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The psychological effects of minimal electrical stimulations of the amygdala in male rats

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Abstract

The male rats with electrodes implanted in the amygdale with (control) or without daily electrical stimulations (ES) were evaluated for behavioural changes.
The animals in the test group showed significantly lower conflict, struggles, and movements for connection to the setup or trying to exit after ES when compared to the control group. The animals under ES became silent, less active, and compatible other rats without resistance for handling.
These findings showed that ES has induced a conditional state behaviour to the setup like opioids that can induce euphoria. This procedure may be useful for treatment of drug dependence.

Keywords: Electrical stimulation; amygdala; rat; psychologic effects; behaviour.

1. Introduction

Peripheral or central electrical stimulations has been used to treat a large number of nervous system diseases, including movement, psychiatric, and seizure disorders as well as chronic pain syndromes (Faingold, 2008). The approach may be localized electrical stimulation of specific sites within the brain as effective treatments of Parkinson and epilepsy disease (Benabid, et al, 2005, Pereira, et al, 2007). The proposed mechanisms involve changes in the levels of modulator, inhibitory or excitatory function, which influence the neuronal networks within the brain. The initial effect of the electrical stimulation procedure may involve rapid short-term mechanisms, such as ion channel and neurotransmitter-mediated functions (Theodore & Fisher, 2007). It had been shown that transcutaneous electrical stimulation could produce pain relief via mechanisms mediated by endogenous opioids (Stux & Pomeranz, 1991). The Amygdala stimulation has induced euphoria in human subjects (Kellett and Kokkinidis 2004), and may be consistent with intracranial self-stimulation in rats even after the seizure development (Brophy et al, 1993). Amygdala stimulation also provokes fear in human and animal subjects (Gloor, 1992; Goddard, 1964; Nam, et al, 2001).

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Conversely, the emotionality of cats to rat or mouse exposure has been increased following partial kindling of the amygdale (Adamec, 1976). It has been demonstrated that the kindling procedure may increase the incidence of defensive behaviours as enhanced emotionality (Kalynchuk, 2000). The first step to kindling, electrical stimulation has positive and negative motivational consequences.

This, in turn, may have implications for understanding the associative processes that contribute to seizure-related psychological disorders. Temporal lobe epilepsy may be accompanied by paranoid psychosis, an association that has led researchers to assess the role of kindling in fear and anxiety (kellett & kokkinidis., 2004).

In addition, these evidences indicate that electrical stimulation may produce fear, emotionality and anxiety in animal models (Almedia et al., 2006). Based on the above findings about the effects of electrical stimulations on endogenous opioids and induction of euphoria and our previous experience during the kindling procedure that could reduce the animal's activity, we evaluated the psychological and behavioral effects of minimal electrical stimulations of the amygdala in male rats.

2. Material and Methods

2.1. Animals

Adult male Sprague-Dawley rats, 250-300 g, were housed in individual cages with unrestricted access to water and Purina Rat Chow. The rats were maintained in temperature (about 22 °C) and humidity controlled local animal facilities equipped with 12 hours on (7:00 a.m. to 7:00 p.m.), and 12 hours off light cycle. The study was performed in accordance with the ethical standards and principles of laboratory animal care (NIH publication) and laws of animal protection.

2.1. Surgical procedure

The animals were anaesthetised with ketamine (50mg/kg) and lidocaine (10 mg/kg, i.p.) and stereotaxically implanted with bipolar stimulating and monopolar recording electrodes (twisted into a tripolar configuration) terminating in the basolateral amygdala of the right hemisphere (co-ordinates: 2.5 mm posterior, 4.8 mm lateral to bregma, and 7.5 mm vertical to dura). The incisor bar was fixed 6 mm above the intra-aural line. Electrodes (stainless steel, Teflon coated, 0.11mm diameter, A-M System, Inc., Carlsborg, USA) were insulated except at the tips. Two other monopolar electrodes were connected to skull screws, placed above the left cortical surface, as earth and differential electrodes.

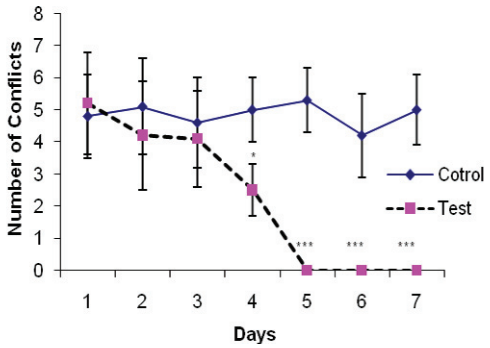
2.3. Electrical stimulation and experimental design

The electrical stimulation procedure was started 10 days after implantation of electrodes. The animals were stimulated daily by 2 second of 100 Hz, biphasic square wave pulses of 0.5 ms per half wave. During the first stimulation session, minimum stimulation threshold (AD threshold) was determined with an ascending series of 25 μA incremental stimulation and 5 minute intervals until at least 5 sec AD recording was achieved as previously described (Saberi et al., 2008). After electrodes implantation the in amygdale and skull the male rats were allocated in two different groups (n=5-7 per group) including control group (without receiving electrical stimulations and test group which received daily electrical stimulation after connection to the setup. The behaviours including the conflict for the connection to the setup, movement distance, struggles for freedom from the cage and the time spend for connection to the setup were determined in each animal quantitatively. Also, total activity, incompatibility, aggression, irritability, conditioning were evaluated before and after connection to the setup for both group.

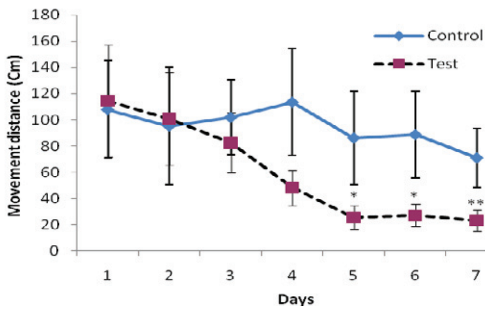
3. Results

The animals in both test and control groups showed high defensive behaviours against connecting to the setup such as struggles, conflicts and rapid movements and craving at the first trial before stimulation.

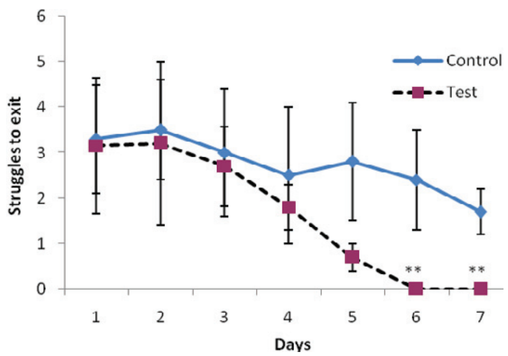
While there was no difference between the pre and post connection of the animals to the setup in the control group, the electrical stimulation induced significant behavioural change in the test group. After electrical stimulation the defensive behaviours defined as struggles for delivery or conflicts decreased significantly in the test group (P<0.001) and the conflicts for connection to the setup reached to the zero during the last three days (fig, 1).



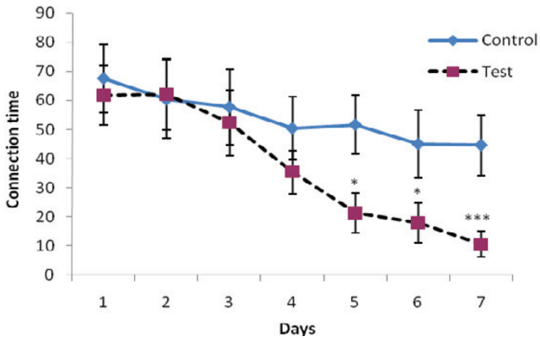
As far as the test group was concerned, although there was a downward trend in the amount of the animal's movements till 4th day with a none significant increment in the control and it fluctuated during the rest of the period. In general the movements became lesser (and slower) but had no significant change in control group. Conversely, the animal's activity and movements after stimulations were significantly (P<0.01)less than before stimulation on day 1 of the test group or in comparison to the control group (fig. 2).



The trying or struggles of animals to exit from the plexy glass cage in the control group was initially increased slowly, and then it was reduced but had no significant change when compared to the first day. Conversely, in the test group exit trying after electrical stimulations underwent a slight decline till the 6th day when it reached to the zero with significant difference (P<0.01) in comparison to the first day of the test or control groups (fig. 3).



Although, the total time spend for the connection of the animals to the setup was reduced for both control and test group, but the difference was not significant for control group when compared to the first day value. Conversely, in the test group the connection time was reduced more sharply during the stimulation procedure and showed significant difference (*P*<0.001) in comparison to the control group (fig. 4).



A wonderful behaviour of some rats was singing and remaining waited in constant state to receive the stimulation without any movement and handling of these animals was very easy and need not protection or glove against biting as was need at the first time or in control. In addition the animals under ES became silent, less active, without incompatibility with other rats in the same box.

Other behavioural changes which were evaluated qualitatively are listed in the table 1.

Table 1: Qualitative evaluation of the rats behaviour following minimal electrical stimulation (ES)

Behaviour type	**Before ES**	**After ES**
incompatibility	high	low
activity	moderate	low
aggression	extreme	Very low
irritability	high	low
Exploratory	extreme	little
conditioning	low	high

4. Conclusion

These results show that electrical stimulation of the basolateral amygdale could produce changes in animal behaviours toward less activity and a silent state with minimum reactivity to the handling or pressures. It seems that they became conditioned for connection to the setup.

Although a wide range of behavioural changes including psychotic behaviour have been observed in temporal lobe epileptics, fear and anxiety-like behaviour have been most often modelled in laboratory animals using the kindling model (Kalynchuk, 2000). The partial kindled cats have displayed increased defensive responses to rats, mice or ES of the ventromedial hypothalamus. In comparison, in this study we applied minimum ES of the amygdale and the behaviours were evaluated in initial stages of kindling procedure. It is suggested that the alterations in interictal emotional behaviour (as observed in the cats) produced by amygdala ES appear to be specifically related to changes in fear or anxiety-like behaviour.

Our study showed that ES causes less resistance to the capture after 4-5 stimulations as indicated by less conflict or struggles for delivery. Previous studies have shown that the kindled rats tested 1 day after the final 100 times amygdale stimulation was substantially more resistant to capture than the sham-stimulated rats. This suggests that interictal emotionality occurs as a result of long-lasting neural changes than short term stimulations without production of any seizure (Kalynchuk, et al, 1999). As a result short term ES may produce more calming and conditioning state than fear and anxiety as shown in long term studies.

The advantage of our study is the assessment of behavioural changes at a stage in kindling before afterdischarges have become generalized. However, because the animals received few stimulations, the findings not directly relate to temporal lobe epilepsy. In addition, although the results of studies of short-term amygdala kindling have documented a wide range of changes in emotional behaviour, they are not consistent with our findings and short term ES more induced calming instead of fear or anxiety.

It has been reported that amygdala stimulation could induce euphoria in human subjects, and clinical experiences have shown that patient requested more ES after the first or second trials. These finding are more related to the release of endogenous opioids which can induce euphoria and a favourite calming (Stevens et al, 1969). This effect is consistent with intracranial self-stimulation in rats even after the seizure development (Brophy et al, 1993). The motivational consequence of the ES observed in this study may be more related to the release of endogenous opioids than other neurotransmitters such as dopamine which has involved in psychotic or emotional behaviours (Watanabe et al., 1998; Kalynchuk et al., 1999). However, reduction of the activity and movement or reactivity may be the signs of depression, but in such condition the irritability and defensive response will not change or even may be increased. More over, the depression like behaviour has been observed in animal which have received high rate of stimulations (i.e. more than 300 stimulations).

In conclusion, these findings showed that ES has induced a conditional and elevated state behaviour to the kindling setup like opioids that induce euphoria. To find out the exact mechanisms further investigations are warranted. This procedure may be useful for treatment of drug dependence.

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