A Multisensory Gamma Entrainment Apparatus for Rodents

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***Abstract* — New treatments are needed for detrimental neurological diseases such as Alzheimer's disease and stroke. Certain auditory and visual stimulation has been shown to reduce neuropathology in rodents. The apparatus discussed in this paper allows researchers to expose rodents to multisensory stimulation at various frequencies while allowing the rodents to remain in their home cage. An attempt to create a noninvasive and wireless EEG for rodents is also described. The design consists of gold cup electrodes, a premade printed circuit board, coaxial cables, a GUI, and a flexible suit that fits on a rat. More testing is needed to complete a functional noninvasive EEG.**

I. Introduction

Neurological disorders such as stroke and Alzheimer's disease cause suffering across the world. Recent research suggests that specific patterns of synchronized multisensory (auditory and visual) stimulation can improve cognition and reduce pathology in mouse models of Alzheimer's disease [1]. Equipment that exposes rodents to user set patterns of synchronized auditory and visual stimulation is necessary for further studying the effects it has on the central nervous system. The equipment should also include an electroencephalogram (EEG) to monitor rodent brain activity as stimulation occurs. In this paper, a design for an apparatus that exposes rodents to multisensory stimulation and measures their brain activity is discussed.

II. Background

The design allows for the multisensory stimulation to be user set to pulse at frequencies that are a multiple of 10 Hz and are between 20 and 80 Hz (inclusive). It can also be set to a random frequency mode, in which a frequency is randomly determined by a uniform distribution from 20 to 80 Hz at the beginning of each pulse. Therapeutic benefits of specific frequencies can be explored, and the random frequency mode can be used for control groups. The 40 Hz frequency stimulation is expected to be used because it is the frequency at which gamma entrainment therapy occurs.

The immediate effects of multisensory stimulation can be observed with an EEG. The main purpose of the EEG is to verify that the brain waves resulting from gamma entrainment are occurring. The EEG is designed to be noninvasive, which removes the need for time intensive and dangerous surgeries required for invasive EEGs. A circuit board from OpenBCI called the Ganglion, an OpenBCI graphical user interface (GUI), and gold cup electrodes are used for recordings. A rat suit was made to hold the circuit board and secure the electrodes in place. The design also requires the use of electrode gel. The EEG is designed to be easy to use, safe, reusable, and fit rats of different sizes.

III. Design

The minimum requirement for use of the apparatus in an experiment is that the stimuli run as expected. Input to the stimuli is controlled with a dial that is a potentiometer. As the dial is turned, the frequency of the stimuli is changed by an Arduino Uno. The frequency that is set by the user is clearly displayed on an LCD screen near the dial.

The desired properties of the EEG include accuracy, preciseness, and production of data that can be saved. Input to the EEG comes from two gold cup electrodes. One electrode is placed on a shaven rat head and superior to the sensorimotor cortex of the rat. The reference electrode is placed on the side of the head, or elsewhere on the rat. The signal from the electrodes is wirelessly transmitted to a computer via Bluetooth. The EEG voltage versus time graph and fast Fourier transform (FFT) per second can be viewed in the OpenBCI GUI. The signal can then be saved in the GUI for later analysis.

IV. Materials and Methods

A. *Multisensory Stimulation*

The potentiometer controls a voltage that is an input into the Arduino Uno. The Arduino Uno microcontroller was coded to detect eight equally sized intervals of voltage. Seven for the frequencies between 20 and 80 Hz, and one for the random frequency mode. The frequency value is displayed on the LCD, and a loop runs that pulses a square wave current through the LED strip with a duty cycle of about 50%. The light is white, and the auditory stimulation is a 10 kHz sound that turns on at the same time as the LEDs and remains on for 1 ms. The design for the duty cycles was taken from [1]. At the end of each pulse, the voltage input from the potentiometer is checked. The box has no floor, so it can be placed to enclose a rat's home cage that remains within the box during stimulation sessions. The piezoelectric speaker is placed on the ceiling of the box and faces down. The LEDs are wrapped around the box. The box is transparent so rodent behavior can be observed during stimulation. The stimulation box is shown in Figure 1. If components break, function can be maintained without technical engineering knowledge by replacing individual parts.

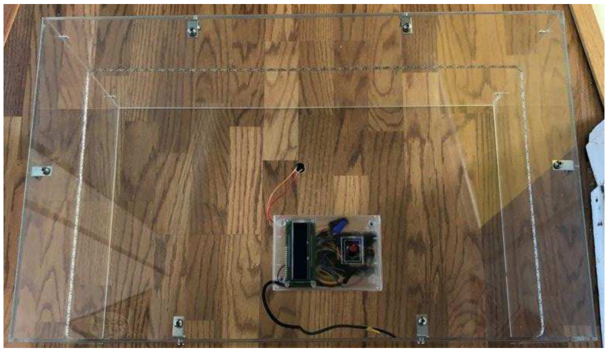

Figure 1. Stimulation Box

B. *Rat EEG*

For EEG testing on a human subject, one electrode was placed at the right visual cortex, and the reference electrode was placed at the left earlobe. The OpenBCI GUI was used to analyze signals. To analyze noise, two electrodes were placed on one human arm to induce a small differential voltage. The suit used to place the electrodes on the rat was made from spandex and Velcro to allow for physical flexibility and use on multiple rats. An unfinished prototype suit was tested on a rat.

V. RESULTS

A. *Multisensory Stimulation*

The frequencies and duty cycles of the stimuli were verified with an oscilloscope and results indicated expected values. With one piezoelectric speaker within the box at the 40 Hz frequency, the amplitude of sound measured within the box was 70 dB. When the piezoelectric speaker was not inside the box, the amplitude of the sound from about the same distance from the speaker outside the box was measured to be about 57 dB. The increase in sound wave amplitude inside the box is possibly due to echoes happening within the box. Outside the box, the measured decibel levels were as low as 50 dB when the piezoelectric speaker was set to pulse at 20 Hz, and as high as 60 dB when the frequency was set to 70 Hz. The intensity of the lights can be controlled with a resister in series with the LED strip. One flaw with the design is that when the dial appears still, the resistances within the potentiometer circuit changes slightly, which can cause the user set frequency value to fluctuate between two frequencies if the dial is not set unequivocally within the boundaries of the interval, which happened only once during testing.

B. *Rat EEG*

Measurements displayed on the GUI for the human EEG resembled those of a typical EEG signal. However, human gamma entrainment, which should be a 40 Hz EEG wave, was not observed with the stimuli, although gamma entrainment has been shown to occur in humans [2].

Before coaxial cables were used, noise due to displacement current from the stimulation circuit was visible in the FFT. Figure 2 shows noise from the stimulation circuit while the 40 Hz frequency was running. After the coaxial cables were grounded and used, noise was reduced (Figure 3).

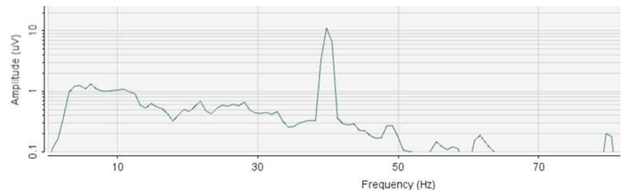

Figure 2. FFT; Noise without Coaxial Cables

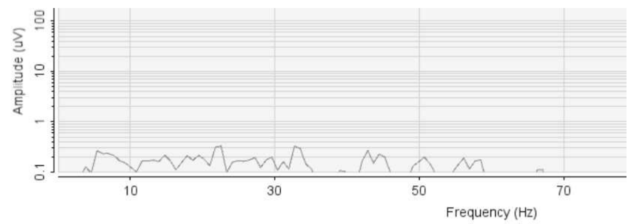

Figure 3. FFT; Noise Reduced with Grounded Coaxial Cables

The prototype EEG suit that was tested fit the rats, although the rats tried to take the suit off, and one rat successfully removed the suit. A more fitting suit was designed to have less material, be more comfortable, and hold the electrodes, but testing was not completed.

VI. DISSCUSSION

The stimulation box works as expected. The stimulation can be run at the correct frequency and is ready for experimentation. The increase in sound amplitude due to the echo may interfere with the intended audio stimulation, which is a problem that may be fixed by padding the walls of the box with acoustic foam. The noninvasive rat EEG is unfinished, but significant progress has been made. The suit must be connected to the coaxial cable gold cup electrodes and tested with a rat.

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