Section: Anatomy

Original Research Article

LOW AND HIGH-DOSE ELECTROCONVULSIVE SHOCK: COMPARATIVE ANALYSIS OF CORTICAL SURFACE AREA IN WISTAR RATS

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Received *: 10/07/2025*
Received in revised form *: 02/09/2025*
Accepted *: 23/09/2025*

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DOI: 10.70034/ijmedph.2025.4.100

Source of Support: Nil,
Conflict of Interest: None declared

Int J Med Pub Health
2025; 15 (4); 553-556

ABSTRACT

Background: Neuroplasticity is the ability of brain to reorganize structure and function in response to stimuli. Electroconvulsive shock (ECS), an experimental analogue of electroconvulsive therapy (ECT), induces morphological and molecular changes in the brain. Neuroplasticity has been demonstrated in the basolateral amygdala, hippocampus and subventricular zone, but cortical correlates remain less well studied. **The aim & objective** is to observe the effect of low and high-dose ECS on cortical neuroplasticity by measuring surface area (SA) of representative cortices in Golgi–Cox stained sections. To estimate and compare the SA of representative - primary, secondary, retrosplenial granular and dysgranular cerebral cortices in Golgi stained coronal sections of control(sham), low dose and high dose ECS treated rats

Materials and Methods: ECS induced cortical sections were obtained of Wistar rat brains previously used in departmental studies that demonstrated amygdalar plasticity. Rats were grouped into control, low-dose ECS, and high-dose ECS groups. Cortical surface area was examined under the microscope, photographed and SA quantified using ImageJ software, and comparisons were made using one-way ANOVA with Tukey's post hoc test.

Results: The mean cortical surface area was numerically higher in ECS-treated groups (low dose: 6.43 ±1.73square milli micron and high dose 6.11±1.12square milli micron)

Conclusion: ECS-treated groups (low and high-dose) showed numerically greater cortical surface area compared to control. However, these differences were not statistically significant ($p > 0.05$).

Keywords: Neuroplasticity, Electroconvulsive shock, Golgi stain, cortical morphometry.

INTRODUCTION

Neuroplasticity is the intrinsic capacity of the brain to reorganize its structure and function in response to endogenous and exogenous stimuli. It plays a vital role in learning, memory consolidation, and recovery from neurological injury. Structural correlates of neuroplasticity include synaptogenesis, dendritic arborization, and gliogenesis. These changes can be captured using morphometric methods with Golgi staining considered for visualizing entire neuronal architecture, dendritic spines, and cortical surface characteristics.[1, 3, 4]

Neuroplasticity is known to occur primarily in hippocampus and sub ventricular zone. The process is regulated by environment, physical activity, genetic, stress, administration of chemical antidepressants and ECT. Studies in rodents and primates demonstrate the persistence of immature neurons in cortical layer II that remain developmentally arrested but are capable of integration during adulthood,[5] similarly, delayed maturation of double cortin-expressing neurons in the

primate amygdala provides a reservoir for adaptive circuit remodeling during critical periods.[6] These findings support that the cortical morphology, including surface area measurements, can serve as an indicator of plasticity.

ECT in humans and ECS in rodents, remain among the most potent biological interventions for inducing structural brain plasticity. ECS induces widespread cellular changes, including increased glial and endothelial proliferation, enhanced synaptic density, and dendritic arborisation.[7,8]

Neurochemical mechanisms reinforce this structural plasticity. Cholinergic signaling through muscarinic receptors modulates excitability and synaptic integration in cortical and amygdaloid neurons. These excitatory and inhibitory responses are closely linked to dendritic remodeling and synaptic strengthening.[9] ECS is also known to activate neurotrophic pathways, including brain-derived neurotrophic factor (BDNF), which increase dendritic growth and synaptic stabilization.[8] These effects are thought to underlie the clinical efficacy of ECT in treatment-resistant depression, where cortical and hippocampal atrophy are prominent features. ECS produces dose-dependent effects: repeated or high-intensity shocks elicit stronger proliferative and morphometric responses, whereas low-dose ECS elicits subtler but measurable changes.[7,8]

Experimental studies have shown similarities in general cell types in basolateral amygdala and cerebral cortex. Light microscopic Golgi cox and electron microscopic studies have revealed remarkable similarity of principal projection neuron in the basolateral nuclei of amygdala to the pyramidal cell in the cortex.

Despite extensive work on spine density and synaptic remodeling, relatively few studies have explored cortical surface area measurements from Golgi-stained sections as a morphometric endpoint of neuroplasticity. Since cortical surface area reflects cumulative changes in dendritic arborization, glial proliferation, and synaptic complexity, it provides an integrative marker of ECS-induced brain remodeling.

Aim and objectives: To estimate and compare the surface area (SA) of representative - primary, secondary, retrosplenial granular and dysgranular cerebral cortices in Golgi stained coronal sections of control(sham), low dose ECS and high dose ECS treated Wistar rats, with the objective of establishing cortical surface area as a structural marker of neuroplasticity.

MATERIALS AND METHODS

Golgi Cox stained slides containing cortex were taken from the collection of previous work done in the department of Anatomy, St John's medical college Bangalore, in which neuroplasticity was observed in basolateral nucleus of amygdala.[1] The cross sectioned slides were of 120µm thick sections of adult male Wistar rats, 2-3 months old; weighing 175-225gms of six control (Sham-no current), six High dose (Suprathreshold of 60mC, High pulse width of 1.5ms, Low frequency of 75pps, Stimulus duration of 2.14sec with amplitude of 250mA), six Low dose (Suprathreshold of 10mC, High pulse width of 1.5ms, Low frequency of 50pps, Stimulus duration of 0.54sec with amplitude of 250mA) ECS treated rats. The sections comprising the areas of cerebral cortex were primary, secondary, retrosplenial granular and retrosplenial dysgranular in the range of -2 to -3 bregma region of rat brain described by Paxinos and Watson C [2].

Inclusion Criteria

Golgi cox stained coronal sections of control, low dose and high dose ECS treated rats.

Exclusion Criteria

Sections of cortices with irregular and incomplete areas.

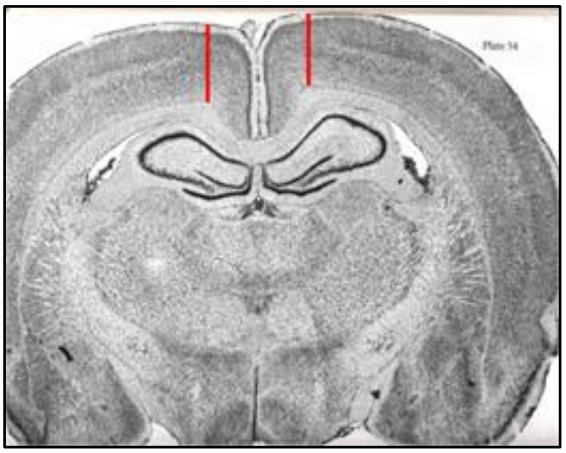

Figure 1: Representative cortices of rat brain at amygdalar complex described by Paxinos & Watson C

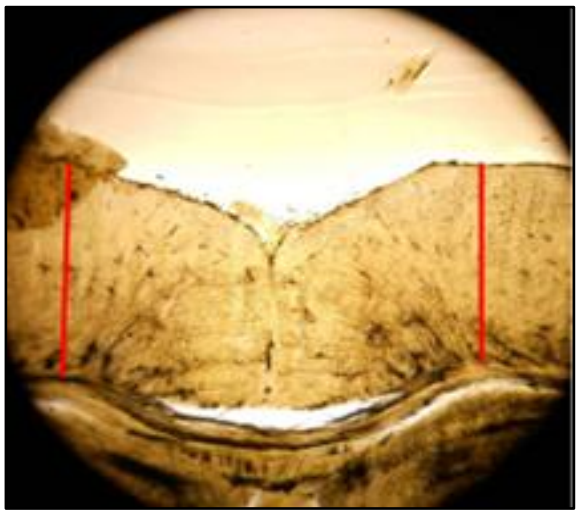

Figure 2: Selected representative cortical area under 4X magnification

Morphometric Analysis: Cortical region from 16 sections of control group, 19 sections of low dose ECS treated and 31 sections of high dose ECS treated were examined under the microscope with 4X magnification; the cortical region that extends from the median fissures to that of highest elevation of

corpus callosum on both sides were identified which comprised of primary, secondary, retrosplenial granular and retrosplenial dysgranular cortices[2].A digital camera (16 megapixel Nikon coolpix S2700) was then placed, photographed and transferred to the computer. The area to be calculated were outlined, standardized and surface area calculated using software Image J analyzer.

The data available was analyzed for comparison between the three groups.

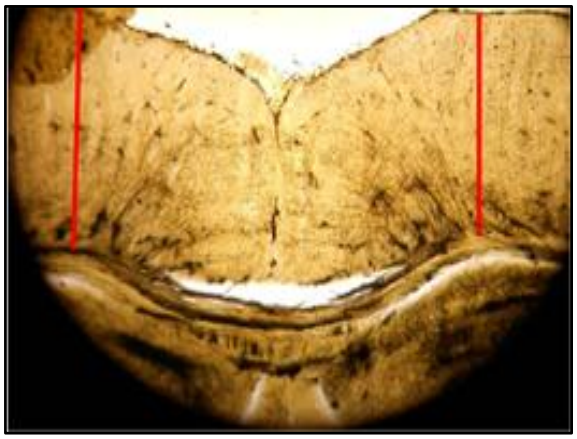

Figure 3: Representative cortical area with Image J

Statistical Analysis: Cross sectional analytical study

Methodology: The total surface area (SA) of representative cortical regions in cross-sectioned slides of the amygdalar complex was measured in control, low-dose ECS, and high-dose ECS treated rats. Results are presented in Table 1 as mean ± standard deviation (SD) and in Figure 1 as box plots. Data were initially evaluated for normality using the rule of thumb (SD < mean/2).

Group differences were assessed using a one-way ANOVA, followed by Tukey's HSD test for post-hoc pairwise comparisons.

Statistical Analysis: The one-way ANOVA indicated no statistically significant differences among the three groups ($p = 0.502$). All statistical analyses were performed in R (version 4.4.1; R Foundation for Statistical Computing) at a 5% level of significance.

RESULTS

The mean cortical surface area was calculated for control, low-dose ECS, and high-dose ECS groups [Table 1].

Numerical differences were observed: Control: 5.92±1.09; Low-dose: 6.43±1.73; High-dose: 6.11±1.12 sq. milli microns.

Statistical analysis did not reveal significant differences among the groups.

Table 1: Mean cortical surface area (sq. milli microns) in control and ECS-treated groups

ECS –Treated groups	Mean± SD±	Min, Max
Control (n=16)	5.92± 1.09	(4.72,8.85)
Low (n=19)	6.43± 1.73	(4.11,10)
High (n=31)	6.11± 1.12	(4.61,8.89)

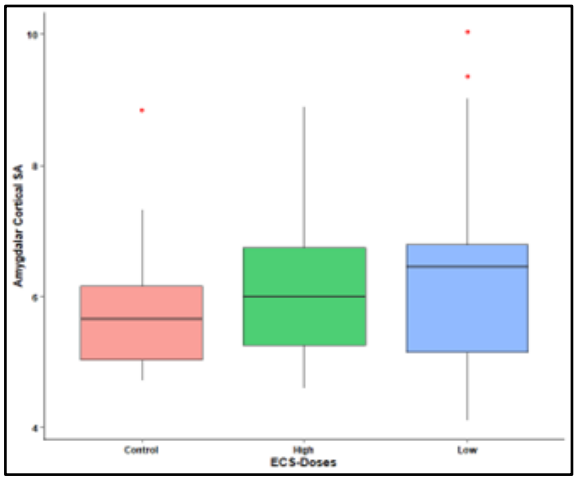

Figure 4: Box plots

Summary of findings

- ECS-treated groups (low- and high-dose) showed numerically greater cortical surface area compared to control.
- However, these differences were not statistically significant ($p > 0.05$).

The trend suggests a possible dose-related effect, but larger sample size or longer treatment duration may be required to demonstrate statistical significance.

DISCUSSION

The present study was undertaken to evaluate the effect of ECS on cortical surface area in Wistar rats, using Golgi-stained sections in which neuroplasticity was observed in basolateral nucleus of amygdale[1] as a morphometric marker of neuroplasticity by measuring the SA in representative cortices (primary, secondary, retrosplenial granular and retrosplenial dysgranular in the range of -2 to -3 bregma region of rat brain described by Paxinos and Watson C[2],Low-dose and high-dose ECS groups exhibited numerically higher cortical surface areas compared to controls; the differences did not reach statistical significance.

ECT is a controversial, non chemical antidepressant and treatment of choice in mania, major depressive disorder and drug resistant patients with depressive disorder. ECS is an animal model of ECT, have consistently been reported to induce widespread structural and functional plasticity in the brain. Previous studies have demonstrated increased synaptic density, [4] enhanced dendritic complexity [5], and cortical glial proliferation, [6] following ECS. Our findings showed a similar trend toward increased cortical surface area in ECS-treated groups,

suggesting morphological remodeling, but variability in the data prevented statistical confirmation.

Several factors may explain the absence of statistical significance. First, the sample size may have been insufficient to detect subtle differences, given the inherent biological variability in cortical morphometric measures. Second, the duration and frequency of ECS exposure might not have been adequate to elicit robust and measurable cortical changes. Earlier reports indicate that repeated ECS administered over longer durations produces more pronounced structural effects.[5,7] High dose ECS attenuated dendrite arborization in the basolateral nucleus of amygdala, which was apparent even after one month of ECS.[1]

Third, the morphometric endpoint employed cortical surface area may integrate multiple cellular processes (dendritic arborization, glial proliferation, synaptic remodeling), and subtle effects in individual components may not translate into detectable area changes within the given experimental timeframe.

High dose ECS attenuated dendrite arborization in the basolateral nucleus of amygdala, which was apparent even after one month of ECS,[1] since this causes functional improvement apparently, so neuroplasticity should manifest in the cortex also. In our study, the low-dose ECS group showed the highest mean cortical surface area, even higher than the high-dose group. This observation, although not statistically significant, is consistent with the hypothesis that excessive neuronal activation may not always correlate with optimal plasticity. Previous work suggests that overstimulation can induce maladaptive changes or even excitotoxic stress, whereas moderate stimulation facilitates adaptive remodelling,[8] thus, the numerical trend in our data could reflect a dose-dependent, between ECS intensity and cortical plasticity.

Our findings must be considered in view of certain limitations. The analysis was restricted to limited cortical surface area that is, primary, secondary, retrosplenial granular and retrosplenal dysgranular areas of cerebral cortex in the range of -2 to -3 bregma region of rat brain. It is possible that only specific areas out of these many regions studied might have undergone notable change in SA. However in our study we have summed up the above regions for comparing without parallel assessment of dendritic spine density or synaptic markers, which could have provided more sensitive correlates of neuroplasticity.

The study provides valuable insights as it supports the feasibility of using Golgi-based cortical surface morphometry as readout of neuroplasticity in ECS models. The observed trend highlights the potential of dose-dependent modulation of cortical structure by ECS, which warrants further investigation with larger cohorts and extended treatment protocols.

CONCLUSION

No statistically significant differences in cortical surface area were found among control, low-dose, and high-dose ECS-treated groups; the observed numerical increases in ECS groups suggest a possible dose-related effect on cortical remodeling. Future studies with larger sample sizes, additional morphometric markers, and longer treatment durations are required to establish cortical surface area as a reliable indicator of ECS-induced neuroplasticity.

Acknowledgement: The authors sincerely thank the Department of Anatomy, St John's Medical College, Bengaluru, Karnataka, India, for providing the slides, and facilities required to conduct this study. We also acknowledge the valuable assistance of the teaching and non teaching staff during the study.

Declarations: This study did not receive any specific grant from funding agencies.

Ethics: The study was done on the Golgi-stained sections, present in the department, in which neuroplasticity was observed in basolateral nucleus of amygdala.

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