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Original Research Article

Impact of Electroconvulsive Shock (ECS) on Hippocampal Neuroplasticity: A Morphometric Analysis in Male Wistar Rats

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Abstract:

Background: The hippocampus plays a pivotal role in memory formation and spatial navigation, its structure and function subject to modulation by various factors, including neuroplasticity. Despite its therapeutic efficacy in severe depression, the specific effects of Electroconvulsive Shock (ECS) therapy on hippocampal neuroplasticity remain poorly understood.

Materials and Methods: This study, conducted at St. John's Medical College, Bangalore, aimed to evaluate the impact of ECS on hippocampal neuroplasticity. Inbred male Wistar rats underwent ECS treatment for six consecutive days, followed by Golgi staining of hippocampal tissue. Morphometric analysis was conducted to assess dendritic node counts.

Results: The study revealed significant differences in dendritic node counts between the ECS-treated and control groups (mean difference: 9.24 nodes, $p \leq 0.002$), indicating ECS's potential to modulate hippocampal neuroplasticity.

Conclusion: ECS therapy may serve as a modulator of hippocampal neuroplasticity, shedding light on its therapeutic mechanisms in neurological disorders. These findings contribute to our understanding of hippocampal function and dysfunction, informing future treatment strategies.

Keywords: Hippocampus, Neuroplasticity, Electroconvulsive Shock (ECS), Golgi Staining, Dendritic Nodes.

Introduction

Plasticity, a fundamental characteristic of the nervous system, enables it to adapt to internal and external environmental changes, whether in physiological or pathological states. Neuroplasticity, a key aspect of nervous tissue, allows for relatively rapid and reversible alterations. It can also influence the translation of genetic information into observable traits, exerting lasting effects. Neuroplastic mechanisms respond to diverse stimuli, natural or artificial, originating internally or externally, with outcomes that can yield either short-term or enduring changes. These changes, occurring during the functional or structural restoration of neuronal circuits, likely share a common foundation across different brain regions. [1] Neuroplastic mechanisms involve the modulation of signal transmission across synapses and interactions among neurons, affecting neuronal communication and the functioning of brain systems. [2]

Neuroplasticity is influenced by various environmental, hormonal, and pharmacological factors, including antidepressant medications and electroconvulsive therapy (ECT). This suggests a role for neurogenesis, a form of neural plasticity, in the brain's ability to perceive, adapt, and respond to stimuli. Understanding adult neuroplasticity, its modulation by environmental influences and psychotropic medications, and its potential as a target for drug development is crucial. [3] The regulation of neurogenesis and neuroplasticity underscores the contributions of both structural and neurochemical adaptations to the effects of psychotropic drugs and responses to stress and environmental stimuli. [4]

ECT, a therapeutic intervention primarily indicated for severe depression and occasionally for schizophrenia and manic episodes, involves the administration of a minor electric current to the brain via scalp electrodes, inducing a controlled seizure. [5]

This study aims to evaluate the impact of Electroconvulsive Shock (ECS) on neuroplasticity by analyzing the branching pattern through node counting within the CA1 region of the rat hippocampus.

I. Materials and Methods:

Inbred male Wistar rats were utilized for the experiments, housed in standard home cages within a controlled 12:12 h light/dark cycle environment, with unlimited access to food and water at the central animal house of St. John's Medical College, Bangalore. All experimental procedures were approved by the Institutional Animal Ethics Committee (IAEC), and utmost care was taken to minimize both the number of animals used and any potential discomfort they may experience. Sacrifice of the rats was carried out through cervical dislocation followed by decapitation. No anesthesia was administered during the experiments to prevent any confounding effects on the results.

Study Design: Descriptive observational study

Study Location: This was performed in Department of anatomy, at St. John's Medical College, Bangalore, Karnataka**.**

Study Duration: 3 years.

Sample Size: 30 samples

Inclusion Criteria: Adult male healthy rats aged 2-3 months.

Exclusion Criteria: Rats injured during ECS and rats affected by infections.

ECS Procedure: Thirty subjects were randomly assigned to ECS and control groups. The ECS group underwent ECS treatment for six consecutive days at 10:00 AM, utilizing electrode gel-coated stainless steel ear clip electrodes. Electrical stimulus was administered using a Naviqure machine, a constant current brief pulse ECT device based in Bangalore, India.

Parameters: Stimulus parameters were computer-controlled with an amplitude of 250mA, pulse width of 0.75ms, pulse frequency of 50Hz, and stimulus duration of 2.14 sec (40mC). Each stimulus induced a tonic-clonic seizure lasting 8-12 seconds. Sham-treated control animals received identical handling but no electrical stimulation. Rats were euthanized after one month, and their hippocampi were processed using rapid Golgi solution. Rapid Golgi staining, a gold standard technique for staining neurons, was employed based on previous studies.

Morphometric Analysis: Hippocampal sections were examined using a Leitz microscope. Neurons meeting specific criteria were selected for the study, including:

1. Dark and consistent silver impregnation throughout all dendrites.
2. Presence of untruncated dendrites.
3. Relative isolation from neighboring impregnated neurons.

Camera Lucida tracings were obtained from randomly selected CA1 pyramidal neurons at a magnification of 625X using a Leitz microscope. Quantification and analysis of dendritic branching points and intersections were conducted using Sholl's analysis.

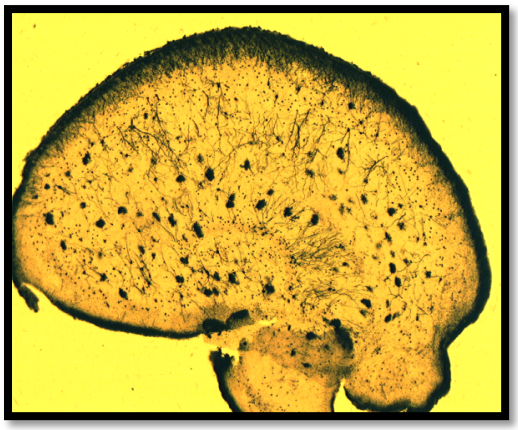

Figure 1

Figure1: Hippocampus CA1 region under 4X

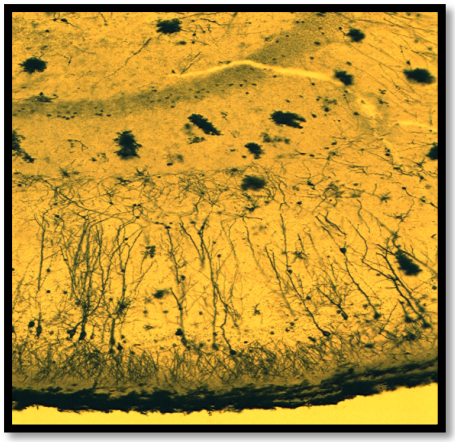

Figure 2

Figure 2: CA1 region under 10X

The Neurolucida Explorer software was utilized to analyze the traced neurons. This software provides detailed information on dendritic intersections, length, and branching points from the soma by computing values in each consecutive concentric segment. The analysis of dendritic branching and intersections extended up to a distance of 250 µm from the center of the soma.

Concentric circles spaced 50-µm apart were employed, maintaining the same magnification as that used for drawing the neurons. With the center of the circle positioned on the center of the cell

body as the reference point, dendritic intersections and branching points were assessed from the soma by computing values in each successive concentric segment. The study of dendritic branching and intersections covered a distance of up to 250 µm from the center of the soma.

Statistical analyses were conducted utilizing statistical software (SPSS for Windows, version 16). An independent sample t-test was employed to assess significant changes in axon length, while Levene's test was utilized to evaluate homogeneity.

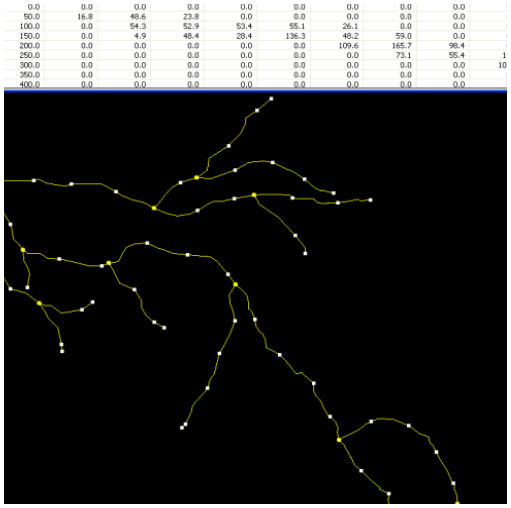

Figure 3: Branching pattern of pyramidal cell in CA1 region of hippocampus

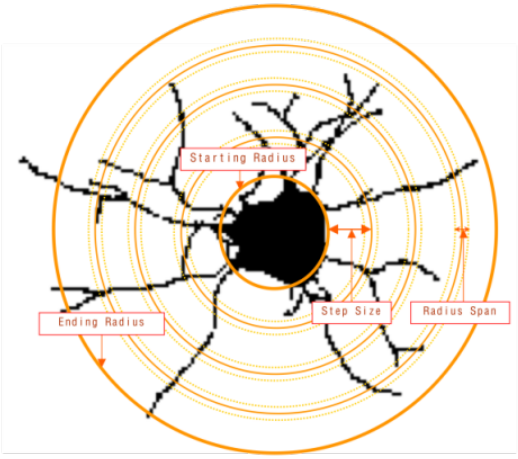

Figure 4: Schematic diagram of sholl's analysis

II. Results

The findings were visually represented in a bar chart. In the experimental group, the mean dendritic nodes were 21.3 ± 5.8, while in the control group, it was 12.81 ± 4.4. The study revealed a mean difference of 9.24 dendritic nodes between the two groups, with a 95% confidence interval. The statistical analysis yielded a p-value of ≤ 0.002, with a 99% power, indicating a significant difference in dendritic node number between the ECS-treated group and the control group.

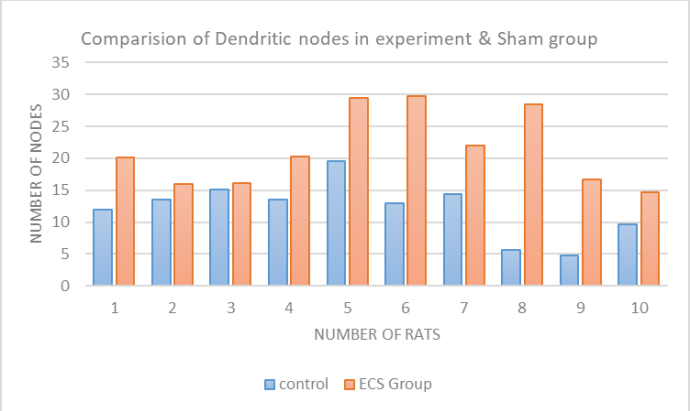

Figure 5: Comparison of dendritic nodes in experiment & sham group

III. Discussion

The utilization of chronic antidepressants, such as Electroconvulsive Shock (ECS) treatment, has been observed to induce various plastic events within the brain, particularly evident in alterations in neuronal morphology across distinct brain regions, notably the hippocampus. These antidepressants not only influence the structural aspects of neurons but also promote neurogenesis, as evidenced by the increase in the number of new neurons. [6,7] This plasticity is particularly crucial as it addresses compromised neuronal connections and plasticity capacity commonly associated with pathological conditions like major depression. The mechanism involves the binding of glutamate to postsynaptic NMDA receptors, triggering calcium influx and subsequently initiating a cascade of changes involving various neurotransmitter and neuromodulator molecules. [8,9]

Antidepressant therapies, including ECS, have demonstrated the ability to enhance synaptogenesis, expedite dendritic arborizations of newly generated neurons, and facilitate spine maturation, particularly within the dentate gyrus cells of the hippocampus. Nonetheless, a direct demonstration of ECS's impact on dendritic complexity in mature granule cells remains elusive. [10]

Meta-analyses propose that depression may stem from disruptions in mechanisms governing cell survival and neural plasticity within the brain. [11] Antidepressants potentially exert their effects by promoting neurogenesis and modulating signaling pathways crucial for plasticity and cell survival. [12,13]

In the current study, Electroconvulsive Shock (ECS) was administered to the CA1 region of normal, healthy rats, elucidating the relationship between ECS and neuroplasticity, particularly in dendritic branching patterns. In conditions of depression, neuronal death and synaptic damage pose significant challenges. Administering ECS to depressed subjects is expected to yield promising results, as demonstrated by the significant findings obtained in this study with healthy subjects.

IV. Conclusion

In conclusion, our study demonstrates the significant impact of Electroconvulsive Shock (ECS) therapy on neuroplasticity within the CA1 region of the hippocampus in healthy rats. These findings suggest the therapeutic potential of ECS in promoting neural plasticity. Further research is warranted to explore its mechanisms and potential clinical applications in neurological disorders characterized by impaired neuroplasticity.

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References

1. S. Sudha, MPhil, PhD, Chittaranjan Andrade, MD, C.R. Mukundan, MPhil, PhD, and J. Suresh Chandra, Spectral EEG Effects of Electroconvulsive Shock Stimulus Parameters The Development of a Rationale for the Optimization of the ECT Stimulus. J of ECT. 2003; 19: 197-10.
2. John Read, Richard Bentall, The effectiveness of electroconvulsive therapy: A literature review. Epidemiologia e Psichiatria Sociate 2010; 4: 333- 47.
3. Andre Russowsky Brunoni, Mariana Lopes, Felipe Fregni, A systematic review and meta-analysis of clinical studies on major depression and BDNF levels: implication for the role of neuroplasticity in depression. Intl J Neuropharmacol. 2008; 11:1169-80.
4. Amar Sahay, Rene Hen, Adult hippocampal neurogenesis in depression. Nature neuroscience. 2007;10(9): 1110- 4.
5. Jessica E. Malberg, Amelia J. Eisch, Eric J. Nestler, Ronald S. Duman, Chronic Antidepressant Treatment Increases Neurogenesis in Adult Rat Hippocampus. J. Neutosci. 2000 Dec;20(24):9104-10.

6. Chittaranjan Andrade, AshwinAkki, Nagaraja Nandakumar, J. Suresh Chandra, Confirmation of Whole-Brain Kindling With Repeated Subthreshold Electroconvulsive Shocks: A Controlled Study. J ECT. 2003; 19(2):81-3.
7. Singaravelu Kuringi, Chittaranjan Andrade, ECS Seizure Threshold: Normal Variations, and Kindling Effects of Subconvulsive Stimuli. J ECT. 2003;19(1):31-7.
8. S. Sudha, Chittaranjan Andrade, C.R. Mukundan, J. Suresh Chandra, Spectral EEG Effects of Electroconvulsive Shock Stimulus Parameters The Development of a Rationale for the Optimization of the ECT Stimulus. J ECT. 2003 Dec; 19(4):197-210.
9. J. Veena, B.N. Srikumar, K. Mahati, V. Bhagya, T.R. Raju, B.S. Shankarnarayana Rao, Enriched Environment Restores Hippocampal Cell Proliferation and Ameliorates Cognitive Deficits in Chronically Stressed Rats. J Neuro Research. 2009; 87:831-43.
10. Cardoso, A., Assuncao, M., Andrade, J.P., Pereira, P.A., Madeira, M.D., Paula-Barbosa, M.M., Lukoyanov, N.V., Loss of synapses in the entorhinal-dentate gyrus pathway following repeated induction of electroshock seizures in the rat. J. Neurosci. Res. 2008; 86: 71–83.
11. Fenghua Chen, Torsten M. Madsen, Gregers Wegener, Jens R. Nyengaard, Repeated electroconvulsive seizures increase the total number of synapses in adult male rat hippocampus. Eur Neuropharmacol. 2009; 19:329-38.
12. Andre Russowsky Brunoni, Mariana Lopes, Felipe Fregni, A systematic review and meta-analysis of clinical studies on major depression and BDNF levels: implication for the role of neuroplasticity in depression. Intl J Neuropharmacol. 2008;11:1169-80.
13. Sudhirkumar U. Yanapallewar, Collen A. Barrik, Mary Ellen Palko, Gianluca Fulgenzi, Lino Tessarollo, Tamalin Is a Critical Mediator of Electroconvulsive Shock-Induced Adhult Neuroplasticity. J Neurosci. 2012 Feb; 32(7): 2252-62.