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The Effects on Social Behaviour & Motor Balance following Repeated Administration of 5-Hydroxytryptophan

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Abstract

The aim of the study was to investigate the effect of repeated administration of 5-Hydroxytryptophan (5-HTP) on social behaviour and motor balance. The quantity of 5-HTP reaching the Central Nervous System (CNS) is affected by the extent to which 5-HTP is converted to serotonin in the periphery. The Beam walking and nestle cotton test were used to access motor balance and social behaviour in mice using two groups of mice weighing 20g-30g (n=10 each).The control group received (15g) normal rodent chow, while the test group received (15gw/w) 5-HTP diet. Daily food intake, water intake and body weight change were measured. The results showed that the frequency of foot slip, distance covered was significantly higher ($p<0.05$) compared to the control while the latency of fall was longer compared to the control. Thus, suggesting that the mice administered 5HTP had better motor coordination and balance compared to control. The nesting score showed no significant difference among the groups. In conclusion, repeated administration of 5-HTP improves motor balance and coordination but did not affect social behaviour.

Keywords: Nestle cotton; Beam walking apparatus; Mice; 5-HTP

Abbreviations: 5-HTP: 5-Hydroxytryptophan; LT: L-tryptophan; SEM: Standard Error of Mean; ANOVA: Analysis of Variance; CNS: Central Nervous System

Introduction

5-Hydroxytryptophan is an aromatic amino acid naturally produced from L-tryptophan (LT). It is obtained commercially by the extraction from the seeds of the plant *Griffonia simplicifolia.* 5-Hydroxytryptophan (5-HTP) has been used clinically for over 30 years [1]. The clinical efficacy of 5-Hydroxytryptophan is its ability to increase production of serotonin. There are some research to support the use of 5-HTP in treating cerebellar ataxia, headache, depression, psychiatric disorders or aid panic disorder, but studies in people with schizophrenia has shown different results [2] and as an appetite suppressant etc. [3-5]. 5-HTP may cause GIT disturbances, mood disturbance, seizure etc. It has also been reported that side effects might result from contaminants in 5-HTP products. However, most of the studies involving the use of 5-HTP were for depression which were done many years ago. At that time, there was a high level of interest in serotonin hypothesis on depression [6]. It is possible that this series of events may have led to the loss of interest in 5-HTP in respect to neurobehaviour. 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 [7].

Materials and Methods

Experimental animals/ grouping

Twenty (20) Swiss mice weighing between 20g and 30g were randomly assigned into two groups of 9 mice each (control and test groups). The control group received normal rodent chow, while the test group was administered 15g of 5-Hydroxytryptophan diet, daily for a period of four weeks.

Experimental Design

The beam has a length of 100 cm, a width of 2 cm and is elevated to a height of 40 cm. The beam is marked at 5 cm and 1 cm intervals. It is composed of wood and is coated with black paint. The camera is located 175 cm above the beam. The subject is scored live and filmed with a video camera.

Procedure

The mice were carried to the test room in their home cages. The mouse was removed from its home cage and placed at one

end of the balance beam. After the mouse has secured its grip on the beam, the trial begins. The maximum length of the trial is five minutes. The mouse is tested under white light, during the dark phase. The beam is cleaned with 70% ethanol and permitted to dry between each trial. What was measured were,

1. **Distance travelled:** The number of line crosses.
2. **Foot Slips:** Number of times one of the mouse's back feet slips from the beam.
3. **Number of turns:** Frequency that the animal reversed direction.
4. **Latency to fall:** Time at which the animal fell off of the beam. If a fall occurred the animal was not placed back on the beam but was returned to the home cage. The trial was not repeated (Figures 1 & 2).

Figure 1: Plate 1: Beam walking apparatus

Figure 2: Plate 2: Mice building nest.

Table 1: Nesting behaviour rating scale.

`Rating	Requirements
1	Nestlet not noticeably touched (90% or more intact)
2	Nestlet partially torn (50-90% intact)
3	Nestlet mostly shredded, often no identifiable nest site, 50-90% shredded, also, less than 50% remains intact, but less than 90% is within a quarter of the cage floor (i.e., not gathered into a nest site but spread throughout cage)
4	An identifiable, but flat nest, more than 90% of the nestlet is torn, the nest is uneven, material is gathered into a nest within a quarter of the cage floor, but the nest is flat with walls higher than mouse body height for less than 50% of its circumference
5	A (near) perfect nest, more than 90% of the nestlet is torn, nest is fairly even, the nest is a crater, with walls higher than the mouse body for more than 50% of its circumference

Nesting behaviour has been used as an assay for social behaviour [8]. Mice were housed individually and tested in their home cages. One hour before giving the mice nesting materials, all enrichment objects in the home cages of the mice were removed. About 3.0g of nesting material were supplied to each mouse in its home cage and allowed for 24 hours. Twenty hours later, the nests were assessed using the rating scale supplied by Deacon R [9] (Table 1). This was based on what was seen.

Statistical Analysis: Data collected were expressed a 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

Beam Walking

The frequency of foot slips of the different experimental groups was recorded as 7.20 ± 0.88 and 2.71 ± 0.42/ 5min for mice fed with control and 5-HTP diet respectively. The frequency of foot slips for the 5-HTP group was significantly different from control at $p<0.05$ (Figure 3). Figure 2 shows the distance covered in the different experimental groups which are recorded as: 41.71 ± 3.99 and 85.50 ± 8.46/5min for mice fed control and 5HTP diet respectively (Figure 4). The distance covered for mice fed with 5HTP diet during beam walking was significantly higher ($P<0.01$) compared to control. The latency of fall of the different experimental groups is as follows: 7.36 ± 10.56 and 15.37 ± 3.48 seconds for mice fed control and 5HTP diet respectively. The latency of fall was longer for the 5HP diet fed mice compared to control at $p<0.05$ (Figure 5). The nesting score in the social behaviour test of nest building was 2.30 ± 0.37 and 2.71 ± 0.42 (%) for mice fed control and 5-HTP diet respectively. There was no significant difference among the groups (Figure 6).

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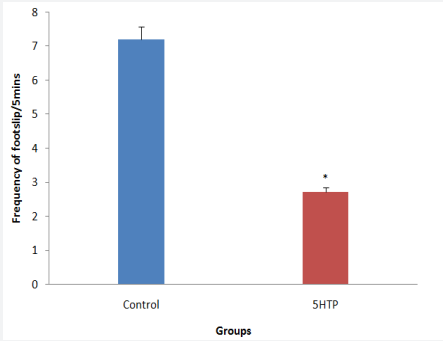

Figure 3: Frequency of foot slip in the different experimental groups during the beam walking test. Values are expressed as are expressed as mean ± SEM, n = 10, *p<0.05 vs. control.

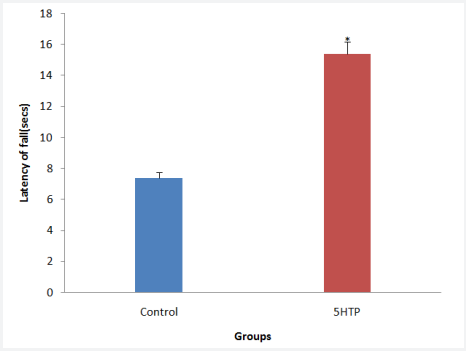

Figure 5: Latency of fall in the different experimental groups during the beam walking test. Values are expressed as are expressed as mean ± SEM, n = 10, *p<0.05 vs. control.

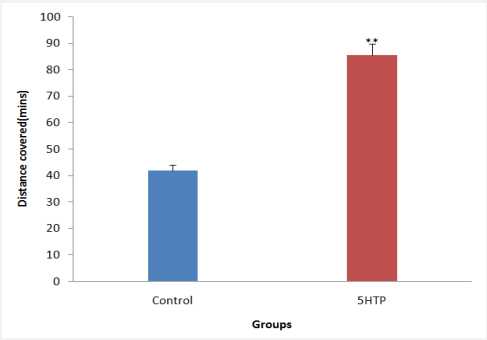

Figure 4: Distance covered in the different experimental groups during the beam walking test. Values are expressed as are expressed as mean ± SEM, n = 10, **P<0.01 vs. Control.

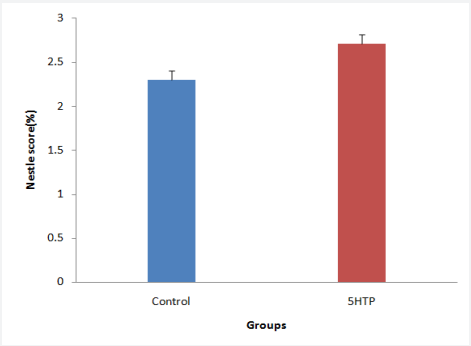

Figure 6: Social behavior score in the different experimental groups during the nestle cotton test. Values are expressed as are expressed as mean ± SEM, n = 10, *p<0.05 vs. control.

Discussion

The nesting score is an assessment of social behaviour. Nesting behaviour which is a reflection of social behaviour in mice may shed light on some significant disorders of human social behaviour such as schizophrenia and autism. Abnormal social behaviour exhibited in mice form a core deficit associated with autism spectrum disorder [10]. Mice in this case huddle together and are able to fluff up suitable beds from their nesting materials [11]. A poor performance in the nesting task may indicate impairment of social relationship in the mice and perhaps a pointer to the presence of autistic behaviour. High level of nesting behavior as indicated in the nesting score (increase grades) indicates increased social behaviour.

The results showed that the mice that were fed 5-HTP diet were not significantly different from that of the control. However, all the mice fed 5HTP diet were able to build their nest well with no one showing any deficit in nest building. Therefore, 5HTP diet did not affect social behaviour and social interaction in mice. Beam walking is a test for motor coordination and balance. The results in beam walking showed that the 5-HTP group showed better motor coordination compared to control. This is because, decreased frequency of foot slips and longer latency of falls indicate a higher level of maneuverability in the beam, thus indicating better motor coordination and therefore the better the motor learning ability [12,13].

Conclusion

In conclusion, repeated administration of 5-HTP diet improves motor coordination but does not affect social behaviour and social interaction in mice. If these results are applicable to humans then repeated administration of 5HTP could be used in the control and management of ataxia, the animal model of Parkinson's disease.

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Authors Contribution

All authors have contributed one way or the other to the success of this paper and there is no conflict in relation to funding or whatsoever that may prevent the publication of this piece.

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