

A Study of Transcranial magnetic stimulation For Extinction about Early Traumatic Memory Description

Zhenzhen Xu

Inner Mongolia University of Science and Technology, Baotou Medical College, China

Abstract: Individuals will experience strong traumatic memories after traumatic events such as earthquakes, car accidents, or loss of loved ones, the most common of which is fear memory. In this experiment, a multi-sensory compound stimulation model (electric stimulation + picture) was used as the conditional stimulus, and the skin electrical response was used as the index of fear response. The effect of retrieval-extinction paradigm on the conditional fear extinction was tested. In addition, high-frequency rTMS was introduced as a treatment. To explore the therapeutic effect of TMS on conditional fear, with the aim of providing new measures for the treatment of PTSD.

Keywords: Retrieval-extinction paradigm; Conditional fear; TMS

Publication date: May, 2020

Publication online: 31 March, 2020

***Corresponding author:** Zhenzhen Xu, zhaogechong@xyzrgroup.com

The experimental results showed that the subjects successfully acquired and regressed the conditional fear, and did not find that the conditional fear recovered during the Recall stage, but TMS failed to function effectively. Finally, based on the experimental results, the effect of the elimination of paradigm intervention and the use of TMS were discussed. The shortcomings of this study were summarized and the future research directions were prospected.

1 Background

Traumatic (fear) memory is defined as a memory that causes the individual's mental, emotional, cognitive and physiological abnormalities, and it is the core

memory type of PTSD (Post-traumatic stress disorder) carries when it damages individuals' psychological and cognitive functions. Transcranial magnetic stimulation, TMS, is a type of mental stimulation that uses an attractive field to cause electric flow at a specific area of one's brain. TMS was at first used to explore nerve conduction, and a device for brain mapping, as a test for neuronal systems, and as a modulator of brain function.

The current mainstay of treatment for PTSD relies on psychopharmacological and trauma-focused psychological interventions. These interventions are useful, but some patients fail to respond. There are recent studies that aim to facilitate exposure-based psychological treatments applying means such as virtual reality or the partial NMDA agonist D-cycloserine. The broadly accepted neurobiological model for PTSD considers it as a stress-induced fear circuitry disorder.

2 Methods

2.1 The practical operation of defining MT

In order to begin a motor threshold determination procedure, turn on the motor evoked potential (MEP) model on the TMS machine and attach the figure-of-eight coil on the patient's head is necessary. Besides, for the motor threshold determination procedure, one will need a treatment cap as an assistant position system to locate the approximate area where M1 is situated. For patients who are anxious about the procedure, applying a few stimulations to the back of the arm is helpful to get the patient familiar with the stimulation.

2.2 The Brainsight TMS navigation system

The Brainsight TMS navigation system is a comprehensive tool that enabling a TMS coil to be located over a specified target location based upon an

individual's image generating from fitting a big database of numerous skull patterns. The generating image on the TMS screen is a 3D curvilinear reconstruction of the brain. The system is Effectively assisting the operator to locate the specific location of the brain and save time that is wasted in the inaccurate search for the location.

2.3 Procedure and Participant

6 participants. One participant understood the wrong experimental task, and one participant failed to acquire the fear, so the effective test was 4. Subjects were right-handed, with no physical illness and mental disorder, normal vision or corrected visual acuity, no color blindness, no hearing impairment, and had not participated in similar situational experiments before. Normal work and rest were maintained during the two days of the experiment to rule out the deviation of the experimental subjects. Before the start of the experiment, the participants were told that during the experiment, a slight electric shock will be applied to the arm. The use and strength of the electric shock instrument are scientifically assessed and will not cause any harm to the human body. If there are any symptoms in the experiment, you can terminate the experiment at any time. All information and data related to the subject will be kept strictly confidential. The subject must sign the informed consent form after understanding the situation. Participants were randomly assigned to two groups, TMS treatment group and behavioral control group.

2.4 Research design

This study used experimental method. Mixed design. The inter-group variables were treated by two kinds of experimental treatments (TMS treatment group, behavioral control group), that is, two methods were used to intervene in fear memory; the intra-group variables were experimental time variables, that is, all subjects were subject to conditional fear acquisition. The dependent variable of the experiment is the level of fear response of the subject.

The behavioral control subjects were treated in the same laboratory using the same experimental procedure as compared to the TMS treatment group. In order to avoid the impact of the experimental materials on the subjects, all materials in the experiment will be balanced.

3 Results

3.1 The first day of fear acquisition

For the data in the acquisition phase, The t-test of SCR values between CS+ and CS- was significant ($P<0.05$). This indicate that all the subjects successfully acquired fear. The t-test of SCR values between the experimental group and the control group was not significant ($P>0.05$). There is no significant difference in the conditional fear learned between the two groups.

3.2 The first day of the extinction phase

For the data of the extinction stage, the SCR average value of the two groups of subjects in the acquisition stage was used as the skin electrical index of fear acquisition, and the SCR average value of the extinction stage was used as the skin electrical index of fear extinction, and the two values were subjected to t test. The SCR values of the acquisition stage in the experimental group and the control group were significantly different from the SCR values of the extinction stage ($P<0.05$), and the extinguished SCR values were smaller than the acquired SCR values, which indicating that the fear extinction of the two groups was successful.

3.3 The second day of the Recall phase

The index of fear recurrence was the average of the SCRs of all trials when the experiment was performed on the next day, and compared with the regressed SCR values. The t-test results showed that there was no significant difference in SCR between Recall stage and extinction stage in two groups ($P>0.05$), which indicating that there was no recurrence of fear after extinction; In the Recall stage, there was no significant difference in SCR values between the experimental group and the control group ($P>0.05$), which indicating that there was no significant difference in the extent of extinction between the two groups.

4 Discussion

In this study, multisensory combination stimulation (electric stimulation + picture) was used as a conditional stimulus to examine the effect of retrieval-extinction a single clue (picture) on the extinction of conditional fear memory.

The study found that both the experimental and control groups successfully completed the acquisition and extinction of fear. In the Recall test on the second day, there was no recurrence of fear in both groups, but there was no significant difference in the SCR values between the two groups, which indicating that there was no significant difference in the degree of fear extinction between the two groups. Possible explanations for this result are as follows. First, although both groups of participants succeeded in fear acquisition, the p-value could not indicate the magnitude of the effect, which means that the specific amount of fear in the two groups could not be compared. And the fear of the two groups was successfully extinguished, but it was not possible to specifically compare the degree of fear of the subject's. It should be considered to further analyze the effect amount. Second, because the acquisition method and the extinction method are relatively simple, the subject may have fatigue effect during the experiment, which affects the skin electrical value. Third, when the subjects were treated with TMS, the location of the F4 brain region may not be accurate, or the subjects in the control group were more sensitive, even if they received pseudo-stimulation, it may have a certain effect.

Based on the previous studies, this study used human-subjects to apply the retrieval-extinction paradigm to more complex conditional fear memories, and proved that the retrieval-extinction paradigm using a single stimulus can be attenuated to some extent by the composite. The fear response caused by the stimulus eliminates the conditional fear caused by the compound stimulus cues. However, this study does not clarify how the stimulation is coded in the process of connection learning. The two stimulation cues of electrical stimulation and picture are stored as a mixed stimulus, or as two stimuli which have a connection with the US but exist difference. When the retrieval is activated, a single cues activates one component or both components are activated. The further research is needed in these aspects.

5 Outlook

The retrieval-extinction paradigm is a major breakthrough in basic research in recent years. It

is a new intervention paradigm aimed at “erasing” fear memory based on the theory of memory reconsolidation. At present, foreign scholars have more research on the cancellation of the paradigm of CS, but the research results are controversial. Some studies have found that the CS retrieval-extinction paradigm can rewrite the conditional fear memory and prevent the recurrence of fear (Schilleretal., 2010). And other studies found that the paradigm failed to prevent the recurrence of fear (Costanzi et al., 2011; Kindt & Soeter, 2013). It can be seen that the intervention effect of CS retrieval-extinction paradigm is not stable. Therefore, it is especially important to re-examine the intervention effect of CS retrieval-extinction and explore the boundary conditions of its effects. Compared with the traditional extinction paradigm, CS retrieval-extinction can eliminate the fear and reduce the recurrence rate of fear memory and traumatic memory. It is a new paradigm of trauma intervention that needs attention in the future, and its effect needs to be further tested in clinical practice. Cause compared with laboratory experiments, clinical problems are more complicated. For example, the CS that induces PTSD is more complicated, the US intensity is greater, the fear formation time is longer, and the individual response is stronger. Complex reality factors increase the difficulty of clinical research, and the introduction of the retrieval-extinction paradigm into clinical practice is an urgent research direction.

And the technique of transcranial magnetic stimulation also provides us with a relatively non-invasive treatment. Although the therapeutic effect was not effectively explored in this experiment, according to previous research results and literature review, repeated transcranial magnetic stimulation may enhance synaptic plasticity, or improve neuroelectrophysiology and cerebral cortex excitability by promoting synaptic remodeling. Or to regulate the level of neurotransmitters to improve cognitive function, so in the future you can consider the use of transcranial magnetic stimulation or the use of transcranial magnetic stimulation combined with other treatments (drugs, counseling, etc.) to treat PTSD.