

## **A. Project Description**

### **1. Project information:**

**Title:** Brain Circuitry Underlying Hearing and Emotions

**Principal Investigator:** Jeffrey Wenstrup, Ph.D., Professor

**Co-Investigator:** Sharad Shanbhag, Ph.D., Research Associate Professor

**Location:** Department of Biomedical Sciences, NEOMED

### **2. Abstract**

Our work investigates neural mechanisms underlying the process by which emotional centers in the brain assign meaning to social vocalizations. Past experiments in our lab have found neurons in the amygdala that respond selectively to social vocalizations. We have examined how contextual cues associated with a social vocalization alter the interpretation of that vocalization by the individual and by neurons in the amygdala. We have shown that the behavioral and amygdalar response to a vocalization is differentially altered by exposure to olfactory cues associated with either mating or predators, and by internal levels of brain chemicals. We now propose to examine the mechanisms of selectivity for vocalizations as well as the source of contextual cues in the amygdala. Using electrical recording of nerve cell activity in the amygdala in response to mouse vocalizations, we will describe how different neurons of the amygdala respond to social vocalizations. Using gene insertion, optical imaging, and histological techniques, we will relate the response to vocalizations of amygdala cells to their connections to other brain regions. Using acoustic methods, we record and analyze mouse vocalizations to study how they change with behaviors.

### **3. Background and rationale**

Our long-term goal is to improve the understanding of neural mechanisms that underlie acoustic communication. This project focuses on the amygdala, a structure known for its role in auditory fear conditioning. For this role, it receives auditory input from the thalamus and cortex, contributes to identifying a stimulus as aversive, and provides for appropriate output connections to control emotional responses (e.g., autonomic responses, freezing, affiliative responses). Our view is that the amygdala plays a critical role in acoustic communication through participation in several processes. Dysfunction in the amygdala may be involved in abnormal relationships between acoustic inputs and emotional responses in conditions such as autism, schizophrenia, post-traumatic stress, and tinnitus. We are interested in how the amygdala combines vocalization-specific and contextual information necessary for interpretation of acoustic, and then connects to brain centers that control behavior. This is the next step in understanding how these neural inputs act on amygdalar neurons to influence behavior.

### **4. Goals and objectives**

Our long-term goal is to improve the understanding of neural mechanisms that underlie acoustic communication. This summer project aims to identify and quantify the mechanisms of vocalization-selective responses. We hypothesize that discrimination and selectivity in response to social vocalizations arises from projections of secondary auditory cortical areas. We further hypothesize that inputs from the prefrontal cortex, ventral tegmental area and hippocampus underlie contextual modulation of auditory responses.

## **5. Investigative methods to be used**

To study how information about social communication sounds is analyzed by the basolateral amygdala, we combine vocalization recordings, neurophysiological and imaging analyses of brain activity with histological analysis of the brain. Vocalizations and associated behaviors are recorded with both audio and video techniques. Neurophysiological recordings utilize multi-electrode arrays to record vocalization responses simultaneously from many neurons. Imaging depends on the injection of recombinant adeno-associated virus (rAAV) coding for a calcium sensing protein that fluoresces when a neuron is active. We use this to measure brain activity over several days and as the result of experience and changes in hormonal state. At the completion of recordings, histological preparation and analysis of brain sections will reveal labeled neurons that connect with the amygdala and the location of neurophysiological and imaging recording sites in the amygdala.

## **6. Proposed method of data analysis**

Neurophysiology: Electrophysiological responses will be plotted and quantified off-line. Initial steps will include exporting of raw data for spike sorting, processing of data using spike sorting software and then integration of sorted data with stimulus information.

Anatomy: Slide-mounted and cleared tissue sections will be examined using fluorescence microscopy and compared with state-of-the-art brain atlas tools from Allen Brain Institute. Sections containing fluorescently labeled neurons or fiber tracts will be digitally photographed and the images stored for further off-line analysis. Analysis will include, but not be limited to, counts of cell bodies in areas of interest and reconstruction of projection pathways from the BLA.

## **7. Significance of anticipated findings**

- The results will describe how neural responses to social vocalizations are distributed within the amygdala, as well as how they are affected by sex, hormonal state and experience.
- The results will identify the brain centers associated with emotional expression that receive information from amygdalar neurons.
- The results will identify brain regions that project to the amygdala to modulate auditory responses. This work will explain how specific inputs to the amygdala contribute to behaviors associated with social communication by sound.

## **B. Summer Research Fellow Training/Mentoring**

All research will be conducted in the Acoustic Communication and Emotions Laboratory, which is part of the Department of Biomedical Sciences at NEOMED. The laboratory includes two faculty, a research scientist, and a research associate. The student will work closely with Drs. Wenstrup and Shanbhag and interact extensively with other laboratory members.

*The laboratory emphasizes collaborative interactions, high expectations and enthusiasm.* The group meets in weekly laboratory meetings where ideas are developed, and technical issues and results discussed. Our laboratory has an extensive record of mentoring undergraduate and professional student trainees since 2009. The fellow will interact with members of the Hearing Research Group (HRG). The highly interactive HRG is composed of members of eight hearing

neuroscience laboratories with a wide range of experimental approaches. The fellow would be expected to present a summary of their summer project to this group.

The fellow will be trained in many of the procedures associated with this project, commensurate with their skill and ability. If interested, the student will participate in neural recording experiments, either using electrophysiological or imaging techniques. The student will participate in histological processing and analysis to prepare brain sections for subsequent neural imaging and tracing. The student will also participate in analyzing the results of neural tracing studies and the neural recording data. Experience or expertise in programming (e.g., Python, MATLAB, Java), histology (including processing of tissue and microscopy) or CAD/CAM is desired but not required. From work in our lab, the student will gain experience in identifying brain regions, histological and electrophysiological techniques, and data analysis.

For more information on this project please contact

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