



**THE EFFECT OF ECT-INDUCED ALTERED BEHAVIOR ON SPATIAL JUDGMENT
AND MENTAL ALERTNESS IN WISTAR RATS**

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ABSTRACT

The study investigated the effect of electro-convulsing therapy (ECT) –induced altered behavior on spatial judgment and mental alertness. Albino wistar rats used were grouped into four groups; control groups treated with saline water as vehicle, mild shock group (2.5mA ECS), high shock group (4.0mA ECS) and Cerebrex drug group (100mg/kg). Prior to the experiment, the rats were exposed to different trials using Barnes maze test, beam maze test, navigation maze test, and elevated plus maze test. The behavioral tests were performed in different trials and altered behavior was clearly exhibited in all the tests; such as Barnes maze (inability to locate the escape hole), beam walk (increased time to walk across the beam), navigation maze (inability or prolonged time to locate the exit hole) and elevated plus maze ((decreased total time spent in the open/close arms). Statistical analysis was performed using IBM-SPSS-version 22.0. The descriptive characteristics were expressed as means \pm sem. The repeated measures of ANOVA and Post-Hoc analyses were used in the comparison of control groups with Mild Shock, High Shock, and Cerebrex groups respectively. Results obtained from the study showed that Mild and High shock had negative effect on cognitive ability, motor coordination, spatial judgment and mental alertness and it also increased anxiety in rats. However, Cerebrex had had a less pronounce effect of cognitive ability, spatial judgment and anxiety but had a positive effect on motor coordination. In conclusion, this study suggested the possibility of ECT could have a profound interference on motor response, spatial judgment and mental alertness in rats.

KEYWORDS: ECT, Cerebrex, spatial judgment, mental alertness, albino wistar rat, maze, shock.

INTRODUCTION

Electroconvulsive therapy (ECT) is a procedure, done under general anesthesia, in which small electric currents are passed through the brain, intentionally triggering a brief seizure. ECT seems to cause changes in brain chemistry that can quickly reverse symptoms of certain mental health conditions. ECT often works when other treatments are unsuccessful and when the full course of treatment is completed, but it may not work for everyone. However, fear of cognitive side effects, such as memory loss and confusion, is often cited as the main reason for not consenting to this type of treatment (Fraser, 2008).

The ECT apparatus is specially designed for neurochemical and neuropharmacological research. A constant output is used, which ensures reproducible results and accurate determination of the ECT threshold

while also pinpointing any variations in the threshold brought about by drugs having specific action on cortex and sub cortical regions. (Ugo, 2019). Spatial ability as the ability to generate, retains, and manipulates abstract visual images. Spatial ability was also defined as the performance on tasks that require the mental rotation of objects, the ability to understand how objects appear in different positions and the ability to conceptualise how objects relate to each other in space (Sutton and Allen, 2011).

Mental alertness refers to the kind of thinking, flexibility and versatility an individual possesses that makes it possible for him to adjust to new situation (Thurston, 1952). Mental alertness was also defined as any function pertaining to the mind, such as awareness, perception, imagination and reasoning (Srivastava, 1986). There are a wide variety of behavioral tests available for laboratory

rodents. This study focuses on spatial judgment and mental alertness. They include beam walk test, Barnes maze task, elevated plus maze task, and navigation maze task.

MATERIALS AND METHODS

Experimental Animal

A total of twenty male wistar albino rats weighing 180-200g were obtained from animal house. The rats were kept in clean disinfected wooden cages with saw dust as bedding in the animal house, with 12hours light/dark

cycle and 50-60% humidity at a temperature of about 30°C and were allowed to acclimatize to the new environment for two weeks, with free access to clean water and animal feed. The rats were weighed using an analytical weighing balance at commencement of the experiment.

Experimental Design

A total of twenty albino wistar rats were weighed and randomly divided into four groups of five rats per group.

Table 1 Experimental Design and Grouping of the Rats.

Groups	Number of animals	Treatment:
Group A (Normal control)	5	Feed + Water ad libitum
Group B	5	Feed + Water ad libitum + Mild shock (2.5mA)
Group C	5	Feed + Water ad libitum + High Shock (4.0mA)
Group D	5	Feed + Water ad libitum + Celebrex (0.5ml/kg)

Group A animals (control) were given clean water and feed only, without any form of shock or drugs, Groups B animals were exposed to mild shock (3 times) only, without any form of drugs using the ECT machine, Group C animals were exposed to High shock (3 times) using the ECT machine and group D was given 0.5ml/kg of Celebrex daily for 3 days after which they underwent a total of nine (9) trials of some memory and learning tests which include: elevated plus maze, Barnes maze, beam walk test and navigational task. The animals were sacrificed after two (2) weeks of treatment.

Electroconvulsive seizures

An electrical current of 2.5mA (mild shock) and 4.0mA (High shock) was generated by an ECT unit and applied via ear clip electrodes on the rats. This current induced a tonic-clonic seizure lasting 2 seconds according to the modified method of King & Glasser (1970).

Barnes Maze Test (Modified method of Barnes, 1979)

- The Barnes maze consists of a circular surface with up to 20 circular holes around its circumference.
- The table surface is brightly lit by overhead lighting. Under one of the holes is an "escape box" which can be reached by the rodent through the corresponding hole on the table top.

The model is based on rodents' aversion of open spaces, which motivates the test subject to seek shelter in the escape box. A normal rodent will learn to find the escape box within four to five trials and will head directly toward the escape box without attempting to escape via incorrect holes. Various parameters are measured including latency to escape, path length, number of errors, and velocity.

Beam Walk

- The beam was 38cm long and a diameter of 2cm. The animals were placed on one edge of the beam and expected to walk across the beam within five (5) minutes and any animal that did not complete the task within 5minutes were removed according to modified method of Carter *et al*, 2001.
- All the animals in each group passed through this test, one at a time and the process was repeated three times day summing up to nine (9) trials.

Navigational Task

- The animals (one at a time) were placed in a navigational maze which has two doors at opposite ends, but they need to go through a puzzle of complex pathway which the animals were expected to find their ways to the other outlet.
- The animals were placed in the navigational maze cabinet and the stop watch immediately starts.
- The time taken by the animals to go from side of the maze through the puzzle to the other end was recorded in seconds.
- The animal was given a maximum of 5minutes to complete the task and if any animal did not complete the set task in 5minutes, it was removed at the expiration of the 5minutes.

Elevated plus Maze (Modified method of Itoh *et al*, 1990)

- The animal was placed on an elevated maze of 32cm high having four open arms of 14.2cm (diagonally).
- The animal was placed in the centre of the four arms and the stop watch started.
- The time taken for the animals to go through the four arms was recorded.
- The maximum time of five (5) minutes was set as the longest allowable time for each animal after

which it was removed if it could not complete its task within 5 minutes.

- The animals were subjected to three trials daily.
- At the completion of the whole research procedure, the animals were sacrificed

ANOVA and Dunnet Post Hoc (multiple comparison) Test was used to compare the mean and P-Value ≤ 0.05 was accepted as statistically significant. Results are presented in tables.

STATISTICAL ANALYSIS

Statistical analysis was done SPSS version 20.0 and the results were expressed as mean \pm SEM. One-way

RESULTS

Table 1 Results from Barnes Maze Test on Spatial memory and mental alertness.

Barnes Maze Task performed in nine trials at 24hr Interval (S \pm SEM)				
Group	Treatment	Trial 1	Trial 2	Trial 3
1	Control (Distilled water)	30.00 \pm 13.05	26.40 \pm 17.39	42.00 \pm 15.45
2	Mild Shock (2.5mA)	164.00 \pm 58.54*	80.00 \pm 45.36	111.80 \pm 58.76
3	High Shock (4.0mA)	57.40 \pm 18.21	32.00 \pm 16.39	27.60 \pm 7.94
4	Celebrex (100mg/kg)	43.20 \pm 5.03	111.80 \pm 27.24	33.00 \pm 6.97

Values were presented as mean \pm sem. N= 5, * means values are statistically significant when compared to the control values

Table 2 Results from Beam walk Task on spatial judgement and mental alertness.

Beam walkTask performed in three trials at 24hr Interval (S \pm SEM)				
Group	Treatment	Trial 1	Trial 2	Trial 3
1	Control (Distilled water)	66.20 \pm 38.61	118.40 \pm 50.62	72.80 \pm 26.69
2	Mild Shock (2.5mA)	89.60 \pm 38.13	78.40 \pm 33.73	162.00 \pm 54.75
3	High Shock (4.0mA)	144.00 \pm 34.83	174.80 \pm 52.81	195.20 \pm 49.23
4	Celebrex (100mg/kg)	92.40 \pm 53.15	85.80 \pm 52.47	70.40 \pm 33.46

Values were presented as mean \pm sem. N= 5, * means values are statistically significant when compared to the control values

Table 3 Results from Navigation Maze Task on spatial judgement and mental alertness.

Navigation Maze Task performed in three trials at 24hr Interval (S \pm SEM)				
Group	Treatment	Trial 1	Trial 2	Trial 3
1	Control (Distilled water)	112.80 \pm 45.82	105.80 \pm 33.40	62.00 \pm 24.82
2	Mild Shock (2.5mA)	77.00 \pm 28.54	57.80 \pm 28.80	68.00 \pm 33.67
3	High Shock (4.0mA)	70.00 \pm 54.09	129.20 \pm 46.77	105.80 \pm 49.17
4	Celebrex (100mg/kg)	87.60 \pm 28.53	164.40 \pm 57.64	111.00 \pm 52.64

Values were presented as mean \pm sem. N= 5, * means values are statistically significant when compared to the control values

Table 4 Results from Elevated plus maze task on spatial judgement and mental alertness performed in nine trials at 24hr Interval (S \pm SEM).

		Elevated plus maze task (S \pm SEM)											
Group	Treatment	Trial 1				TRIAL 2				TRIAL 3			
		Right	Left	Closed	Semi closed	Right	Left	Closed	Semi Closed	Right	Left	Closed	Semi Closed
1	Control (Distilled water)	12.60	12.00	27.60	128.80	21.60	9.00	26.00	19.40	9.20	6.20	74.60	103.80
		\pm 5.70	\pm 3.391	\pm 6.64	\pm 49.83	\pm 4.78	\pm 4.59	\pm 6.35	\pm 9.29	\pm 4.79	\pm 2.85	\pm 48.08	\pm 58.52
2	Mild Shock (2.5mA)	11.80	8.40	77.20	28.20	9.00	4.60	77.20	114.60	3.60	5.80	20.20	120.20
		\pm	\pm	\pm	\pm 8.80	\pm	\pm	\pm	\pm	\pm	\pm	\pm 6.55	\pm

		4.16	4.16	54.08		2.89	1.03	40.87	56.86	1.03	2.60		58.84
3	High Shock (4.0mA)	8.20 ± 1.49	6.00 ± 1.30	4.80 ± 2.13	125.80 ± 62.49	26.00 ± 3.16	10.60 ± 3.03	68.60 ± 51.15	11.20 ± 3.87	7.20 ± 1.88	7.40 ± 0.51	118.80 ± 66.65	18.60 ± 7.69
4	Celebrex (100mg/kg)	8.40 ± 1.94	8.20 ± 2.06	118.40 ± 62.98	58.00 ± 40.98	19.40 ± 11.13	10.60 ± 4.09	11.20 ± 5.89	187.60 ± 61.20	9.20 ± 4.79	6.20 ± 2.85	74.60 ± 48.08	103.80 ± 58.52

Values were presented as mean ± sem. N= 5, * means values are statistically significant when compared to the control values

DISCUSSION

The research work investigated the Effect of ECT-Induced altered behaviour on spatial judgement and mental alertness in wistar rats. Results extrapolated from the various cognitive task showed significant impact on how electroconvulsive shock could pose on spatial judgement and mental alertness exhibited by the rats under standard laboratory conditions. Results from Table 1, showed the different times spent in completing the Barnes maze task by locating and entering the escape box in different trials carried out by the rats in the Control, Mild shock, High shock and Celebrex group. It was observed that, rats exposed to 2.5mA of Mild shock spent 164.00 ± 58.54 sec in Trial 1, 80.00 ± 45.36 sec in Trial 2 and 111.80 ± 58.76 sec in Trial 3. It was observed that when compared to the Control group, Mild shock increased the time it took the rats to locate the escape box in all Trials. This could be as a result of alteration in behaviour on spatial judgement and mental alertness due to shock because rodent is naturally motivated to avoid open spaces and bright lights, and therefore attempts to find the drop box of the maze. This agrees with the research done by Tyng *et al.* (2017) on optimization of apparatus design and behavioral measures for the assessment of visuo-spatial learning and memory of mice on the Barnes maze.

During the Balance Task, when compared to the Control group, it was observed that the animals spent a longer time on the beam in Trial 3. From the result, it can be deduced that exposure to Mild shock caused the rats to be very active in Trial 1 and Trial 2 but reduced their performance and prolonged the time they spent on the beam. This suggests that Mild shock induced fatigue and also altered spatial judgment and mental alertness in the rats. The results also showed a steady increase in time spent on the beam by rats exposed to High shock indicating alteration of spatial judgment and mental alertness had occurred leading to reduced performance and response. A few foot slips but no fall was also observed on the rats exposed to the High shock. However Celebrex group spent 92.40 ± 53.15 sec, 85.80 ± 52.47 sec, and 70.40 ± 33.46 sec on the beam in Trial 1, 2 and 3 respectively. The result from this study is in line with the observations done by Gvozden *et al.*, 2014 on Anxiogenic effects of chronic exposure to nandrolone decanoate (ND) at supraphysiological dose in rats.

The result from Table 2, showed the different times spent in locating the exit hole of the Navigation maze task in

different trials by the rats in the Control, Mild shock, High shock and Celebrex group. It was observed that Mild shock increased the response and performance of the rats suggesting increased spatial judgement and mental alertness. However, in Trial 3, the rats exposed to Mild shock spent 68.00 ± 33.67 sec in completing the navigation task. This suggests that Mild shock had a positive effect on spatial judgement and mental alertness in the rats. From the result in Fig 3, the chart showed the different latency period in open arms of the elevated plus maze in different Trials by the rats in the Control, Mild shock, High shock and Celebrex group. It was observed that there was a general Latency decrease in the Mild shock, High Control and Celebrex group when compared with the control in the open arms (right and left). When the rats explore the open arms (right and left), they tend to show curiosity. Shorter time spent in this arm suggests anxiety or reduced spatial judgement and increased mental alertness due to fear. The result of this study corroborates with the study by Harrison *et al.*, (2006) on Enhancement of anxiety and modulation of TH and pERK expression in Amygdala by repeated injections of corticosterone. Their findings showed that rats exposed to electric shock spent significantly less ($p < 0.05$) in the open arms compared with that of the Control group.

In the Elevated plus maze, increased activity in the open arms (right and left), reflects a conflict between the rodents preference for protected areas such as the closed arm and the semi-closed arm and their innate motivation to explore novel environments. The results from the elevated plus maze shows that Mild shock and High shock and Celebrex increased the anxiety level of the rats making them to spend more time in the closed and semi-closed arm of the maze as compared with the rats in the Control group and reducing their ability to explore the open arm thus reducing their spatial judgement and increasing mental alertness mental alertness in the animals. The elevated plus-maze is a conflict test in which novelty produces both approach (open arm) and avoidance (closed arm), interpreted as curiosity and anxiety or caution. (Handley and McBlane, 1993).

CONCLUSION

The present data demonstrated that the repeated ECS protocol used induced altered spatial judgment and mental alertness. Several previous studies have reported ECS-induced learning and memory deficits in rodents. Cognitive impairment, particularly anterograde and retrograde amnesia, is one of the most common side

effects of ECT but this study has shown that Electroconvulsive shock can also alter spatial judgment and mental alertness.

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