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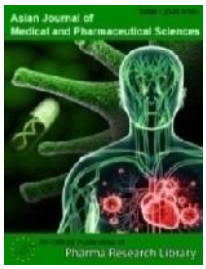

R E S E A R C H A R T I C L E

Interplay Brain Between Stress Markers and Cognito-Motor Behaviour and Coordination In Starvation- Induced Stress In Rats

Olorunfemi O.J.[*], Bohr E.L.S., Okosiemiama S.C., Okopido I.S, Okpe E.

Department of Human Physiology, Faculty of Basic Medical Sciences, College of Health Sciences, University of Port Harcourt, Choba, Port Harcourt, Nigeria.

A B S T R A C T

The impact of stress (which is a common daily occurrence) is strongly influenced by the type and duration of the stressor. The study was done to ascertain the effects of starvation-induced stress on cognito-motor behavior and coordination and also its effect on brain stress metabolites in rats usingsome neurobehavioral tasks such as Navigational maze task, Beam walking task, elevated maze task and Hand grip test. Twenty five male albino wistar rats after two weeks of acclimatization, were weighed and randomly divided into five groups (groups 1, 2, 3, 4 and 5) of five rats in each group. While group 1 is the control group, group 2 were given caffeine. Group 3 received epinephrine which was administered intraperitoneally. Group 4 received dopamine and group 5 were starved. Results on cognitive assessment showed groups treated with catecholamine demonstrated improved cognitive responses compared to the groups treated with glucose and caffeine. The results further showed that cognito-motor coordination and balance were significantly ($p<0.05$) affected by starvation-induced stress noticed in the starvation. All forms of stress demonstrated a significant ($p<0.05$) anti-anxiolytic effect. In other words, some forms of stress can be necessary adaptive measures for survival and with only transient changes within the brain while others can inflict detrimental changes in the brain structure and function.

Keywords: Starvation-induced stress, cognito-motor behavior, navigational maze task, beam walking task.

A R T I C L E I N F O

A U T H O R D E T A I L S
Olorunfemi O.J.
Faculty of Basic Medical Sciences,
College of Health Sciences, University of Port Harcourt,
Choba, Port Harcourt, Nigeria
MS-ID: AJMPS3706

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C O N T E N T S

1. Introduction

People (Over 400 million) suffer from a mental or behavioral disorder, and this accounts for about 12% of the global burden of disease (WHO, 2002). Several disease states ranging from psychiatric disorders like depression, anxiety etc and cognitive dysfunctions to cardiovascular disease, peptic ulcers, premature aging are affected by stress, which plays key role in their progression (Kaur and Kulkarni,2009). Stress involves complicated immunological, biochemical mechanisms and the human body responds to it with a fight-or flight reaction. Thus, as defined in this context, it is the body's method of reacting to a challenge. Most importantly, cognitive functions are affected by stress (von Zerssen, 1976).

Thus, recent studies suggest that stress affects the brain which could affect learning and memory etc. Also, stress-related hormones are known to alter physical structures in the brain. Some studies have shown that information does not get relayed across nerve cells because of the shrinking of dendrites caused by stress hormones thereby resulting in failure to send or receive signals. Therefore, the cognitive, behavioral status of an organism is remodeled following the lifelong self-adjustment and self-optimization processes to meet the ever changing demand.Stress affects everyone. Life is filled of stress. Therefore, stress affects every aspect of life that we must all deal with.

2. Materials and methods

The guideline of the care and use of animals in research/teaching was strictly followed (NIH Publication No. 8593, revised 1985) and the experimental research was conducted in the animal house (pre-clinical) of the University of Port Harcourt, Rivers state, Nigeria.

The recommendations from the 16th Annual Assembly of the World Medical Association held in Edinburgh in October, 2000 on ethical guidance for biomedical research was adhered to in the course of this research.

Drugs and Chemicals

Epinephrine was purchased from Wuhan Grand Pharm. Group, co, Ltd, China. The solvents and chemicals were used. Other drugs and substance used include caffeine, dopamine and glucose.

Collection of Experimental Animals

Twenty-five (25) male Albino wistar rats were used for this study and were housed in the animal house, College of Basic Medical Sciences, University of Port Harcourt. The animals were treated professionally under laboratory conditions and ethics guiding the use of animals in experimentation.

Acclimatization of animals

After identification, the animals were allowed to acclimatize for two (2)weeks. The animals were weighed and housed in a wire gauze cage under standard conditions (Temperature 25-29^{o}C, 12 hours' light/dark cycle).

Animal grouping

The animals were divided into five groups. Each group comprise of five male Albino wistar rats. The first groups (control group 1) were given glucose. The second group received caffeine. The third group was given epinephrine. The fourth group was administered dopamine while the fifth group was starved.

Group 1 - (control) was treated with glucose 1mL/kg.
Group 2 – was administered caffeine 50mg/kg
Group 3 – was administered epinephrine (2.0lg/kg)
Group 4 – was administered dopamine(2.0lg/kg)
Group 5 – was starved (12 hours daily), feeds was removed from 6am to 6pm each day.

Cognitive and Motor Function Tests

Cognitive and motor functions were carried out on the experimental animals with the following tasks;

- Navigation task
- Elevated maze task
- Hand grip task
- Beam walking task

Navigation Maze Test

The navigation maze test is a test of cognitive motor functions for rodents that relies on distal cues to navigate from start locations a tour puzzle which looks like a complex branching passage through which the rat is expected to find a route. Performance of the maze is quantified by measuring the time it will take the rat to find the exit route. Navigational Maze Study is broadly used in behavioral neuroscience to examine memory and spatial learning.

Beam Walking

Each of the rats in this study, was placed on one end of an elevated cylindrical beam of about 38cm long and was expected to move to the other end of the beam. Performance on the beam is quantified by measuring the period of time that it takes for the rat to cross the beam. Beam Walking Test is used to access anxiety and fine motor coordination and balance. (Tinhet al., 2011).

Hand grip

This objectively quantifies the muscular strength in rats. In this study, the rat's forelimbs was placed on the grid while the other part of the body was suspended. Each rat was monitored and time at which they lose grip was carefully noted using a stop watch.

Duration of Study

This research study lasted for a period of eight (8) weeks which comprises of two weeks of acclimatization and six (6) weeks of administration.

Epinephrine Administration

Before the rats in test group 3 were engaged in cognitive tasks, about 0.1ml/150g body weight of rat of 1mg epinephrine ne was administered intraperitoneallywith the aid of 1 ml syringe.

Statistical Analysis

SPSS version 20.0 was used for statistical analysis and the results were expressed as mean ±SEM and relative percent change. One-way Analysis of Variance (ANOVA) and Post Hoc Test were used to compare the mean and P-Value ≤ 0.05 was accepted as statistically significant. Results were presented in tables and bar charts.

3. Results and discussion

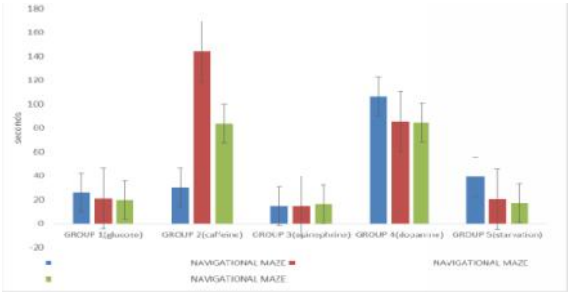

Fig 1: Cognitive Response duringnavigational maze test across the group

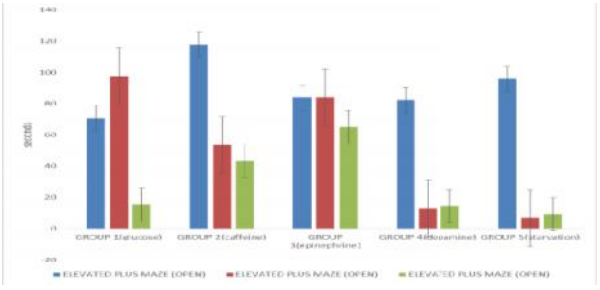

Fig 2: Activities from opened elevated plus maze test across the test groups and the control

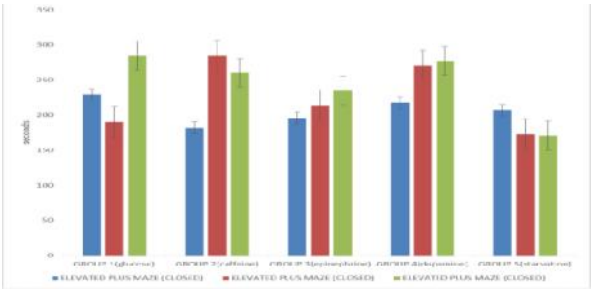

Fig 3: Activities from closed elevated plus maze test across the test groups and the control

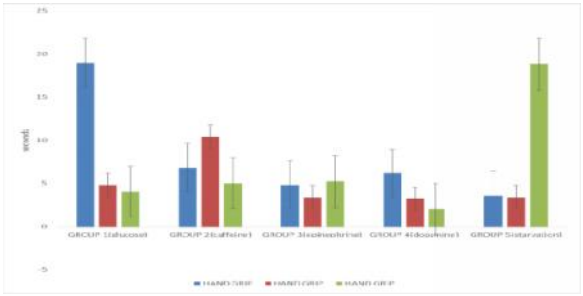

Fig 4: Activities from hand grip test across the test groups and the control

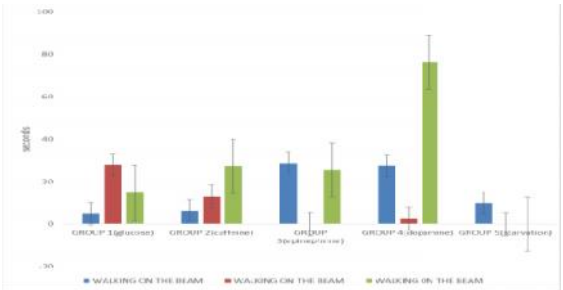

Fig 5: Activities from walking on the beam test across the test groups and the control

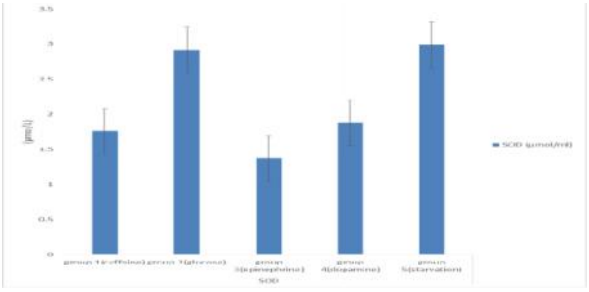

Fig 6:SOD levels resulting from treatment across the test groups and the control

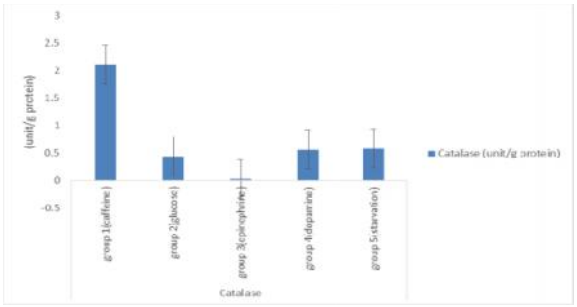

Fig 7: Catalase levels resulting from treatment across the test groups and the control

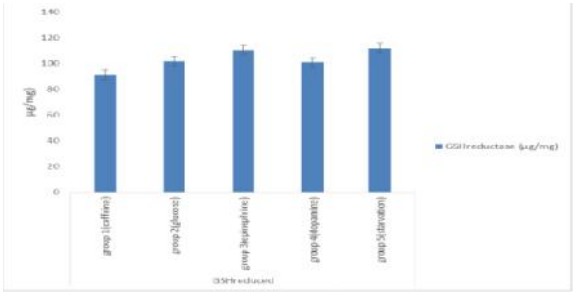

Fig 8:GSH reductase patterns resulting from treatment across the test groups and control

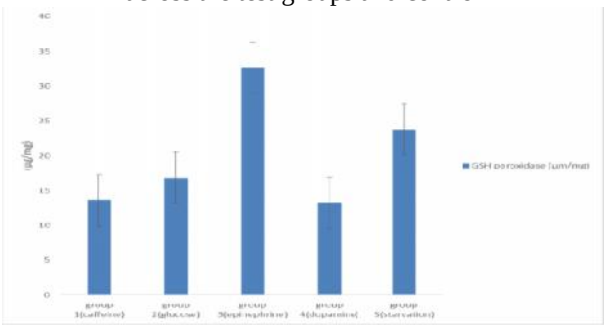

Fig 9:GSH peroxidase pattern resulting from treatment across the test groups and control

Discussion

This study investigated the effects of starvation-induced stress on cognito-motor behavior and brain stress markers in albino wistar rats. The experimental procedure was done using the following test; Navigational maze tests, Beam walking test, Elevated maze test (open and closed arm) and hand grip test.Navigational maze test is a test of cognitive motor functions for rats that relies on cues to navigate from start locations to the exit end through a labyrinth (Michael et al, 2010).

In other words, Navigational maze task is employ in behavioural neuroscience to study spatial learning and memory. It can be a very precise study of learning, memory and spatial working and be capable of also assessing damage to cortical regions of the brain (Hoogeand De deyn,2001). It is also used as a tool to study drug abuse, neural systems, neurotransmitters and brain development.

In the navigational maze test involving three trials at fifteen minutes' interval, epinephrine-treated group demonstrated the most significant improvement in the performance followed by the starvation group. The time taken to perform the navigation is a clear reflection of cognitive astuteness of the animal in challenging situations. The caffeine-treated group alongside the dopamine-treated group performed significantly the slowest as indicated by the amount of time taken in meandering through the labyrinth. This observation was corroborated by the work of Smith et al, 1999 that stated that all doses of caffeine significantly affect cognitive performance and also decrease brain activity". Dopamine on the other hand, also has effects on learning; some evidence indicates it improves working memory while it impairs other complex functions (Brozoski et al, 1979).

In group 5, the task was fast compared with group 2 and 4. A study done on the effect of starvation/fasting on cognition in rats' shows that there was improved prefrontal-cortex-mediated cognitive function such as mental flexibility. In contrast, hippocampus-related cognitive performance was not affected by starvation/fasting (Rima et al, 2016). The above result agrees with previous research, that stress can weaken learning and that memory can be improved by stress (Nielson et al, 2005).

The Elevated plus maze is an animal model used as a general tool in neurobiological anxiety research. Results from the elevated maze test as shown in figures 2 (open) and 3 (closed) revealed in all test groups that the rat spent more time in the closed arm compared to the open arm. This observation is in concert with the fact that rats are generally nocturnal animals and actively seek for a closure for their activities. This shows that stress, no matter the form or duration enhances the presence of anxiogenic-like activity. This is in accordance with the work of Lisa and Israel.It is important to note that physical stress equally affects learning and memory though the duration, frequency and risk-reward of each stress plays a role.

Beam walk test is used to access anxiety and fine motor coordination and balance. This test is used to ascertain the ability of the animal to remain upright and to walk on an elevated and relatively narrow beam. This test is also used to detect motor deficit due to age, central nervous system lesion and genetic and pharmacological manipulations in young and old rodent (Tinh et al, 2011). Generally, observations from the beam walk study as shown in figure 5 revealed that the control group 1 treated with glucose traversed the quickest the entire length while starvation group 5 recorded no performance at all.

Motor coordination is principally adjusted in the cerebellum. A main player in modulation of cerebellum is GABAergic neurotransmitter in cerebellum. Observations from the beam walking test as shown in figure 4 revealed that there was a significant ($p<0.05$) change in the time it took for the groups to traverse the beam in the third trial.In group 5, there was passivity observed in the 2nd and 3rd trials and hence therewas no movement as opposed to the 1st trial which traverse the beam in a recorded time of 9.80 ± 5.09.

A study done by Schindler on the effect of dopamine on locomotive activity in rats' shows that there is an increase locomotive activity, thus they show an increase in behavioral response to dopamine administration. Another research done by Davey et al in 2002 evaluated the connection between diverse stressors and motor performance and it was observed that there was a decrease in performance mostly to physiological factors (e.g dehydration and insufficient energy resources).

Hand grip test is a motor function test that measures the strength of the forepaw. The hand grip test is a uncomplicated non- invasive technique designed to assess rats muscle force in vivo by taking gain of the animal's predisposition to grip a horizontal metal bar/grid while suspended by its tail. Experimental animals are allowed to grasp the grid with their forepaws and are then pulled from the base of the tail until they release the grid. Observation from the hand grip test in table 4.5 denotes that there was significant ($p<0.05$) change in the time it took the animal to hold on to the meter grid. Thus, from the table, group 1 and group 4 had a progressive reduction in time. While in group 5 there was an increase in the time.

From results for brain stress markers, it was observed that groups 2,4, and 5 had higher levels of Superoxide dismutase (SOD) in comparison to the control. While for groups 3 it was lower. For Catalase, there is a decrease in its level across all the groups when compared to the control group. Glutathione reductase values were seen to be higher in all the groups. Finally, for glutathione peroxidase there was an increase in the values in comparison to the control group. Glutathione peroxidase acts as a cysteine reserve during food deprivation (Cho et al., 1981) and is a major source of cysteine for lymphocyte. Brain makers are antioxidant enzymes that function as blockers of free radical process.The implication for the above biochemical activities is that starvation as a form of stress could trigger rise in stress response and can result in the availability of these markers in the blood. The increase in the level of cellular lipid peroxidation easily gives rise to levels of malonaldehyde, glutathione indicating cellular provocation and response.

4. Conclusion

In conclusion, the results show that starvation-induced stress affects some cognitive functions and behavior in rats. The various tests employed in the study clearly demonstrated the direct interference of starvation-induced

stress could have in cognitive awareness and motor activities. The impact of stress on cognito-motor behavior and coordination and brain stress markers seemed to be minimized by drugs although the effect may cause short-term neurological problems. The impact of stress on cognitive functions and behavior is strongly affected by the type and duration of the stressor. Hence, stress can have a negative or positive modulator effect on cognitive functions (which includes the learning and memory processes) and motor function/coordination.

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