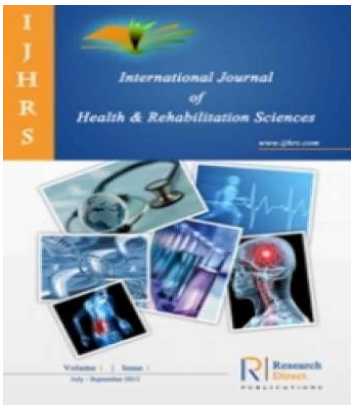

Effect of Brain Computer Interface (BCI) in stress induced loss of cognition in hippocampus of wister albino rats

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ABSTRACT

Background: Brain-computer interface (BCI) is a collaboration between a brain and a device that enables signals from the brain to direct some external activity, which interface enables a direct communications pathway between the brain and the object to be controlled. By reading signals from an array of neurons and using computer chips and programs to translate the signals into action. The Magneto encephalography (MEG) is to record the firing of the neuron and absorb the brain activity as the magnetic field travels from region to region with in the brain. It has the potential to enhance the life style of the disabled person. The MEG Brain Computer Interface (BCI) impact on medicine and healthcare now may be subtle but is still revolutionary.

Objectives: The purpose of this study was to develop novel methods and systems for rehabilitation and control of assistive devices using signals from the brain – BCI on motor coding and on neural plasticity.

Materials and methods: The experiment was carried out in 24 albino rats with Magneto encephalography (MEG). All the rats underwent BCI procedure except the first and second group which was exposed to fake intervention. The objective of this proof of concept closed loop BCI experiment was for the subject to control the positive movement of a rat in the radial arm maze to take the food even altered position which was recorded in the system.

Results: An important finding in the present study was the enhancing effect of BCI against neurodegeneration. It shows that these rats achieve to learn the task. It suggests that the BCI activated the neurons in the hippocampus and makes it sufficient for normal acquisition.

Conclusion: Stress induced hippocampal degeneration leads to significant impairment of cognitive functions especially in calculation, immediate recall and attention. In this present study, stress induced loss of cognition was studied by activating the neurons of the hippocampus by grid electrodes of BCI system.

Keywords: Magneto encephalography (MEG), glucocorticoid, hippocampal formation & grid electrodes.

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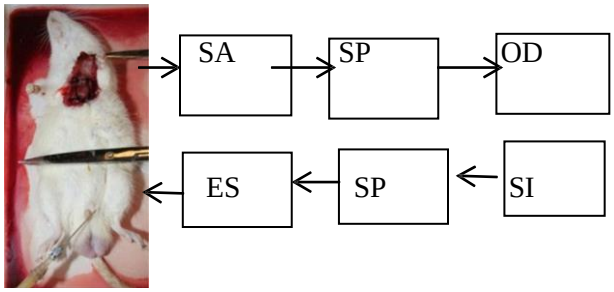
INTRODUCTION

Brain computer interface (BCI) in learning and spatial memory is one of the important ongoing projects in the field of research. Stress induced deficiency of learning and memory has been inevitable for the upcoming generations due to their changing lifestyle. Chronic stress (CS) extracts a high price from our bodies as well as our minds [1]. Many degenerative diseases, as well as premature aging are associated with chronic nervous tension. One of the principal cognitive effects of stress is disruption of learning and memory. Mainly it leads to significant impairment of cognitive functions especially in calculation, immediate recall and attention [2]. The documented effect of stress on learning and memory function raises the question of what anatomical pathways are impaired, either transiently or permanently. As far as the neuropathology associated to stress is concerned, there will be a defect in cortical and subcortical centers [3,4,5,6], mainly the hippocampal formation [7,8,9]. The field of neuroscience has evolved greatly and it is now clear that the hippocampal formation plays a pivotal role in learning and memory [10]. A leading thought is that the volume of the BCI helps to decrease the number and severity of CS-inhibit the adverse effects of CS on retention of learned tasks. There is a great need for safe and effective prevention strategies to combat the ravages of stress on our nervous system. The hippocampus is directly related to memory capability[11]. Hippocampus is believed to be particularly vulnerable to oxidative stress due to a relatively high rate of oxygen free radical generation without commensurate level of antioxidative defenses [12]. The cytotoxic acetaldehyde produced from oxidation of stress can be further oxidised to acetate by acetaldehyde dehydrogenase enzyme and is capable of producing reactive oxygen species [13] and leads to a depletion of the antioxidant defenses in the hippocampus [14]. Here in this study, BCI establishes the link between the human brain and the external signals. BCI is a smart system that sends external signals into specific portion of the brain to enhance its natural activity. BCI's are designed to restore sensory function, transmit sensory information to the brain, or stimulate the brain through artificially generated electrical signals. The Magnetoencephalography (MEG) detects the tiny magnetic fields created as individual neurons fire within the brain. It can pinpoint the active region with a millimeter, and can follow the movement of brain activity as it travels from region to region within the brain. BCI systems use MEG to detect signals from the brain when it is activated with standard input signals.



SA— Signal Acquisition
SP--- Signal Processing
OD---- Output Display
ES---Electrode System
SI --- Standard Input

FIG.1.BLOCK DIAGRAM OF THE SYSTEM

The objective of this study was with the help of BCI loop, the subject can control the positive movement in the radial arm maze which allow to take the food. It was recorded in the system. An important finding in the present study was the enhancing effect of BCI against neurodegeneration. It shows that these rats achieve to learn the task.

Experimental Procedure

The experiment was carried out in young adult male wistar albino rats, (body weight 180± 10 gms, aged 2 months) were maintained in the animal room at a controlled temperature (26°± 2°C) and a light and dark cycle (12 hrs light and 12 hrs dark) for 2 months. They were provided with food and water ad libitum. All experiments were cleared by institutional ethical committee (IAEC.No.Ana.M.Sc/002/2010). The animals are divided into four groups, 6 animals for each group, so totally 24 rats were used.

No. of groups with description:

Control group:

Group I – The rats were housed in complete non-stress condition. The control group animals were housed and maintained for 2 months from the start of the experiment. After that the animals were sacrificed.

Experimental group:

Experimental animals were divided into 3 groups
(Group II, III and IV).

Group II – Animals induced stress with cold water (18±2 ºC) for 4 hours for 1 month.

Group III – Animals treated with BCI.

Group IV – Animals subjected to cold stress for 1 month and then treated with BCI

.

Stress protocol:

The rats were subjected to cold water swimming stress for 10 minutes, a day for a period of one month. Animals were forced to swim in a plastic bucket (Dimensions 45x20x25 cm in diameter) filled with of cold water (18±2ºC) under

observation. The stress period was selected based on a pilot study to obtain the maximum percentage of cell degeneration in the Hippocampal region. Although habituations were observed in the general behavior, cell degeneration was complete [15].

MATERIALS AND METHODS

The experiment was carried out for a period of 2 –4 months with 24 albino rats. Before starting the experiment, the rats were made to acclimatize to the laboratory environment for one week. Then rats were randomly divided into 4 groups of 6 (n=6) animals each. Age: 2 months. All the rats underwent BCI procedure except the first and second group which was exposed to fake intervention. The objective of this proof of concept closed loop BCI experiment was for the subject to control the positive movement of a rat in the radial arm maze to take the food which was recorded in the system. The rat was tasked to alter the position in the maze by a fixed increment by respectively engaging into mental operations increasing cognitive load (e.g mental arithmetic) or relaxing. The trial was deemed successful if the rat managed to manipulate his/her cognitive load (and thus their alpha power) to achieve the goal with short latency time. The position of the food pallet was not fixed and changed randomly with equal probability between trials. The experimental setup is illustrated in fig.1 in that 3 electrodes were placed on the scalp in the position of P1, O2, and T3. These were used to record EEG signals from each subject as well as stimulate in a common reference montage at a sampling frequency of 256Hz. The alpha power for each electrode was calculated individually using MATLAB and then averaged to obtain a single value. The alpha band power was defined as the power of the EEG data filtered between 8-13Hz. This value was calculated once per second. The mean of the positive activity was recorded. During this period, the rats were trained in a 30 min session/day to study the behaviour for following 30 days until acquisition of a stable baseline of responding was reached.

The rats were treated humanely and in compliance with the recommendations of Animal Care Committee. All experimental procedures were carried out between 04.00 to 08.00 pm. To assess hippocampal dependent spatial learning and memory, all rats were trained in a complex maze task [16]. After the induction of stress and BCI treatment at the end of the 8th week, the positive behavioral activities were accessed by performing four times per day for four weeks. Over the time, rats tend to run the maze with fewer and fewer errors, more and more quickly. By graphing the number of errors over time, learning and memory of the rats were assessed. After the scarification procedure, fixation was done using 4% paraformaldehyde in 0.1 M phosphate buffered saline, through transcardiac perfusion. Fixed tissues are stained with H&E and counting of neurons were done by using histomorphometry.

RESULTS AND DISCUSSION

An important finding in the present study was the enhancing effect of BCI against neurodegeneration. It shows that these rats achieve to l e a r n the task. It suggests that the BCI activated the neurons in the hippocampus and makes it sufficient for normal acquisition. So the task acquisition and memory modulation mediated in hippocampus was due to neuroprotective & neurogenesis effect of BCI. In group III, highly significant effect of BCI was noticed in normal acquisition and retrieval of memory. It suggests that BCI not only reverses amnesia in stress induced rats as shown in group IV and also it improve the memory as shown in group III. This suggests that BCI modulates retention in hippocampus required for learning the task. An intact hippocampus was found to be essential for task acquisition. The retention was enhanced in group III rats suggests that BCI strengthened the contribution in hippocampus makes to a level that could influence behavior. This interpretation further suggests that BCI influence and mediates the modulatory effect of acute stress on memory.

Table 1: Mean ± SEM of positive behavioral activity (number/count) during the days of training after BCI and/or stressed rats

Group	Day 1	Day 2	Day 3	Day 4
Group I	1996.1±71.02	2016±51.01	2120±48.02	2428±36.42
Group II	1837±29.51	1625±72.50	1421±49.50	1570±60.10
Group III	2049.91±47.03	2121±59.91	2095±68.02	2327±15.67
Group IV	3599.91±87.03	3121±89.91	3225±58.02	3527±25.67

The overall mean behavioural activity was calculated from the above table (n=6). The above results showed that during stress, the behavioural activity of group II was decreased as when compared with all other groups. But in group III and IV, the overall positive mean behavioural activity was Post- hoc tests revealed that comparing the mean of positive activity of all the 4 groups, group IV has higher significant positive value. This showed that BCI treated group was better than other groups.

increased as compared with all the other groups. The ANOVA test carried for positive behavioural activity showed that the difference in mean values between the groups were statistically significant ($F= 55.21$; $P<0.001$).

It was proved in the present study that the beneficial effects of BCI on cognition had been demonstrated in behavioral studies. New cells were important for hippocampal dependent learning, but perhaps only required for encoding spatial information in the long term. There was also

evidence that the newly-generated cells may serve specific functions during learning or recall of certain tasks, distinct from the function served by mature granule cells. For example, both cell proliferation and total cell number in the dentate gyrus was negatively correlated with a rat's locomotor activity in response to exposure to novelty [17]. So, the new cells may serve an important role in the recognition of novelty and in producing an appropriate response in a novel context [18].

Table 2: Mean ± SEM of total number of neurons during the days of training after BCI and/or Stressed rats. (CA – Cornu Ammonis)

Group	CA1	CA2/3	CA4
Group I	222.9±14.2	271.7±5.7	188±9.5
Group II	192.5±12.2	216.9±9.3	160.8±5.5
Group III	202.7±10.2	261.2±6.8	190±7.5
Group IV	282.7±10.2	291.2±6.8	260±7.5

The above results showed that during stress, the total number of neuron was decreased in group II as when compared with other groups. But in group IV, it was increased as compared to all the other experimental groups. So, this shows that BCI improved the total number of neurons in the experimental group. The ANOVA test done for total number of neuron which showed that the difference in overall mean total number of neurons between the different groups were statistically significant ($F=2.94$; $P<0.05$). Comparing the mean total number of all the experimental groups, group III had significant value. This shows that BCI treated group was better than other experimental groups. These findings compared with previous research demonstrating the impairment of spatial learning and memory of stress induced rats in the radial arm maze 19, [20].

This suggests that these newly formed cells may serve a function in the encoding or recall of spatial information that was distinct from that served by more mature granule neurons. It was also possible t h a t the young cells may be important for encoding information about the timing of specific memories. The dentate gyrus allows the differentiation of similar memories by production of distinct, non-overlapping representations in the CA3 region [21.] However, memories that occur temporally close to each other to remain associated [22]. So, presence of more number of mossy cells and mature neurons as well as immature neurons in the hippocampus in fructus treated group was very much useful in cognition as well as in depression.

Deficits in spatial ability in stress exposure mainly in maze studied by Goodlett and Peterson, et al.,1995.

Although the neural changes underlying the deficits induced by stress exposure remain ambiguous. But there were at least two possible explanations for the differences in performance group II in the maze. First, the brain area underlying spatial cognitive abilities was affected by stress exposure and secondly, HPA (Hypothalamo-pituitary-adrenal axis) hyper responsiveness to stress. So, the deficits in spatial navigation demonstrated group II may be attributable, due to hippocampal damage. Finally, stress exposure had been shown to produce alterations in hippocampal structure and function, changing mossy fiber branching, arborization and hippocampal pyramidal cell number in CA1 as well as in CA3 [29,30]. It reduces the affinity of hippocampal NMDA receptors for binding glutamate [23.]

So, finally improved performance in BCI group in latency time and total path length appeared to result from neuroprotective effect of BCI against stress induced hippocampus and there were significant differences among groups in latency to perform the task. The ANOVA test done for positive activity shows that the difference in time taken to achieve the target between the groups were statistically significant ($P<0.05$). Comparing the mean positive activity of all the 4 groups, group IV had significant value. This shows that BCI treated group was better than other groups. So BCI treated rats performed well in behavioral and cognitive tasks including conditioned aversion learning, spatial learning and memory as well as resulting in decrease in HPA responsiveness. This shows that BCI induced the positive behavioral activity and thereby it improves the learning and memory. As the set of newly generated neurons available at the time of encoding would be similar for memories formed in close temporal proximity, their involvement in encoding could help tie memories together in time 24. Total number of mature neurons and positive activity were increased in group II and IV which proves that BCI had neuroprotective effect and its estrogen property. This neuroprotective effect of BCI increases the pyramidal and granular cells in hippocampus. This newly borned cells very much useful in hippocampal plasticity. So, discovery of adult hippocampal neurogenesis had stimulated the efforts to understand the relationship between newborn cells and hippocampal dependent learning and memory.

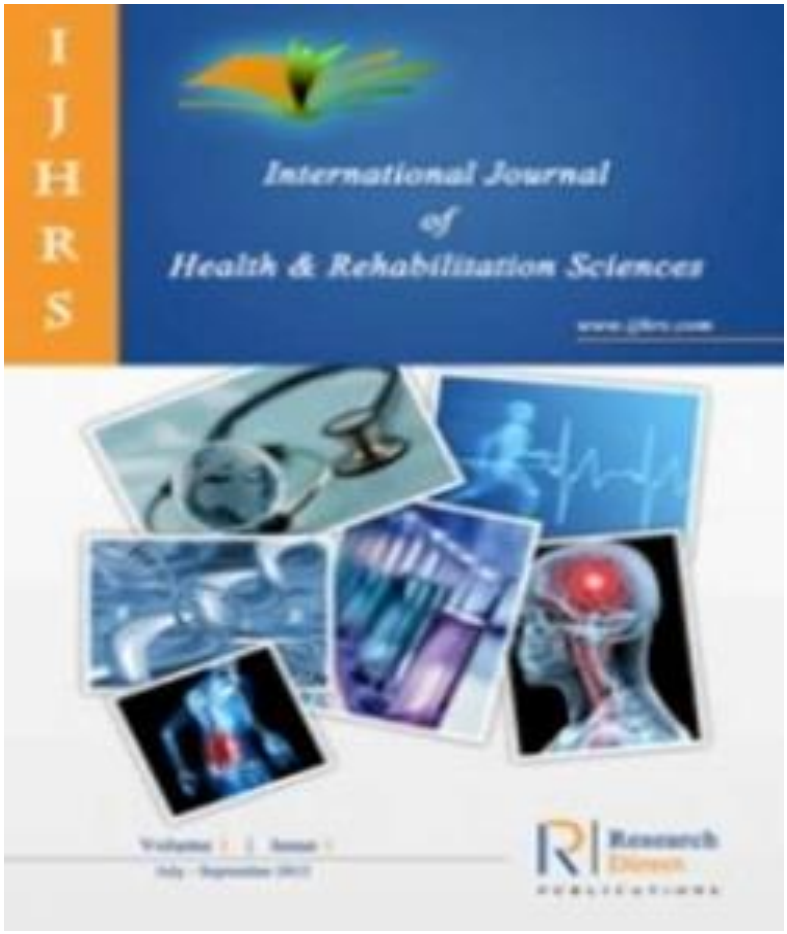
CONCLUSION

BCI improves the behavioral activities of stress induced hippocampus. Regulating the cells of the brain in stress induced hippocampus as well as in normal, BCI can be used as adjunct for the treatment of depression. Presence of more number of neurons reveals that there may be a migration of progenitor neural stem cells from the ependymal layer of sub ventricular zone. Neuronal activity in the hippocampus declines with age [25]. These concurrent events may precipitate decreased cognitive functioning with stress and advancement of age. BCI induced activation of neurons with resultant induction of an ERK-Akt-CREB-BDNF signaling pathway mediates neuroprotection and preservation of cognitive

function BCI. The study thus adds to a growing literature supporting a potentially important role of BCI in mediating neurogenic beneficial effects in the brain.

FUTURE SCOPE

In future, BCI induced neurogenesis may also be of considerable clinical interest with the development of neural stem cell technology for replacing lost neurons. The results of this study suggest that administration of BCI had induced neurogenesis on hippocampus which suggests that BCI could serve to stabilize brain morphology and physiology



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