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## RESEARCH ARTICLE

### Mechanical Pain Induced-Acute Stress Attenuates Mental Alertness and Behaviour in Wistar Rats

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#### ABSTRACT

The study was carried out to ascertain the effects of induced-acute stress on mental alertness and behaviour in rats using Navigational maze task, Elevated maze task, Light/dark box task, Analgesic-metre (paw-withdrawal) task, Open field task. Twenty albino wistar rats were acquired. After two weeks of acclimatization, the rats were weighed and divided into four groups (groups 1, 2, 3, and 4) of five rats in each group. While group 1 received only feed and water serving as the control group, group 2 had their tails clipped during cognitive function test. Group 3 received 0.1ml/150 body weight of rat of a standard drug (epinephrine) administered intraperitoneally. Group 4 received a 0.1ml/150 body weight of rat of a standard drug (Dopamine) administered intraperitoneally. From the observations obtained, it showed that alertness and fine motor coordination and balance were significantly ( $p < 0.05$ ) enhanced by catecholamine drugs, they were also significantly ( $p < 0.05$ ) decreased by physical stress. All forms of stress demonstrated a significant ( $p < 0.05$ ) anti-anxiolytic effect. Stress can be an essential adaptive mechanism needed for survival and with only transient changes in the brain, while others can cause overreaction and deregulation of the hypothalamic pituitary adrenal (HPA) axis thus inflicting detrimental effects on the brain structure and function. Therefore, stress can be either negative or positive modulator of the cognitive functions, which includes learning and memory.

**Keywords:** mental alertness, Analgesic-metre, Navigational maze task, cognitive function test, Elevated maze task.

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## 1. Introduction

All through life, some psychological and biological factors like stress, fear, arousal, aging and anxiety affect learning and memory process (Schrijver *et al.*, 2002). It can also drain our emotional reserves; contribute to depression, anxiety, fatigue, and irritability; and punctuate our social interactions with hostility and anger. Stress is the combination of psychological, physiological, and behavioural reactions that people have, in response to events that threaten or challenge them. Stress can be good or bad. Sometimes, it can be helpful, providing people with extra energy, mental alertness they need.

The mental alertness is dealt as any function pertaining to the mind, such as awareness, perception, imagination, reasoning and the like. It is a state of wakefulness with concentrated attention; it involves active participation of mental faculties of the brain. (Paykel, 1998). Research which investigates the connection between diverse stressors and motor performance have revealed a decrease in performance mostly to physiological factors (e.g. blood lactate concentrations, dehydration, and insufficient energy resources) (Davey *et al.*, 2002), or psychological factors (distraction from relevant information sources, disruption of movement automatically by attending to motor execution).

## 2. Materials and Methods

### Collection of Experimental Animals:

20 healthy albino wistar rats of both sexes, weighing 120-125g, were used in experimental research. The animals were purchased from the animal house in Pharmacology Department, Faculty of Basic Medical Sciences, University of Port Harcourt, Choba Rivers State. They were fed with standard rat diets (palletized poultry feeds) and distilled water throughout the period of study (except otherwise stated). The duration of the study was for four weeks, 7 days (1 week) for acclimatisation and three weeks for experimental processes.

### Drugs:

Catecholamine drugs (dopamine and epinephrine) were purchased from Z.J.J.T. Pharmaceutical Factory, China and were administered via the intra-peritoneal route.

### Experimental Design:

Group 1 was the control group which consist of five rats. They were fed with normal poultry chow and distilled water and were administered normal saline. Group 2 animals were also given chow and distilled water, and had their tail clipped. Group 3 animals were fed with chow and distilled water and 0.1 ml of epinephrine drug was administered. Group 4 animals were fed with chow and distilled water, and 0.1 ml of dopamine drug was administered.

**Experimental Tests:** To determine the effects of the drugs, the following tests were carried out on the wistar rats, 5 minutes after drug administration. Each experimental test was carried for 5 minutes for each test on every rat in all the groups, and results duly recorded.

### Paw Withdrawal Test:

Analgesy-meter machine was used to determine the pain bearance and response of the rats. The test was carried out

by applying force to the paw of the rat, the plinth increases at a constant rate, thereby enabling reproducible measurements to be made. The machine stops' running immediately the pedal is released, at the point of paw withdrawal, recordings on the analgesy-meter were taken. After each test, the slide is returned to its starting point by lifting and pushing to the left. The force is measured on the scale calibrated in 10-gram steps, by a pointer to the slide. This test was used in determining the anti-nociceptive activity of the drugs.

### Elevated Plus Maze:

The elevated plus maze is a widely used behavioural test for rodents, it assess the anti-anxiety effects of pharmacological agents and steroid hormones. Was carried out using the elevated plus maze instrument to determine the mental alertness of the rats. The rat was placed at the central platform like a cross, facing 2 open arms, and 2 closed arm, and the latency for the rat to move from the open arms to one of the closed arm was recorded, the number of head dips on the open arm was recoded. Following entry into the arm, the rat was allowed to explore the apparatus for 5 minutes. An increase in open arm activity (duration/or entries) reflects anti-anxiety behaviour.

The drugs (epinephrine and dopamine) was administered to group 3 and group 4 rats, and allowed to undergo same training using elevated plus maze apparatus.

### Light Dark Box Test:

The light/dark test is based on the innate aversion of rodents to brightly illuminated areas and on the spontaneous exploratory behaviour of rodents in response to mild stressors, that is, novel environment and light. The test apparatus consists of a small dark safe compartment (one third) and a large illuminated aversive compartment (two thirds). The distance travelled in each chamber, total number of entries between each chamber, and the time spent in each chamber was recorded. The most consistent and useful measurement is the time spent in light box, since this provides the most consistent dose-effect results in pharmacological evaluations

### Open Field Test Apparatus:

The open field test is based on rat's natural aversion to open areas and its willingness to explore new areas. It is used to measure anxiety states as well as locomotion and exploratory activity in rodents. Animals with minimal anxiety are likely to move about the area and perform other behaviours such as grooming and rearing, while animals with increased anxiety may freeze (not really move about), other behaviour such as urination and defecation were also recorded, and they provide the information about the animal's anxiety state. Animals in control groups show a willingness to explore, while animals treated with drugs increased anxiety-related behaviour.

### Navigational Box / Opaque Maze:

Opaque maze / navigational box study is broadly used in behavioural neuroscience to examine the spatial learning and memory. It can be a very accurate study of learning, memory and spatial working and can equally evaluate damage to cortical regions of the brain (D'Hooge and De-deyn, 2001).

This maze is a tour puzzle in the form of a complex branching passage through which the rat is expected to find a route.

### Stress-Inducing Objects

**Tail Clip:** The tail clip is regarded as a stressful activating stimulus (Antelman *et al.*, 1975) and can influence the rat's cognitive decisions and actions. The essence of tail-clip is to increase mechanical pressure on the tail of the rat throughout the period of experiment. The tail-clip was padded with a soft material to avoid injury to the rat. The clip is padded with a soft material to avoid injury to the rat. Clip will be on the tail throughout the period of experiment. The essence of the clip is to increase mechanical pressure on the tail of the rat. Tail clip is regarded as a stressful activating stimulus (Antelman *et al.*, 1975) and can influence the rat's cognitive decisions and actions.

### Statistical Analysis:

The statistical analysis of the results obtained from the study was done using the ANOVA (Analysis Of variance) method. Statistical Package for Social Science (SPSS) and Microsoft excel. The level of significance was set at  $P < 0.05$ . The results obtained were represented as Mean Standard Error of Mean (S.E.M).

## 3. Results and Discussion

The effect of induced-acute pain on mental alertness and behaviour in rats was studied. The experimental procedures for the investigations included the following tasks; Navigational maze task, Elevated maze task, Open field task, paw-withdrawal task, light/dark box task. Even though stress is an essential mechanism for survival, it also disrupts normal brain structures and functions (Karim *et al.*, 2013). Observations from the elevated plus maze showed that control group 1 was significantly ( $P = 0.05$ ) the best in all test groups, when compared to other groups. The rats spent more significant time in the closed arm when compared to open arms, control group 1 spent the most time in closed arms, while dopamine group spending the most time in open arms, followed by epinephrine group, then tail-clip group. This shows that stress, no matter the form or duration enhances the presence of anxiogenic-like activity. Results from the paw-withdrawal test as shown in table 14 in all test groups, shows that there was significant ( $P = 0.05$ ) increase in pain bearance in Dopamine group (group 4), and this was followed by control group (group 1) which was able to withstand the pain, but not as much as dopamine group, then the epinephrine group 3 in that order.

there was significant ( $P = 0.05$ ) decrease in pain bearance in tail-clip group. The percentage performance analysis showed that the performance of the dopamine group was enhanced significantly by ( $P = 0.05$ ) increase, and the best. This seems to agree with Wood, 2008 who stated that low dopamine may contribute to increased pain (wood, 2008) it is associated with enhanced pain response.

Observation from the navigational maze study as shown in Table 13 revealed that there was a significant ( $P = 0.05$ ) change in the time it took to navigate through the maze. Comparatively, dopamine and epinephrine drugs International Journal of Medicine and Pharmaceutical Research

significantly improved the ability of rats in their respective groups (group 4 and group 3) to complete the task faster when compared to the control group 1 and tail-clip group 2 which completed the task at longer duration of time, shows a significant ( $p < 0.05$ ) improvement in spatial learning and memory. Quantitatively, the percentage performance analysis revealed that group 4 (dopamine) performance was enhanced significantly ( $p = 0.05$ ) the best followed by the epinephrine group (group 3), group 2 (tail clip) and group 1 (control) followed in that order. Results from the open field test as shown above in FIG 8 and 6 showed that, in all test groups, the rats spent significant time at the corners and wall area when compared to centre stage of the open field, with control group 1 spending more time in contact with the walls and corner areas.

Dopamine group 4 there was a significant ( $P = 0.05$ ) increase in accessing all parts and patronised the centre more frequently, and travelled the highest distance, followed by tail-clip group 2. Tail-clip group 2 had anxiogenic effect due to the tail-clip attached to its tail which was a source of distraction and increased its stress and anxiety. From the result obtained, while control group showed highest rate of anxiogenic-like effect, dopamine group 4 displayed the highest rate of anxiolytic-like effect. Observation from light/dark task as shown above in FIG 9, 10, and 11. Control group 1 showed the highest example of anxiogenic effect because it spent the highest time in darker and protected compartment, when compared to other groups. Dopamine group 4 showed the highest anxiolytic effect, and there were an increased number of transitions between both compartments in dopamine group 4, and the time spent in light box was more when compared to other groups, followed by epinephrine group 3. This clearly shows that dopamine and epinephrine drugs have anxiolytic effects in them.

## 4. Conclusion

The impact of stress on cognitive functions and behaviour is strongly influenced by the type and duration of stressor. Stress can be an essential adaptive mechanism needed for survival and with only transient changes in the brain, while others can cause overreaction and deregulation of the hypothalamic pituitary adrenal (HPA) axis thus inflicting detrimental effects on the brain structure and function. Therefore, stress can be either negative or positive modulator of the cognitive functions, which includes learning and memory.

**Conflict of Interest:** We declare no conflict of interest.

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