International Journal of Herbs and Pharmacological Research
IJHPR, 2017, 6(1): 25 - 30
ISSN: 2315-537X www.arpjournals.com; www.antrescentpub.com E- ISSN: 2384-6836

RESEARCH PAPER

ASSESSING THE EFFECT OF ANXIETY RELATED BEHAVIOUR FOLLOWING REPEATED ADMINISTRATION OF 5-HYDROXYTRYPTOPHAN IN MICE

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Published: 31st January, 2017

Endorsed By: *Innovative Science Research Foundation (**ISREF**) and International Society of Science Researchers (**ISSCIR**).*
IndexedBy*: African Journal Online (AJOL); Texila American University; Genamics; Scholarsteer; EIJASR; CAS-American Chemical Society; and IRMS Informatics India (J-Gate)*

ABSTRACT

The effect of repeated administration of 5-Hydroxytryptophan diet on anxiety, was studied using two groups of Swiss mice (control and test) weighing 18-28g (n=10 each).The control received 100g of normal rodent chow, while the test received 1g of 5-Hydroxytryptophan in 99g of rodent chow per day. Water was given *ad libitum*, while daily food and water intake, as well as body weight changes, were monitored during the 31-day study. The light/dark box was used to access anxiety related behaviour. The result showed that in the light/dark transition box, the light box duration was significantly higher ($P<0.05$) in the test group, while the frequency of stretch attend posture, frequency of grooming and duration of grooming, were lower in the test group ($P<0.05$ and $P<0.001$ respectively), signifying a decreased level of anxiety in the test group. Thus, repeated administration of 5-Hydroxytryptophan may decrease anxiety/fear.

Keywords: 5-Hydroxytryptophan, Anxiety, Light/dark transition box and Mice.

INTRODUCTION

5-Hydroxytryptophan (5-HTP) is the intermediate metabolite of the essential amino acid L-tryptophan (LT) in the biosynthesis of serotonin. Intestinal absorption of 5-HTP does not require the presence of a transport molecule, and is not affected by the presence of other amino acids; therefore, it may be taken with meals without reducing its effectiveness. Unlike LT, 5-HTP cannot be shunted into niacin or protein production. Therapeutic use of 5-HTP bypasses the conversion of LT into 5-HTP by the enzyme tryptophan hydroxylase, which is the rate limiting step in the synthesis of serotonin (Osim and Wyllie,1991).5-HTP is well absorbed from an oral dose, with about 70% ending up in the blood stream. It easily crosses the blood brain barrier and effectively increases central nervous system (CNS) synthesis of serotonin (Timothy *et al*., 1998).

In the CNS, serotonin levels have been implicated in the regulation of sleep, depression, anxiety, aggression, appetite, temperature, sexual behaviour and pain sensation. Therapeutic administration of 5-HTP has been shown to be effective in treating a wide variety of conditions, including depression, fibromyalgia, insomnia, bringe eating associated with obesity chronic headaches, and insomnia(Guilleminault *et al*.,1973;Van Prag*et al*.,1986;Den Boer *et al*.,1990;Chalkwick *et al*.,1995;Timothy *et al*.,1998). It may be worthwhile to find out whether repeated administration of 5-Hydroxytryptophan diet can affect behaviour. This was of particular interest when we consider the challenges that confront human behaviour and how behavioural disorders still remain a global concern (Messman, 2005).

Human behaviour is believed to be influenced by endocrine and nervous systems. The complexity in the behaviour of an organism is correlated with the complexity of its nervous system. Thus, organism with more complex nervous systems (like humans) has a greater capacity to learn new responses and adjust their behaviour. This behaviour is influenced by physical and psychological changes that result from a complex state of feeling described as emotion (Cacioppo and Gardner, 1999).Therefore, this study was aimed at investigating the effect of repeated administration of 5-Hydroxytryptophan on anxiety related behaviours in mice.

MATERIALS AND METHODS

Experimental animals/grouping: Twenty (20) Swiss white mice weighing between 18-28g was obtained from the animal house of the Department of Pharmacology, University of Calabar, Nigeria, were used for this study after approval by the College Ethical Committee of the University of Calabar, Nigeria. The animals were acclimatized under standard laboratory conditions and given free access to normal feed and clean tap water. The animals were randomly assigned into two (2) groups; a control and a test group. The animal in the control group received normal rodent chow only, while the test group received mixed feed of 1g 5-Hydroxytryptophan per 99g of rodent chow making 1% of the diet for 31days.This is sequel to the fact that the determined LD_{50} for intra-peritoneal administration of 5-Hydroxytryptophan was 937.04mg/kg.

Experimental Design: The light/dark transition box was used to access anxiety and fear related behavior. Mice were carried into the test room in their home cages and were handled by the base of their tails at all times. Each mouse was picked up using a plastic bucket and placed in the centre division of the large compartment facing the floor. The mouse was allowed to explore the transition box for 5 minutes. Entering into the chamber is defined as the placement of all four paws into the chamber. During the period of 5 minutes, behavior scored using a stop watch was frequency of grooming and duration of grooming; light box duration, frequency of rearing and stretch attend posture.

Statistical Analysis: Data collected were expressed as Mean ± SEM (standard error of mean), analysis of variance (ANOVA) and the student't' test were used for analysis. "P" value less than 0.05, was considered statistically significant.

RESULTS

Grooming frequency in the light/dark box:The frequency of grooming for mice fed control and serotonin precursor diet was recorded as 2.60± 0.34 and 1.57± 0.20/5mins respectively. The graph in figure 1 shows that mice fed serotonin precursor was significantly lower ($p<0.05$) than that of the mice fed control diet.

Grooming duration in the light/dark box: Figure 2 compares the grooming duration between the two groups of mice respectively. The grooming duration shown in figure 2 was 14.53 ± 2.78secs (control) and 1.75± 2.78 (serotonin precursor). Mice fed with the serotonin precursor diet showed, a lower grooming duration compared to control ($p< 0.001$).

Light chamber duration in the light/dark transition box: The values for the light chamber duration are: 146:58± 8.02 (control) seconds and 170.00 ± 26.02 seconds (serotonin precursor).The duration of time the animal spent in the Light Chamber in the group of mice fed serotonin precursor diet was significantly higher ($P<0.05$) compared to control(Fig.3).

Stretch attend posture (sap) in the light/dark transition box: The frequencies of stretch attend posture between the two groups are: 2.40± 0.39/5min (control) and 1.57 ± 0.53/5min (serotonin precursor) respectively. The frequency of the SAP for the serotonin precursor fed mice was significantly lower ($P<0.05$) compared to control group. See figure 4.

Frequency of rearing in the light/dark box: The frequency with which the animal stand on his hind legs was recorded as 40.57± 4.45; 8 and 30.20± 2.56/5min for mice fed control and serotonin precursor diets. Mice fed serotonin precursor diet showed, a lower frequency of rearing compared to control ($p<0.05$) (Fig 5).

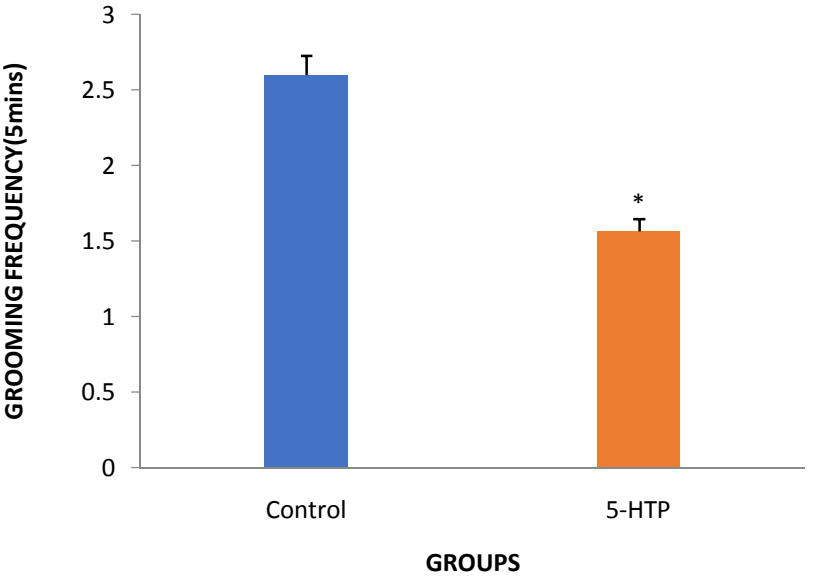

Fig 1: Frequency of grooming in the different experimental groups during the light/dark transition box test.Values are expressed as mean ± SEM, n = 10;*p<0.05 vs. control.

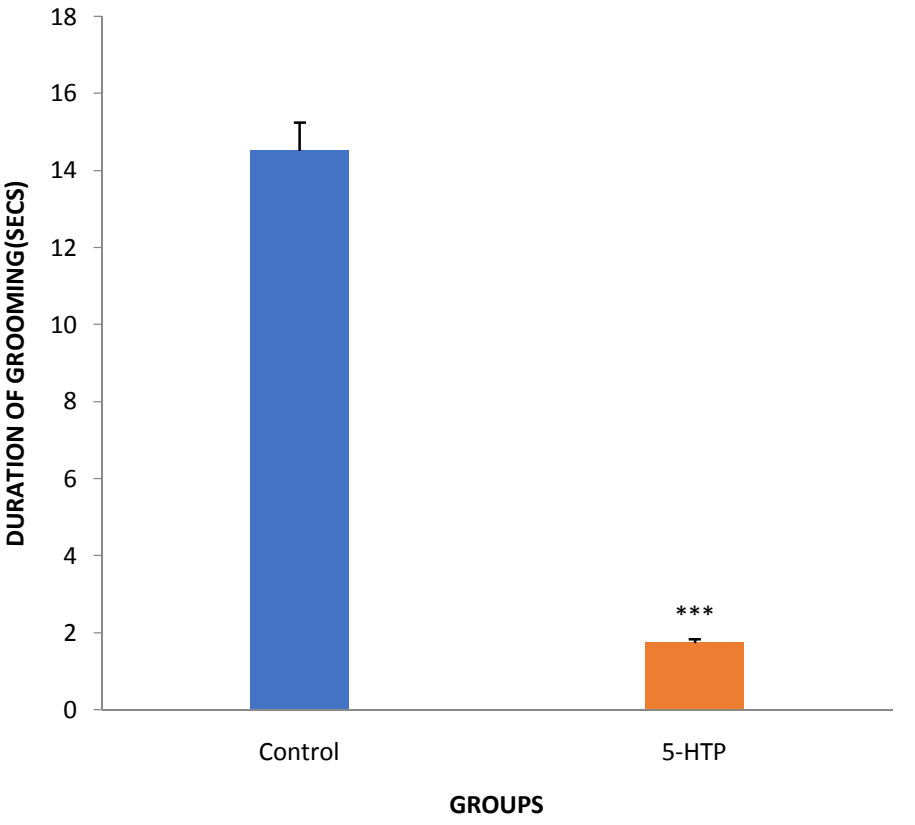

Fig 2: Duration of grooming in the different experimental groups during the light/dark transition box test.Values are expressed as mean ± SEM, n = 10;*p<0.001 vs. control.**

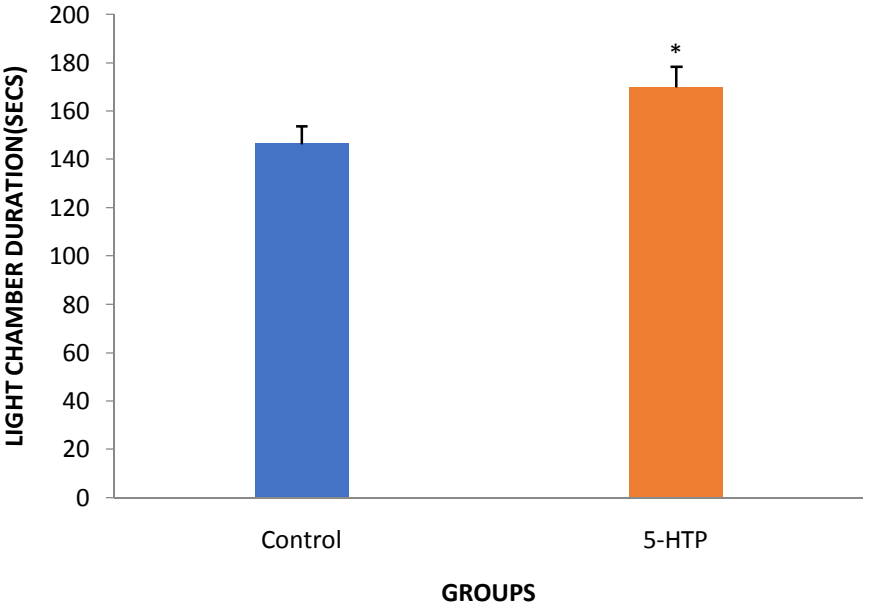

Fig 3: Light box duration in the different experimental groups during the light/dark transition box test.Values are expressed as mean ± SEM, n = 10;*p<0.05 vs. control.

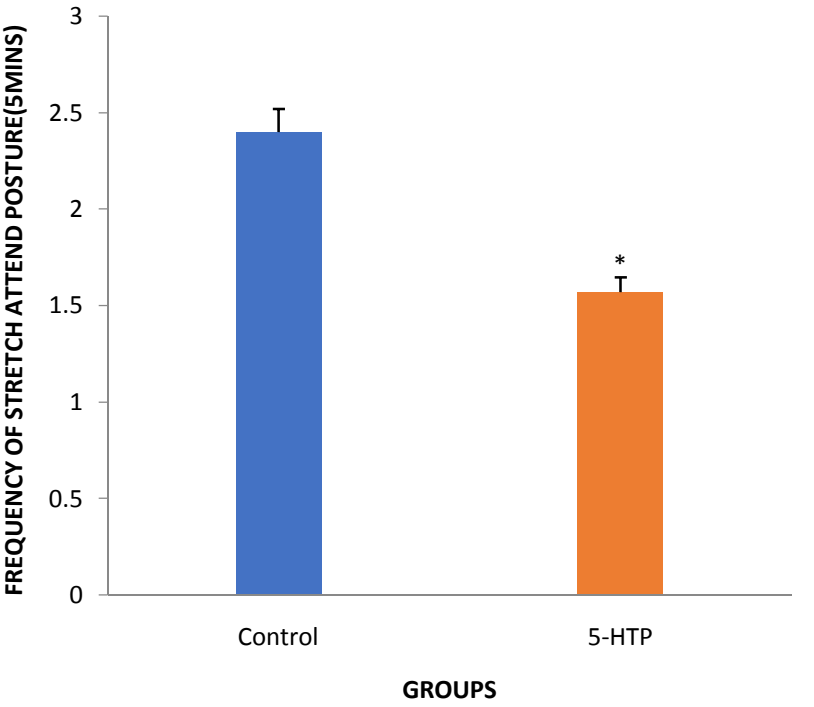

Fig 4: Frequencies of stretch attend posture in the different experimental groups during the light/dark transition box test.Values are expressed as mean ± SEM, n = 10;*p<0.05 vs. control.

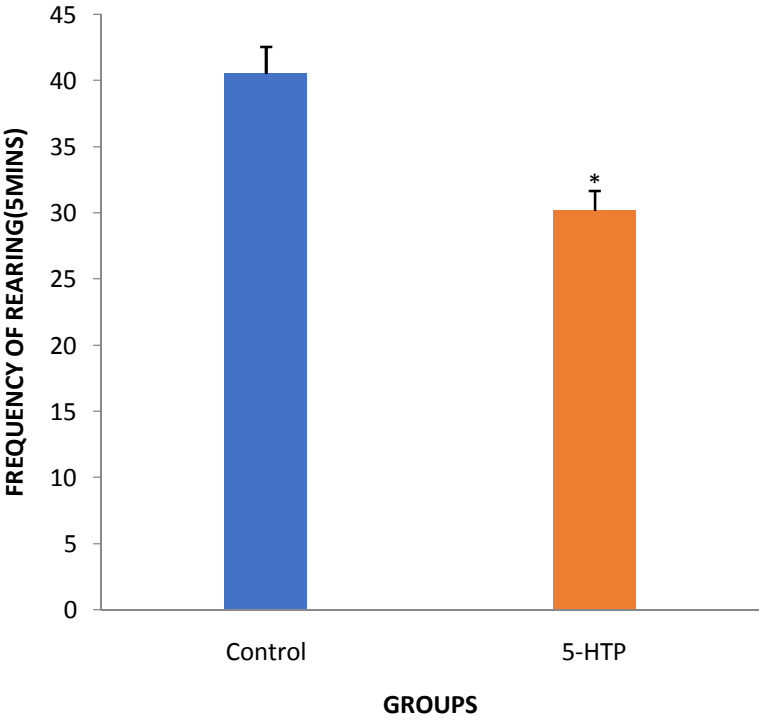

Fig 5: frequency of rearing in the different experimental groups during the light/dark transition box test. Values are expressed as mean ± SEM, n = 10; ***p<0.05 vs. control.

DISCUSSION:

In order to assess the effect of repeated administration of 5-Hydroxytryptophan diet on anxiety related behaviours in mice, the light and dark transition box (LD) was employed. This method is similar to that of Brown *et al* (1999), who used the light and dark transition box to assess locomotion and anxiety behaviours of animals in the novel environment. In the light box, the light chamber duration for the test group of mice was significantly higher when compared to control. The frequency of stretch attends posture (SAP), which is a measure of anxiety in the 5-Hydroxytryptophan group was significantly lower compared to control. The grooming frequency and duration was also lower in the test group compared to control. Similarly, the rearing frequency of the test group was also significantly lower compared to control.

The decrease in anxiety related behaviours, following repeated administration of 5-Hydroxytryptophan is in consonance with the report of Aduema(2016), which showed that the consumption of common beans which 5-Hydroxytrytophan was the principal active constituent caused decreased anxiety/fear. Fear and anxiety are basically controlled by neural circuitry involving the amygdala mostly and the hypothalamus. Electrical stimulation of the amygdala for instance is associated with fear and feeling of terror in the animals (Osim, 2008).

Thus, it is possible that the presence of this compound (5-Hydroxytryptophan) could be responsible for the anxiolytic property which acts by inhibiting the excitability of the amygdala by increase in the threshold of response of the cells of these nuclei, thereby reducing fear related behaviour in the mice (Costal et al., 1989; Adolph et al., 2005). It is also possible that those mice did not show anxiety and fear related behaviour because 5-Hydroxytryptophan may have increased the level of brain serotonin and thus facilitated the calming, relaxing and mellowing serotonin circuits (Young &Teff, 1989).

In conclusion, if the result of these findings is extrapolated to man, then, repeated administration of 5-Hydroxytrytophan can be used to ameliorate panic disorders.

ACKNOWLEDGEMENT

We acknowledged Mr. and Mrs. B.A. Aduema, Dr. Nmaju, and Associate Prof. A.A. Nwankwo for their priceless support.

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AUTHORS CONTRIBUTION

All the authors played important roles towards the success of this publication