trial, the mouse would be presented with sounds that had a modulation rate in between the two target sounds and would have to make a choice as to which side the sound likely corresponded to. If an animal is proficient in learning the task, they should be able to discriminate between the fast and slow target modulations very well and we would expect their performance to decrease as we present them sounds with an intermediate level of modulation. Likewise, animals on the frequency discrimination psychometric mode would be presented with intermediate frequencies in addition to the two target frequencies and would have to discriminate between them.

An additional bias mode stage was created for circumstances where the animal was getting below 30 percent correct on either the left or right side. Mice were moved to this stage after one day of biased performance on the Stage 3 paradigm and were required to get above 30 percent correct on both sides before being moved back to Stage 3. This training paradigm was created to help prevent the animal from developing a bias to either the left or right-side ports, which would prevent the animal from properly learning the task.

Results

Results from Frequency discrimination task training in Cohort 1

On average it took 18 days and 7661 trails for the 9 mice from this cohort to learn the entire frequency discrimination task from Stage 0 to the end of Stage 3. This time is considerably shorter when compared to the animal cohort that was leaning the human speech sound discrimination task. The animals spent most of their training time (on average 8 days and 6044 trails) on Stage 3. This is expected because Stage 3 requires the animal to learn the frequency discrimination task. The other 10 days were spent on Stages 0-2 where the animal learned to acclimate to the rig environment and learned how to initiate the trials.

When the animals first started learning on the Stage 3 training paradigm, they struggled to perform well on the task and were getting around 50 percent of the trials correct. This is what we would expect to happen in this scenario because the mice have not learned the task and are simply guessing during each trial. However, as their training sessions progress, they get better at discriminating between the high and low frequency sounds and get over 70 percent of the trials correct over a two-day consecutive period (Figure 4).

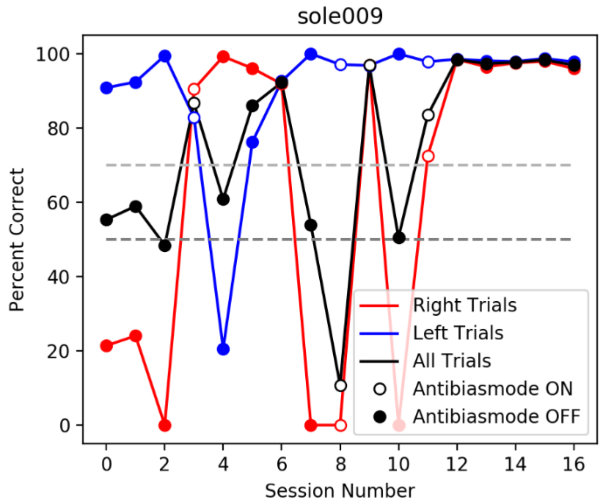

Figure 4. Progress of one animal learning the Frequency discrimination task

This graph displays the progress of one mouse over 16 days of learning the Frequency discrimination task. At first the mouse struggles to discern between the high and low frequency sounds and is guessing during each trial. However, as the animal progresses in training sessions, they eventually learn to distinguish the two target sounds and can get around 90 percent of the trails correct on any given training session. This graph also shows that the animal struggled with becoming biased on certain training days and spent 4 days in bias mode over the training period.

The results from this first cohort were important because it gave us an idea of how long it took to train the animals in this frequency discrimination task and enabled us to compare the progress of the next cohort that learned the frequency discrimination task after learning the AM task.

Results from the AM discrimination task training in Cohort 2

In total 7 out of the 9 animals in this cohort learned the AM discrimination task. For these 7 animals it took on average 39 days to pass all four stages of the training protocol. These seven animals spent most of the time (31 days and 25619 trials) on the Stage 3 training paradigm (Figure 5).

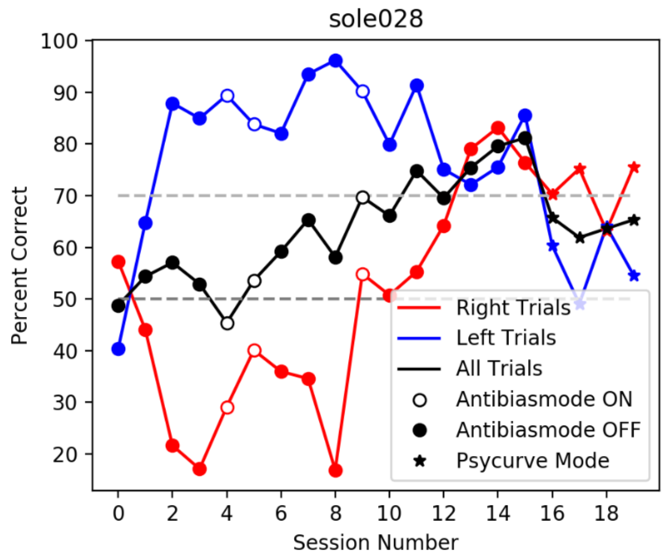

Figure 5. Progress of one animal learning the AM discrimination task

The graph above shows one animal's performance over several training sessions. This animal successfully got above the 70 percent threshold on both the left and right sides for two consecutive days and was then moved to the psychometric mode. The days the animal performed on the psychometric stage is displayed by the star points on the graph. Note that the animal experienced a drop in their performance on the left and right side when they moved onto the psychometric mode.

This is expected because Stage 3 requires the animal to correctly discriminate between the fast and slow AM rates. After the animals passed the first four learning stages, they were transferred to the psychometric mode training paradigm where the animals demonstrated their ability to categorize a range of AM sounds (Figure 6).

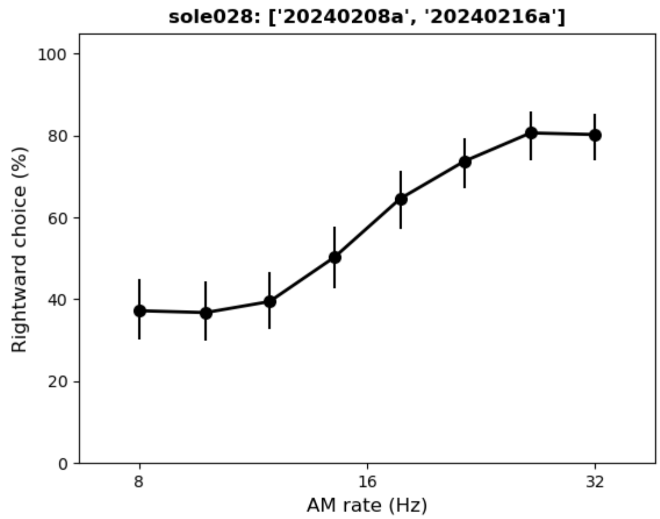

Figure 6. Mice in a freely moving training paradigm can learn to discriminate a range of AM rates.

The psychometric graph above displays the percentage of rightward choices one mouse made during two training sessions. The graph highlights the mouse's ability to discriminate multiple AM rates as it is going to the right when the fast modulated sound is presented over 70 percent of the time and is going to the right less when the slow modulated sound is presented. The mouse also struggles to discriminate sounds that have an intermediate level of modulation between the two target sounds as its performance approaches 50 percent.

It is also worth noting that two animals in this cohort were unable to learn the AM discrimination task during training. These animals were trained over 60 days and their performance remained around the 50-60 percent correct range. This indicates that by the end of the training period, the mice were still guessing when presented with either the fast or slow AM stimuli (Figure 7).

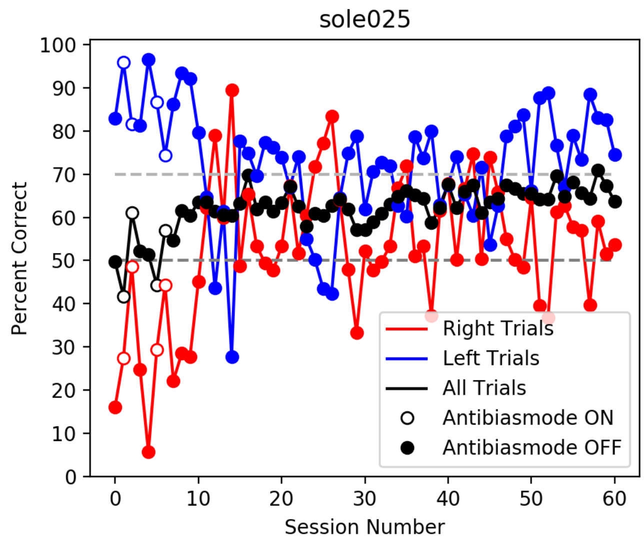

Figure 7. Progress of one animal learning the AM discrimination task

This graph highlights that this animal struggled to learn the AM discrimination task. Over 60 training sessions, the animal was still below the 70 percent threshold on either of the two target sounds, indicating that the animal is still guessing each time it is presented with one of the target sounds.

Results from the Frequency discrimination task training in Cohort 2

After spending four to five days on the psychometric training paradigm, 6 out of the 7 animals that learned the AM discrimination task were moved onto Stage 3 of the frequency discrimination task. Only 6 out of the 7 animals moved onto learning the frequency discrimination task because one of the animals finished learning the AM task too late and was unable to be moved to the frequency discrimination task. In total, all six of these animals learned the frequency discrimination task. On average, they spent 6 days and 4720 trials on the Stage 3 paradigm. Their performance at the beginning of the Stage 3 training sessions was around 50 percent, but quickly improved with successive training sessions (Figure 8).

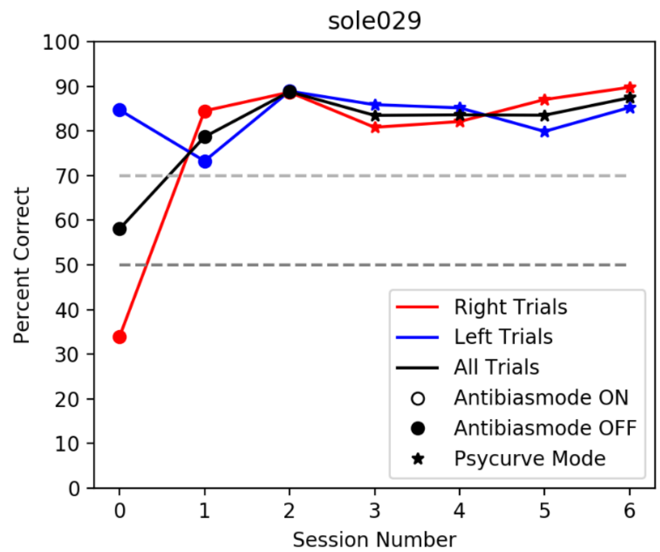

Figure 8. Progress of one animal learning the Frequency discrimination task

The graph displayed above highlights the performance of one mouse learning the frequency discrimination task following completion of the AM task. During three days of training, the animal performed above the 70 percent threshold for two consecutive days.

Once mice completed the Stage 3 training criteria, they were moved onto the psychometric mode for the frequency discrimination task. Mice were kept on this psychometric stage for 4 to 5 consecutive days and showed strong performance in their ability to discriminate a range of frequencies (Figure 9). The animals were still able to discriminate between the two target stimuli in the psychometric stage, but their performance worsened with stimuli that had frequencies in between the two target sounds.

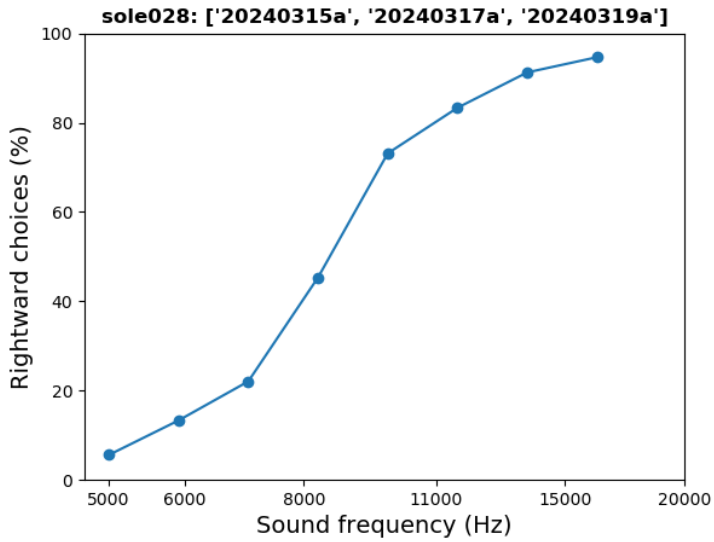

Figure 9. Mice in a freely moving setup can discriminate between a range of frequency sounds

This graph displays the performance of one animal averaged across three training sessions. This psychometric curve displays that the mouse can correctly discriminate between the high and low frequency sounds and can also discriminate sounds that have intermediate frequencies between these two target sounds.

Results from the alternating task

After the six mice demonstrated proficiency in both the AM and frequency discrimination tasks, we moved them to the final training task that required them to alternate between the AM and frequency psychometric training paradigms every other day. All six mice switched between performing the AM and frequency discrimination tasks but were slightly better during the days when they performed the psychometric frequency discrimination task (Figure 10).

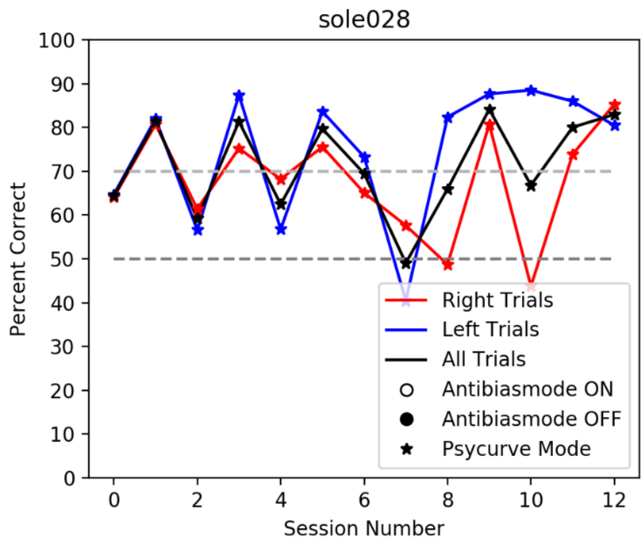

Figure 10. Displays the performance of one animal alternating between the AM and Frequency psychometric mode every other day

The animal performs better on the days where they are on the frequency psychometric mode (denoted by the odd training session numbers) and their performance drops on the days when they are performing on the AM psychometric mode.

Discussion

Mice Learned the Frequency discrimination task

All 9 mice in cohort 1 successfully learned the frequency discrimination task in a freely moving rig setup. Throughout the Stage 3 training process, the mice showed a gradual increase in task performance. They were initially getting around 50 percent of the total trials correct in any given session, indicating that they were guessing between the left and right ports when the target sounds were presented. This performance improved with increased training sessions and within a week, the mice were getting above the 70 percent correct threshold for both target sounds. With this cohort, we successfully categorized their ability to learn the frequency discrimination task, as on average, it took 9 days for the mice to acclimate to the rigs and another 8 days to successfully learn the discrimination task. This finding corroborates earlier studies analyzing mouse and rat learning of frequency discrimination tasks that found that on average it takes mice 18.1 training sessions to learn the frequency discrimination task (Jaramillo et al., 2014). Although this prior study used a slightly different training protocol, it still provides a useful benchmark to compare the results from my frequency discrimination training task.

Mice Learned the AM discrimination task

In cohort 2, 7 out of the 9 mice successfully learned the AM discrimination task in a freely moving rig setup. The two mice that were unsuccessful at learning the task spent 62 days on the Stage 3 training paradigm. The reason why these mice failed to learn the task is difficult to deduce. The mice rotated rigs during every training session to minimize the potential risk of rig functioning impacting mouse performance on the discrimination task. Alternatively, the intensity randomization for the AM task might have made it harder for certain mice to distinguish between the fast and slow target stimuli because the target sounds were never presented at the same intensity every single time. It is possible that at lower intensities, the mice have a harder time recognizing the difference between these two AM rates.

Mouse performance on the AM discrimination task also varied, with some mice being able to pass Stage 3 in 16 days while others took 57 days. Similarly, we saw a slight drop in the animal's overall performance when they were moved to the psychometric stage. Despite the mice having more difficulty discriminating the AM stimuli in between the two extremes, all seven animals were still proficient in discriminating between the two target AM stimuli in the psychometric stage, adding confidence in our ability to determine that the mice learned the AM task.

Additionally, the wide variance in mouse performance might aid evidence to the idea that the randomization of sound intensity makes the AM task harder to master. However, we would need to train mice on the AM task with a fixed sound intensity to confirm that sound intensity modulates the difficulty of the AM discrimination task.

Mice Learned the Frequency discrimination task faster after learning the AM discrimination task

All six mice successfully learned the frequency discrimination task and were also able to discriminate a range of frequencies in the psychometric training stage. Interestingly, the six mice that learned the frequency discrimination task after the AM task spent on average 6 days in the Stage 3 training paradigm, a two day decrease from cohort 1, which took 8 days on average to pass Stage 3. Despite this average decrease, there was still a wide range in cohort 2's learning of the frequency discrimination task, with Stage 3 completion taking between 3 to 11 days depending on the animal. This is contrasted with cohort 1, whose range was smaller, taking the mice between 6 to 12 days to pass the Stage 3 training paradigm. Given that there were only 18 mice in total between these two cohorts, more training data with other mice is needed to confirm whether the variation in the frequency Stage 3 training duration between cohorts is due to chance or due to prior learning from the AM discrimination task.

It is also worth noting that the two mice that learned the AM discrimination task the fastest, also quickly learned the frequency discrimination task. These two animals passed the AM Stage 3 training criteria in 16 and 18 days and passed the frequency Stage 3 training criteria in 4 and 3 days respectively. This result demonstrates that we can successfully teach a single animal to learn multiple auditory discrimination tasks over a 10-week training period. This result is promising because it demonstrates that mice can learn additional auditory discrimination tasks and that their ability to learn these additional tasks might be impacted by the learning of prior tasks.

Mice Could Alternate between the Frequency and AM discrimination tasks

By the end of the training period, we trained six mice from cohort 2 to alternate between the AM and frequency psychometric tasks. The mice exhibited strong performance in the frequency psychometric task but showed a slightly lower performance in the AM psychometric task when compared to their performance on the frequency psychometric task. This difference could be due to the stimulus intensity randomization adversely impacting mouse performance on the AM task but having no effect on the frequency psychometric task. Despite the mice performing slightly better in the frequency psychometric task, this result indicates that we can get mice to alternate between two separate auditory discrimination tasks.

Future Direction

Now that we have established the time it takes the mice to learn both the frequency and AM discrimination tasks, we can move to characterize the response of neurons in the auditory cortex to these sounds. This research is important because it enables us to understand how the firing properties of individual neurons are transformed through the auditory learning process. We can accomplish this goal by measuring the neural activity of these mice with a Neuropixel probe while they are alternating between the AM and frequency discrimination tasks. Using the Neuropixel probe enables us to record from a wide array of neuronal populations in the auditory cortex. After the training sessions with these animals are completed, the brain of these animals undergoes histological analysis to ensure that the recordings were in the correct target area, and we can then analyze how neural firing changes as the animal performs the discrimination tasks.

Currently, there is a project underway to optogenetically suppress the auditory cortex of mice from cohort 2 that learned the AM discrimination task. This will enable us to test the necessity of the auditory cortex in performing amplitude modulated sound discrimination tasks.

Since we know that mice can learn the AM and frequency discrimination tasks in a freely moving set up, we can also create additional experiments where we implant electrodes into a naive cohort and train them to perform either task in a freely moving rig. This would then enable us to track how the auditory cortex of these mice changes throughout the learning process and will enable us to better understand how auditory learning works in a mouse model.

In addition to these experiments, we can continue to perfect our training model by streamlining the habituation process for the freely moving rig setup and by investigating if mice can learn additional sounds that hold relevant features for speech sound learning.

Hopefully through these future experiments, we can gain a better understanding of how the auditory system processes novel sounds and how neural speech coding develops.

Bibliography

Ehret, G. and Riecke, S. (2002). Mice and humans perceive multi harmonic communication sounds in the same way. Proceedings of the National Academy of Sciences of the United States of America, 99(1):479–482

Gidon, A. et al. Dendritic action potentials and computation in human layer 2/3 cortical neurons. *Science* **367**, 83–87 (2020).

Harris, K., Bartho, P., Chadderton, P., Curto, C., de la Rocha, J., Hollender, L., Itskov, V., Luczak, A., Marguet, S., and Renart, A. (2011). How do neurons work together? Lessons from auditory cortex. Hearing Research, 271(1):37–53

Jaramillo, S., & Zador, A. M. (2014). Mice and rats achieve similar levels of performance in an adaptive decision-making task. *Frontiers in Systems Neuroscience*, *8*. https://doi.org/10.3389/fnsys.2014.00173

Larkum, M. E., Nevian, T., Sandler, M., Polsky, A. & Schiller, J. Synaptic integration in tuft dendrites of layer 5 pyramidal neurons: a new unifying principle. *Science* **325**, 756–760 (2009).

Leaver AM, Rauschecker JP. Cortical representation of natural complex sounds: effects of acoustic features and auditory object category. J Neurosci. 2010 Jun 2;30(22):7604-12. doi: 10.1523/JNEUROSCI.0296-10.2010. PMID: 20519535; PMCID: PMC2930617.

O'sullivan, C. P., Weible, A. P., & Wehr, M. (2020). Disruption of Early or Late Epochs of Auditory Cortical Activity Impairs Speech Discrimination in Mice. *Frontiers in Neuroscience*, *13*.

Recanzone, G., Schreiner, C., & Merzenich, M. (1993). Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *The Journal of Neuroscience*, *13*(1), 87–103.

Polley, D. B., Steinberg, E. E. & Merzenich, M. M. Perceptual learning directs auditory cortical map reorganization through top-down influences. *J. Neurosci.* **26**, 4970–4982 (2006).

Porter, B. A., Rosenthal, T. R., Ranasinghe, K. G., & Kilgard, M. P. (2011). Discrimination of brief speech sounds is impaired in rats with auditory cortex lesions. *Behavioural Brain Research*, *219*(1), 68–74.

Town, S.M., Wood, K.C. & Bizley, J.K. Sound identity is represented robustly in auditory cortex during perceptual constancy. *Nat Commun* **9**, 4786 (2018).

Wang, M., Liao, X., Li, R. *et al.* Single-neuron representation of learned complex sounds in the auditory cortex. *Nat Commun* **11**, 4361 (2020).

Weinberger, N. Specific long-term memory traces in primary auditory cortex. *Nat Rev Neurosci* **5**, 279–290 (2004).

Wolfe, J. M., Kluender, K. R., & Levi, D. M. (2020). *Sensation & perception*. Sinauer Associates: Oxford University Press.