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Article

Novel Behavioral Test to make Changes in the response of neurotransmitters in the brain of Alzheimer's (Auditory Stimulation)

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ABSTRACT

Clinical medicines that act on neuro mediator-related locations are virtually always used to treat neurological illnesses. This suggests that intercellular chemical signaling has a significant impact on how brain networks function. Over the past 25 years, a range of micro-voltammetric sensors and methods have been created to examine neuro mediators in intact brains in vivo. Objective: A more comprehensive understanding of the rat's brain and the response of neurotransmitters in the brain aid in future clinical studies Design: In this experiment, we will add a sound source with a frequency of 950 Hz to 1100 Hz to the Morris water maze to measure the auditory memory of the rat. The experiment was conducted on 6 rats (control) and 6 rats (induced by aluminum chloride)**.** It was observed that the rats' memory improved, and a change in their behavior and response was better. Can some diseases of the nervous system be treated with sound effects? Does sound affect the movement of neurotransmitters in the brain? We will discuss in this experiment the changes that have been observed in order to answer all these questions. Results: before modification Induced rats by aluminum chloride were placed on a quarter of the platform for seconds less than after modification (add a sound source). the control before modification Control rats were placed on the platform for fewer seconds than after modification. (Add a sound source).

Keywords: 950 Hz; 1100 Hz; Frequency; long-term memory; learning or memory.

1-Introduction

Alzheimer's disease (AD) is a long-term neurodegenerative condition distinguished by cognitive and memory deficits. About 50 million people worldwide suffer from AD, which is characterized by deficits in cognition, memory, and other types of cognitive dissonance. [1].

In this study, the change in rat behavior upon exposure to an external stimulus was presented in an experiment demonstrating learning and memory capacity (the modified Morris Water Maze (MWM) test). The crossing counts were carefully tallied and recorded, making this significant. And it aids in the development of fresh therapeutic approaches for a variety of neurological ailments that have a brain chemistry deficiency. If clinical trials become more developed in the future, especially for Alzheimer's disease, Sound-induced analgesia depends on a low signal-to-noise ratio (SNR) relative to ambient noise in rats. We looked at whether consonant sounds, such as enjoyable music for humans, would have analgesic effects in rats with inflammation-related discomfort brought on by an injection of complete Freund's adjuvant (CFA) into the hind paw. Because loud noises (over 75 dB) force rats to run away [2], the main findings in this paper, improve the performance of the Morris maze device (a new idea) and contribute to the search for new treatment methods for the central nervous system.

2. Experimental

2.1. Materials and chemicals

$AlCl_3$ was attained from Sigma-Aldrich, USA.

2.2. Experimental animals

The Wistar rats used in this experiment weighed between 130 and 150 g.

All rats were confined in a clean environment underneath a tidy box with a temperature of 22-24 °C and a 12-hour cycle of light and darkness. Throughout the trial, free access to food and water was given to every animal.

2.3 Experimental design

In groups A and B, all animals were divided into two categories. Animals in group A (control group, n = 6) are kept under control and fed a normal diet without receiving any treatment. Group

B (indicating that group n = 6) To trigger AD in rats, 175 mg/kg of $AlCl_3$ is administered orally for 25 days, followed by 0.9% NaCl (5 ml/kg) from the 25th to the 36th day. $AlCl_3$ was dissolved in distilled water and administered orally at a dose of 0.5 ml per 100 g of body weight. 2.4 Modified Morris Water Maze (MWM) Test. The MWM test was used to evaluate the animals' learning and memory. the 175 cm-diameter, 45 cm-deep dark pool. The water was split into four quadrants, with the northeast representing the first, the southeast the second, the southwest the third, and the northwest the fourth.

In the third quadrant, there was an unnoticeable spherical platform with a 10 cm diameter. Skimmed milk was used to make the water opaque, and the platform was positioned 1 cm below the surface. Animals could use the three signals to determine the paths to the platform because they were mounted to the walls surrounding the pool. The video recorder was manually utilized to track the speed, duration, and path of the rats. Install a frequency generator in the target quadrant that emits frequencies of 1000 Hz. The crossing numbers, its intended location quadrant time, the opposite quadrant time, and all other data have been meticulously collected and analyzed. As explained in **Figure 1**.

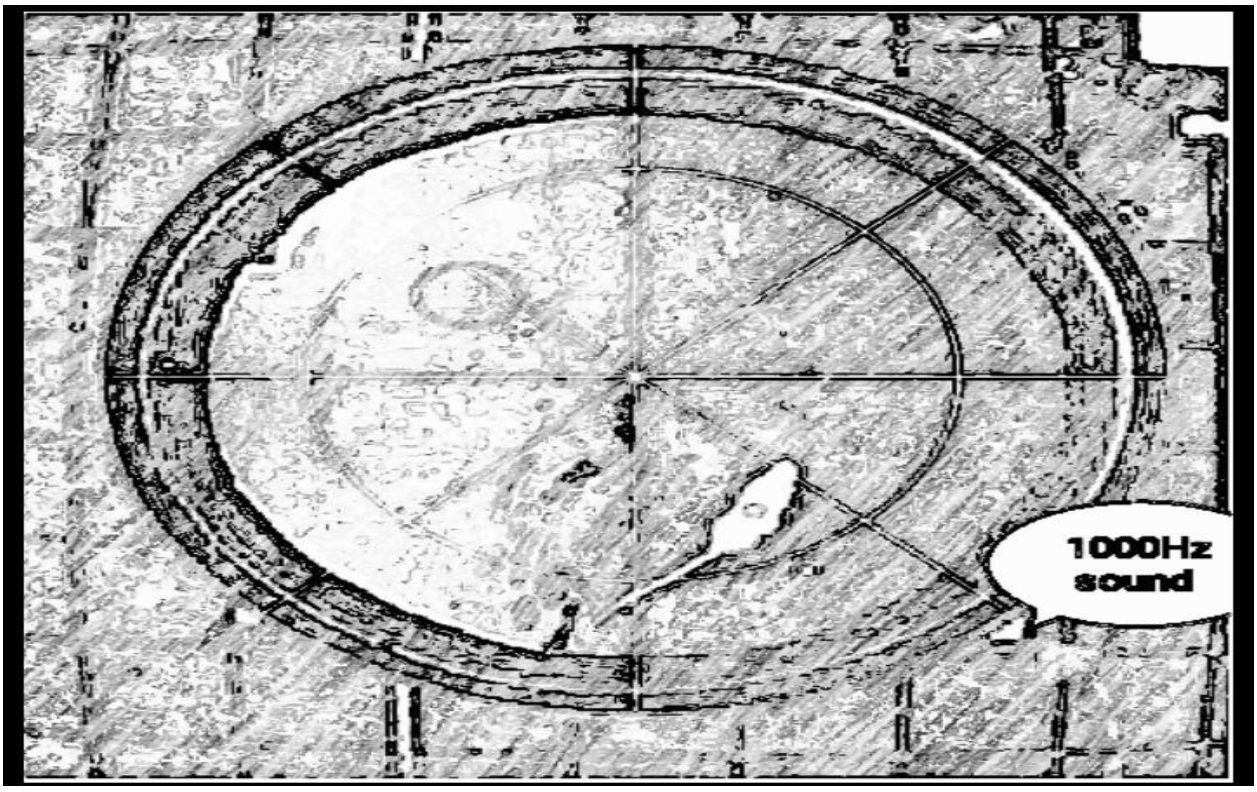

Figure.1. Description of the modification to the device and where to add the sound source.

3-Results

Sound frequency Improves the performance of the Morris maze device, improves learning and memory in rats, and helps manage Alzheimer's disease.

Rats' duration in the target quadrant after the modified MWM test was observed to increase because sound frequency changes the amount of tumor necrosis factor-alpha, superoxide dismutase, Ach, and NF-KB in the brain. measure these parameters, TNF-a conc. In control rat 1, 69.17 pg/mg, and in control rat 2, 62.69 pg/mg (before adding sound frequency 1100 Hz to the Morris water maze), but after adding sound, 55.42 pg/mg and 51.37 pg/mg, respectively. While inducing rat 1. 260,06 pg/mg and inducing rat 2. 224,30 pg/mg (before adding sound frequency 1100 Hz to the Morris water maze), but after adding sound, 190,87 pg/mg and 178,56 pg/mg, respectively.

SOD in control 1. 3,28 u/mg/protein and in control 2.3,97 u/mg/protein (before adding sound frequency 1100 Hz to the Morris water maze), but after adding sound 3,55 u/mg/protein and 4 u/mg/protein, respectively. While the induced rat 1. 0,95 u/mg/protein and the induced rat 2. 0,89 u/mg/protein increased to 2,89 and 1,91 u/mg/protein, respectively, when adding sound frequency 1100 Hz to the Morris water maze, Ach in control rat 1, 3,39 ng/mg, and control rat 2, 3,67 ng/mg before modified MWM, but after modified MWM, 3,77 ng/mg, and 3,85 ng/mg, respectively. while in induced rat 1, 66,2 ng/mg and in induced rat 2, 58,9 ng/mg after modification became 11,38 ng/mg and 16,99 ng/mg, respectively.

NF-KB in control rats 1.1, 41 ng/mg, and in control rats 2 (1, 25 ng/mg) before modified MWM, but after modification 1, 43 ng/mg and 1,38 ng/mg, 38 ng/mg respectively. While in induced rats 1. 4,08 and induced rats 2. 4,49 ng/mg this before modification, while after modification, become 2,85 ng/mg and 3,14 ng/mg, respectively.

Table 1. Effect of sound frequency 1000 Hz on the control group, on the time spent in the target quadrant (sec) in the Morris Maze Test.

Rat number	Before (Sec)	After (Sec)
1	32	30
2	27	42
3	25	39
4	34	40
5	24	34
6	23	33

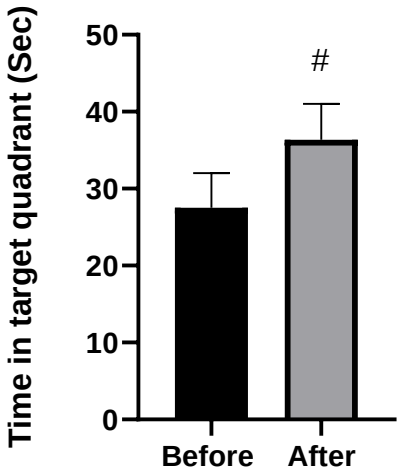

Figure 2. Effect of sound frequency on the behavioral activity of the rats in the control group. # Significant vs before, $P < 0.05$ using unpaired t test. Statistical analysis was carried out using GraphPad Prism 8.0.2.

Table 2. Effect of sound frequency on induction group, on the time spent in the target quadrant (sec) in the Morris Maze Test.

Rat number	Before (Sec)	After (Sec)
1	18	25
2	12	29
3	24	34
4	11	24
5	10	26
6	29	40

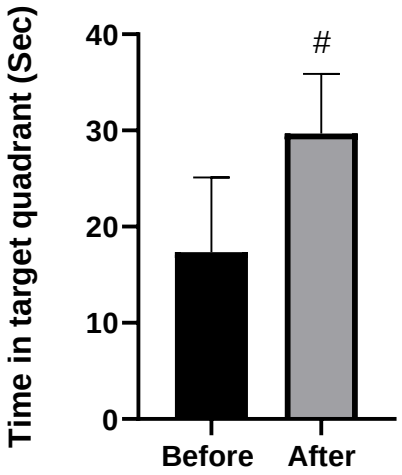

Figure 3. Effect of sound frequency on the behavioral activity of the rats in the induction group. # significant vs before, $P < 0.05$ using unpaired t test. Statistical analysis was carried out using GraphPad Prism 8.0.2.

4. Discussion

The mineral element aluminum (Al) is constantly present in the environment. Since the brain is so sensitive to oxidative damage, it is a primary target of aluminum poisoning. As a result, identifying medications or natural remedies that protect against Al-mediated neuronal cell death is a potent method for both treating and preventing neurodegenerative diseases. Rats treated with Al showed a decline in memory and learning. [3] Aluminum chloride suppressed TNF-a, SOD, NF-KB, and Ach. [1] The cerebral cortex was shown to have decreased glucose oxidation and glutamatergic and GABA neurotransmitter cycling. [4] The Association of Tumour Necrosis Factor- and Myeloperoxidase Enzyme with Severe Asthma is a nonsignificant variation of two biomarkers. [5]

A study from 2019. While not statistically significant, 432 Hz tuned music was linked to somewhat lower mean (systolic and diastolic) blood pressure values, a significantly lower mean heart rate (4.79 bpm, $p = 0.05$), and a slightly lower mean respiratory rate (1 r.a., $p = 0.06$). The subjects were happier and more engaged with their music listening after the sessions in which they

listened to music set to 432 Hz. [6] Therefore, many effects on humans and animals are due to sound frequencies.

Through the results of the study, we find that the modification in the device and the addition of a sound source lead to a change in the behavior of the rats and their memory, and this proves the hypothesis that changing the sound frequencies helps in the management of Alzheimer's disease and stimulates a change in brain chemistry.

5. Conclusion

The data suggest that the time spent by rats in the target quadrant after the modified MWM test increased. This means an improvement in learning and memory in rats as a result of the effect of frequencies on the brain. Alzheimer's disease may have been improved by certain sound frequencies. Additionally, we observed an improvement in the learning and memory of the control rats. Noise at different frequencies can change the behavior of rats. It can also change the human brain.

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- **Conflict of Interest**

The authors declare no conflict of interest.

6. References

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