Fear Recognition in Mice based on Neurochat Implantable BCI

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Keywords: Brain-Computer Interface, Neural Signal Acquisition, Fear Response.

Abstract: Establishing the connection between the animal brain and external equipment through the brain-computer interface and realizing the exchange of information between the brain and the outside world is the basis for many imaginations of future science and technology. This project improved the production of the brain-computer interface collection component-Neurochat series, which realized the signal collection from brain waves, to local field potentials and neuron spikes, and successfully identified the fear response of mice.

1 INTRODUCTION

1.1 Brain-Computer Interface

In 2008, neurobiologists at the University of Pittsburgh claimed that monkeys could manipulate mechanical arms to feed themselves by using brain computer interface (BCI) (Velliste 2008). In April 2021, Neuralink, a BCI company owned by Elon Musk, showed the world their practical brain-computer interface technology and automatic implantation of surgical equipment so that a monkey can play video games with his mind. This also provides unlimited possibilities for the future of BCI (Vourvopoulos 2019, Wu 2020, Shi 2018, Tomislav 2018, Chai 2017). Through interdisciplinary research such as neuroscience, signal detection and machine learning, it is popular in the medical and entertainment industries, especially in the field of virtual manipulation (Patil 2008).

At present, the methods of obtaining information by brain computer interface include invasive and non-invasive. Non-invasive is safe for humans and animals, but the acquired EEG signals are not accurate. Invasive type damages the animal brain, but the potential of a single brain cell can be accurately recorded. We improved and fabricated a set of invasive brain computer interface elements neurochat series, which were implanted into the superior colliculus (SC) nucleus of mouse brain through electrodes. In the experimental environment, sound and visual stimuli were used to verify and stably trigger the animal's instinctive defense behavior. According to the collected EEG signals, we can judge whether the mice have instinctive fear. The experimental results prove the effectiveness of the brain-computer interface system made in this project, and provide a basis for the next theoretical research and practical application.

1.2 Fear and Instinctive Defensive Response

In nature, in order to survive, animals have an innate fear of danger signals from the external environment and induce them to make innate behaviors. The generation of this instinctive fear defense depends on the animal's sensory nervous system basically, such as using smell to perceive predator's scent information, using vision to observe the predator's figure, and using the auditory system to perceive predator's sound information.

The instinctive defense response of animals has three main manifestations: Startle, Flight and Freezing. Startle is a short-term startle response caused by high-intensity sound, which is mainly regulated by the cochlear nucleus (CN) located in the lower brainstem and the specific loop is CN-pontine. Flight can be directly induced by noise or light stimulation in the awake state. Freezing mainly

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occurs under the condition of auditory fear. It is rare for mice to induce freezing behavior by simple sound stimulation. The superior colliculus has many advanced functions and is one of the important nuclei in the midbrain. However, for SC research, most of the predecessors focused on vision-related fields. Through the Neurochat brain-computer interface system, we conducted a preliminary study on the role of SC in the fear and instinctive defense response loops in terms of vision and hearing.

2 MATERIALS AND METHOD

2.1 Neurochat BCI System

The overall system architecture diagram is shown in Figure 1.

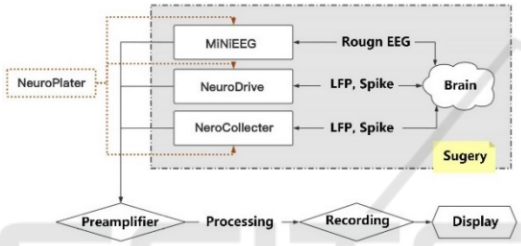

Figure 1: Overall system design diagram.

This project uses NeuroCollector to complete the signal collection with a single fine-tuning electrode. The structure diagram is shown in Figure 2 and the electrode driving operation logic is shown in Figure 3. We will describe the design and production of the Neurochat overall system separately.

Figure 2: Single fine-tuning electrode structure diagram.

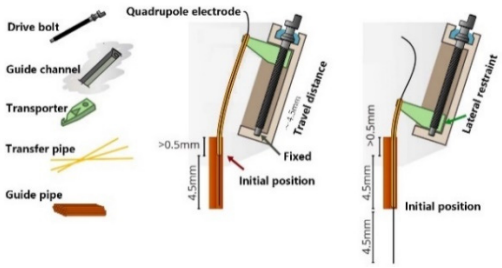

Figure 3: Single fine-tuning electrode driving operation logic.

The recording system we chose is a self-built system based on RHD2000 (Intan, USA).It is a multi-channel recording system and the Intan Technologies RHD2000 Interface software is used for signal acquisition and control. Its software supports monitoring signals from any channel and transfers the collected data to the front-end PC in binary format. Finally, the data file is imported into MATLAB (MathWorks, USA) for subsequent processing and analysis.

2.2 Auditory Stimulation Method

The mouse is placed in a behavior box containing two chambers as shown in Figure 4 and the mouse is free to explore in the behavior boxes on both sides. Two cameras are used to capture the behavior information of the mouse at the same time. When the mice moved freely to the central area of the chamber, they were randomly and non-repeatedly given sound stimulation with an intensity of 30-80db each time, and the behavioral results were recorded and analysed.

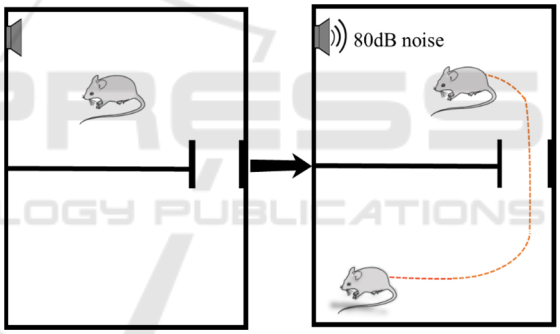

Figure 4: Stimulating behavior paradigm.

2.3 Visual Stimulation Method

For visual stimuli, we adopt the same behavioral paradigm. When the mice move freely to the central area of the chamber, randomly and non-repetitively give looming stimuli with a contrast of 25%-100% each time, record and analyze the behavioral results.

2.4 Surgery

We choose mouse with a body weight of about 20 g, normal hearing, and good condition for operation preparation. Mouse was prepared for surgery within 3-5 days before the experiment. The animal is prepared for surgery as follows: anesthetize with the equipped 1.5% sodium pentobarbital solution or isoflurane. After anesthesia, the mouse head is

depilated with a shaving device and shaving cream, then wiped with alcohol and then smeared with iodophor for disinfection. Use sterile scissors to cut the scalp to an appropriate size to expose the bregma of the mouse. Use a stereotaxic instrument for leveling to ensure that the front and rear fontanelles of the mouse are in a horizontal state. Four skull nails are symmetrically implanted on the surface of the mouse skull for fixation and then locate the SC.

Figure 5: Mouse implanted with NeuroCollector

The SC location coordinates of the mouse are 2.8-4.5mm behind the bregma, and the maximum distance beside the midline is 1.75mm. After marking, the skull is drilled to open the window, the dura mater and pia mater are removed and stop bleeding. After the exposed area is clean and free of blood clots, the electrode is slowly lowered at a speed of 10 micrometers per second and inserted into the nucleus of SC. Use biological silica gel and white wax to seal the skull window, and then use dental cement to paste a shallow circle on the skull nail and the surface of the skull. After drying, the whole adjustable electrode device NeuroDrive or the single adjustable electrode device NeuroCollector is pasted and fixed on the mouse skull with dental cement to ensure that the device can remain stable and does not produce relative displacement with the skull due to the free movement of the mouse. Figure 5 shows a mouse successfully implanted with NeuroCollector.

3 RESULTS

3.1 Auditory Response Verification Experiment

Since the SC receives a large number of axon inputs from the auditory nucleus, we first verified the mouse's auditory stimulus response. In a sound-shielded room, we perform sound stimulation on mice: give different frequencies of pure tones or noises, and record neurophysiological activities at the same time

As shown in Figure 6, A is the recorded real-time data, which reflects the action potentials evoked by 10 auditory stimuli. B is the sum of action potentials accumulated by all stimuli (PSTH diagram: histogram of time distribution after stimulation). C is a scatter plot, the horizontal axis is the time and the vertical axis is the length of the stimulus sound, and the corresponding scatter plot of the complete sound sequence stimulus is drawn.

3.2 Auditory Response Verification Experiment

We found that high-intensity noise could very stably induce the instinctive defense behavior flight of awake mice. When the mouse is out exploring, giving 80db and 70db sound stimulation can stably induce the mouse's flight behavior. When the sound intensity is 60db, the probability of flight is 67.5%; when the sound intensity is 50db and 40db, the proportion of flight is 37.5%; when the sound intensity is 30db, the mouse will not show the defensive behavior of flight, but maintain the state of free movement.

At the same time, as the stimulus intensity decreases, the maximum speed of the mouse in the process of generating a flight also decreases in a stepwise manner. This indicates that as the intensity of the stimulus increases, the mice show stronger and stronger defensive behaviors, and auditory stimulation is more likely to induce the mouse to produce flight. Figure 7 is an analysis diagram of the trajectory and speed of the mouse after hearing 80db sound stimulation. In subsequent experiments, we used 80db sound intensity for stimulation.

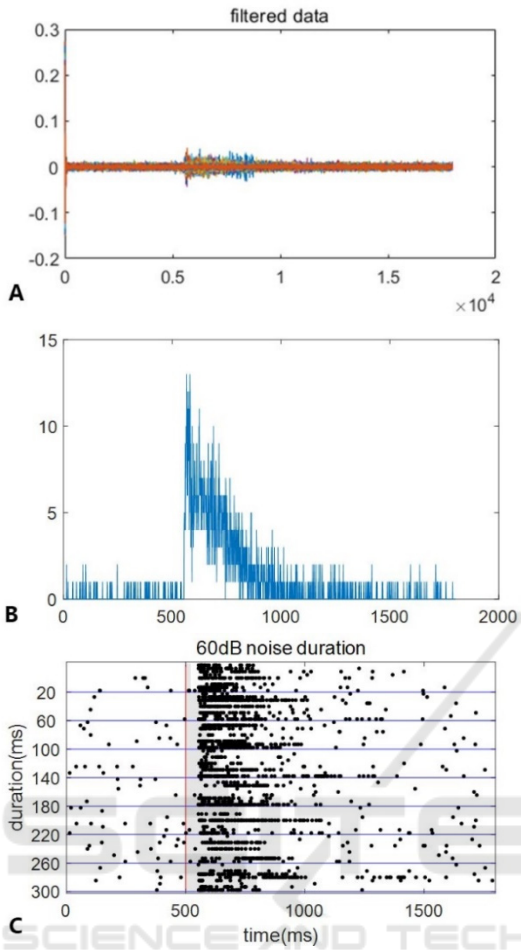

Figure 6: An example of data analysis of neuron response to noise in SC.

We record the changes of SC neuron activity signals after mouse received auditory stimulation and count the number of action potentials within 3ms, as shown in Figure 8. During the recording process, the intensity of the sound stimulation we gave is 80db and the duration is 5s. In the sound interval, the mice developed instinctive fear, which caused defensive behaviors, and a large number of neurons were fired. After the sound was over, the mouse completed their defense. The calcium signal quickly weakened and returned to the baseline level, that is, when the mouse heard noise stimulation and produced defensive behaviors, SC neurons fired in large numbers, which was related to the instinctive fear emotion.

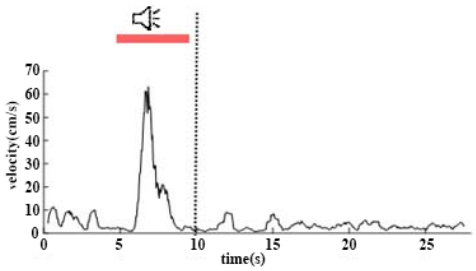

Figure 7: The speed analysis graph of the mouse after hearing 80db sound stimulation.

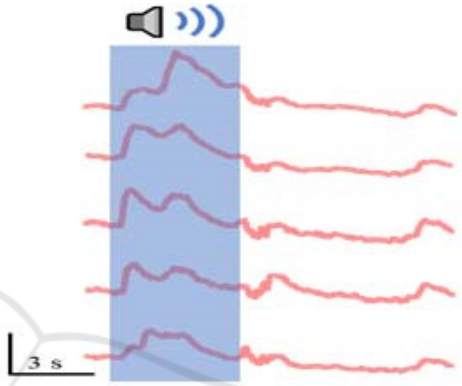

Figure 8: Cell firing and change rate in SC after sound stimulation to mouse.

3.3 Visual Instinct Fear Experiment

For the visual system, giving different speeds and contrasts of looming (visual approximation) will also induce the flight and freezing behavior of mice. When a mouse is out exploring, no matter what the contrast of the looming stimulus is given, it will make the mouse have flight behavior. When the mouse is in a corner, given the looming stimulus, there is a 60% probability that the mouse will have a freezing behavior, 40% of mice will have flight behavior. At the same time, as the intensity of the stimulus decreases, the maximum speed during which the mouse generates a flight also linearly decreases. This shows that as the stimulation intensity increases, the mice show stronger and stronger defensive behaviors, among which the flight behavior tendency is more pronounced. Figure 9 is an analysis diagram of the trajectory and speed of the mouse after being stimulated by looming with a contrast of 100%. In subsequent experiments, we gave a looming stimulus with a contrast of 75%.

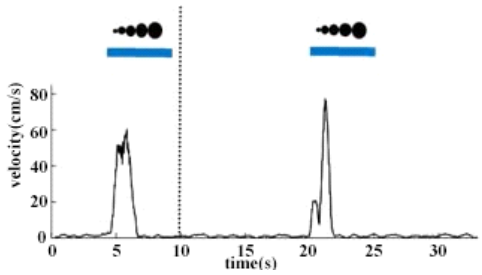

Figure 9: Analysis of the trajectory and speed of the mouse after being stimulated by looming with a contrast of 100%.

Next, we recorded the changes in the SC neuron activity signals after the mouse is stimulated by visual looming and the results are shown in Figure 10. During the recording process, we give looming stimulation with a contrast of 75%, similar to the result of auditory stimulation. In the stimulation interval, the mouse produced flight/freezing defense behavior, and the signal rose rapidly. After the stimulation, the mouse completed their defense. In behavior, the calcium signal quickly weakened and returned to the baseline level. That means, when the mouse felt visual stimulation and produced defensive behavior, SC neurons were fired in large numbers, which indicates that SC is related to visually evoked defensive behaviour.

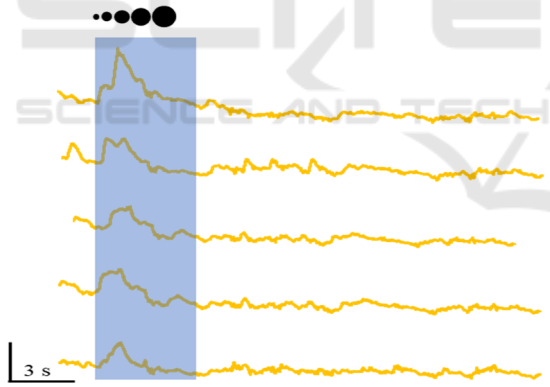

Figure 10: Cell fire and change rate in SC after looming stimulation to mouse.

In the next step, we will establish a Support Vector Machine (SVM) model, take neuro-electrophysiological signals as the input, and take whether the mouse produces defense response as a criterion for fear, trains SVM and analyzes the mouse's fear emotions. Using f1 score as the standard, evaluate the analytical effect of the model, complete the two-classification problem, and realize whether the mouse has fear or not and predict the subsequent response.

4 CONCLUSIONS

Through the self-improved brain-computer interface Neurochat, this project realizes the signal acquisition requirements of brain computer interface from EEG to local field potential and then to neuron spike potential, and successfully analyzes the instinctive fear of mice. It is proved that our system scheme is feasible and effective.

The various methods integrated by the project system have mature theoretical foundations, and there is a huge market space for applications in the fields of neurocognitive science, electrophysiology, and brain-computer interface. The field of brain-computer interface is known as the highway for communication between the human brain and the outside world (Belwafi 2018). It is the key core technology of the latest human-computer interaction and human-computer hybrid intelligence, and its application prospects are unlimited. Using Neurochat series can provide experimental evidence in a multi-faceted, multi-layered, and humanized manner, and provide help for the further application of brain-computer interfaces (Lee 2010, Gao 2020).

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