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ORIGINAL ARTICLE

MODIFIED CAGE-CROSSING ACTIVITY TESTING VARIABLE AND MICE BEHAVIOR

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ABSTRACT

The purpose of this research was to assess the strong modulative effects on the brain and behavior by the cage-crossing exploratory test parameter. This was an observational study. Reserpine, Nux-vomica (*Strychnus nux-vomica*), Bhilwa and chlorpromazine were the medications for the research. These drugs were pharmacologically active in a broad spectrum. We also tested the efficacy of these drugs as agents with modulatory brain and cage-crossing parameter measurement behavior. 25 mice belonging to both sexes have been included in this study. The animals of the study were divided into five groups of five animals each group. Four groups were given drugs and one group was kept as control. This trial was conducted in mice (20-35 g) of both sexes. Under room temperature, mice were placed. Ad-Libitum was approved for tap water. 30 minutes after medications were given, two-minute intervals of animals were observed for ten minutes. The tablet was crushed in 10 ml of water and 1 cc was given. Cage-crossing was the screening method used. *Strychnous nux-vomica* was shown to have a significant effect on cholinergic system, CNS activity and frequent cage-crossing (103±90.80) when used at a dose of 0.07mg. Rauwolfia serpentine is an active alkaloid particularly present in the spine (102.8±92.4) no significant cage-crossing effect has been observed. Anacardium (86.6±61.8) and chlorpromazine (90.8±74.08) reduces effects. Based on the authentic evidence-based of these herbs, this study was undertaken to evaluate these medicinal products for CNS activity on albino-mice.

Keywords: *Strychnus nux-vomica*, *Semecarpus anacardium*, cage-crossing exploratory test.

INTRODUCTION

Cage-crossing is a measure of the effect of activity and exploration that affects movement and investigation when confronted with a new domain or item, the creatures frequently display designs that are comprehensively defined as exploration, e.g., motion around the earth, positioning towards strangeness, and touching or sniffing new objects. Exploration is conceivably furnishing creatures with new data on sources of sustenance, shelters or prospects. Again, by entering another environment or taking care of a novel boost, the creature may also increase its risk of predation, hostility or different hazards. Whatever the animal explores or avoids the oddity has been portrayed as the result of a methodology, keep away from a clash once or as a harmony in the midst of neophilia and neophobic propensities. Neophilia is defined as the fascination that a creature has shown towards an article or place, essentially on the grounds that it is novel, while neophobia is the abhorrence that a creature has shown towards drawing closer to a novel protest or spot.

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These terms, neophilia and neophobia, were seen as an individual interest-based way of dealing with and fear-based evasion of a novel stimulus (Greenberg R, 2003); (Leussis *et al*., 2006).

In 1964, Bossier and Simen introduced the cage-crossing apparatus (Boissier *et al*.,1964). Since then, it has been widely used to study drug effects through a cage-crossing test to explore the behavioral response seen by different drugs. Home cage is a plastic box. Control and treated mice were left in the cage and their movements were recorded (visually) in all corners of the cage in 10 minutes from one corner of the cage to another, even if the mice were standing on their hind limbs and trying to touch the wall of the cage. This is also considered to be a single count. The test circumstance has been changed by separating the container into square compartments (16x10cm). So that other behavioral changes may be seen. In this way, the significance is scored when the mice rise to the hind legs and the paws of the face lie on the part of the divider, and the cross is scored when the creature moves across the divider from one compartment to another (Hughes *et al*., 2007). Anxiety plays a key role in the pathogenesis of mental problems.

It is now clear that without information on clinical and the organic portions of tension and sorrow, it is difficult to offer patients treatment options. We used animal models as "trial arrangements grew in one animal category with the end goal of concentrating on phenomena happening in different species". Mice and people share more than 90% of their qualities, and creature models are seen as a useful tool in the medical sciences, especially when people cannot consider the effect of anxiety due to moral reasons. Subsequently, one of the present difficulties is to use the best clinical and neuropharmacological means of brain and behavior (Paterson *et al*., 2001) (Borsini *et al*., 2002) (Raison *et al*., 2003) (Nemeroff *et al*., 2004). Herbal medicines are one of the major research frontiers. The effect of some herbal medicine on the psychopharmacological profile was observed in our study. Chemical investigation of herbal drugs helps us to explore the further use of these herbs/alkaloids and/or better understanding of the adverse effects that could be seen by the use of these herbal products (Meyer *et al*., 2004). Nux-vomica is the dried ripe seed of Strychnus Nux-vomica Linne belongs to family Loganiaceae. Strychnus is the Greek name for a number of poisonous plants. Nux-vomica derived from two Latin words that mean a nut that causes vomiting.

Nux-vomica is the dried ripe seed of Strychnus Nux-vomica Linne belonging to the Loganiaceae family. Strychnous is the Greek name of a number of poisonous plants. Nux-vomica is derived from two Latin words that mean a nut that causes vomiting. The seeds bark and leaves of *Strychnous nux-vomica* contain Strychnine, a highly toxic substance that severely damages the nervous system. Strychnine at minute doses has a beneficial effect on the body, promotes the digestive system and improves urination. Strychnine is extremely toxic as a CNS stimulant at high doses (Baumeister *et al*., 2002) (Bisset *et al*., 1989). The alkaloid produces excitation of all parts of the CNS and blocks the inhibition of post-synaptic spinal pulses (Cai *et al*., 1996). Reserpine alkaloid isolated from the Snakeroot plant (Rauwolfia serpentina) belongs to the Apocynaceae, a small evergreen shrub. Rauwolfia serpentina extracts have been used in this study. The active constituents of Rauwolfia serpentine are indole alkaloids such as Reserpine, Rauwolfine, Serpentine, Sarpagine, Yohimbine and Ajmaline. In 1940, the Indian physician recognized two distinct properties of Rauwolfia, one as a hypotensive effect and the other as a sedative effect. They began to use the agent for clinical purposes (Sha *et al*., 1989) (Benjamin *et al*., 1994). Reserpine produces its antihypertensive effects by depleting Catecholamine (adrenaline/ noradrenaline) from peripheral sites.

The hypertensive effect is mainly due to a reduction in cardiac output and peripheral-resistance. A high dose causes hypothermia

and respiratory depression. Cardiovascular effects of reserpine include hypotension, reduced heart rate and cardiac output (Lever *et al*., 2006) (Epstein *et al*., 1984). Anacardium (*Semecarpus anacardium*) is also called making nut, is a small tree belonging to the Anacardiaceae. A tincture is made from crushed seeds (marking nut). Anacardium patients have a very peculiar sensation of a hook or a pin on the surface of the body, as well as a sensation of a plug causing a pressing, penetrating pain. These sensations, whenever they are present and in whatever condition, make it a rare first remedy.

Chlorpromazine is a group of tranquillizing drugs called phenothiazines that are valuable in the treatment of psychotic disorders. Phenothiazines have anticholinergic activity. Chlorpromazine, marketed with the name Largactil, is frequently used to reduce extreme tension and anxiety and agitation. Largactil was the farmer's most widely used medicine to treat mental illness and remains one of the standard medicines. Phenothiazine family medications are most helpful in the treatment of schizophrenia. Its action is to block dopamine receptors at the neural link, reducing the neuronal response. Phenothiazines and clozapine have been accredited for nervous disorders. Antipsychotic drugs may have negative symptoms, such as dullness of physical and mental function, dyskinesia and sedation. Chlorpromazine induces muscle relaxation and attenuates schizophrenic catatonia. Chlorpromazine lowers the threshold for seizure. Phenothiazine blocks alpha adrenergic receptors and causes hypotension and ejaculation failure. Chlorpromazine has a quinidine-like effect on the cardiac potential. So, it could cause some brady arrhythmias. Chlorpromazine inhibits ACTH secretion, growth hormone, gonadotropins, ADH and insulin (neuroendocrine blocking effects) (Laurence *et al*., 2001) (Murray *et al*., 2003). Chlorpromazine is a classical neuroleptic. Acts to reduce dopaminergic neuronal firing in particular areas of the brain. It is used as a psychotropic standard (Eckel *et al*., 2004).

MATERIALS AND METHODS

A study was conducted on twenty-five mice of both sexes. These animals were divided into five groups of five animals each. Four groups were given drugs and one group was kept as control.

Type of Study

The observational animal study was approved by the Research Ethics Committee of the University of Karachi. Different neurobehavioral parameters such as cage-crossing, latency, defecation, urination, area traveled/crossed, area/squares crossed in the inner area, distances in the outer area, self-grooming have been monitored. Behavioral data were recorded in a spreadsheet that was divided into 60-120-s time blocks during each 10-minute trial.

Subjects and housing

We selected healthy mice from the animal house of the Faculty of Pharmacy and Pharmaceutical Sciences of the University of Karachi. They were given doses for 21 days. After 21 days of dosing, the activity was shown on different models. The animals in this experiment were male and female mice. The animals were kept in a single room, maintained for temperature and humidity, and designed for 12-hour light: dark cycle (lights on at 6:00 pm). The animals were housed in the same-sex pairs of plastic and wire mesh home cages (25cm x 45cm x 15cm) with ad-libitum access and water.

Apparatus and experimental design

The cage apparatus consist of a basal polyvinyl platform (8mm x 250mm x 350mm) which is mounted on four base aluminum legs. Two polyvinyl square ends (20mm x 20mm x 40mm) are mounted on the two short sides of this platform. These square finishes are fixed with two bearings and are joined by a steel pole (6mm x 350 mm). A polyvinyl holder is attached to two parts of the steel rod on which the second upper platform (4mm x 170mm x 250mm) is mounted. In order to facilitate the modification of the edge of the upper stage

tilting, the two long sides of the lower stage are equipped with an extra polyvinyl square and a metal screw is conveyed. The box was located in a separate test room with a darkened white light. Each animal was checked 10 times in a cage-crossing device, once a day for two sets of five consecutive days. All tests were performed at a fixed time, i.e., from 9:00 a.m. to 1:00 p.m., and the trials on males and females were alternated throughout the day. Each trial lasted 10 minutes, with an interval of two minutes. Thus, every time the animal crosses the Centre line of the cage, the weight shift of the animal causes the cage to tip to the other side. Between each trial, the floor and the walls of the apparatus were cleaned with a 70% alcohol solution.

Behavioral checking

Behavioral data were calculated on a spreadsheet of all animals divided into 60-120 sec on time blocks. The following behavioral pattern has been recorded:

Cage Crossing

The animal moves from the corner of the cage to the other and the movement of the animal has been recorded in all corners of the cage, even if the animal is standing on its limbs and is trying to touch the wall of the bee. This is also considered to be the first count.

RESULTS AND DISCUSSION

All mice weighed 20 to 35gms. Our final analysis applied to all 25 mice who completed the study protocol. The values of the parameter were compared and analyzed by the student t-test version for statistical significance analysis using the student t-test, which revealed a non-significant distribution of behavioral data. The number of parameters was analysed using the student t-test followed if there was a significant analysis to detect statistically significant differences between groups. The significance level was set at $p<0.05$ and $p<0.1$. All values have been expressed as mean ± SEM.

Table 1: Dosage Drugs

DOSAGE	DRUG
Dosage	Drug
0.06mg	Reserpine
0.07mg	Nux-vomica
0.08mg	Anacardium

30 minutes after the drug was given, animals were observed for 10 minutes with an interval of 2 minutes. Tablets crushed in 10 ml of water were given 1 cc. Screening methods used for cage-crossing. Mice (20-35g) of either sex was used in this study.

A group was observed to control drugs. Mice had been placed under room temperature. Ad-libitum was allowed tap-water. Drugs and corresponding doses were used in a cage-crossing test; mice were treated with different drugs. There was a significant increase in cage-crossing reactions in mice when treated with Nux-vomica at doses of 0.06 ug / g - 0.09 ug / g compared to control.

Animal anxiety and depression scientific categorization may take into account the nature and type of stressors used, with the continuum of creature models used as part of the test exploration extending from "fundamental" to complex homologous models (Finger *et al*., 1972) (Newport *et al*., 2002) (Muigg *et al*., 2009). The exploratory behavior of rodents has recently gained interest in a number of areas of behavioral pharmacology. However, according to Renner in 1990 (Hughes *et al*., 2007), the impressive discussion still covers the issue of how best to quantify exploratory responses in laboratory animals? However, the same research has argued that constraining a creature to be an enclosed box, or on an open stage, does not allow a creature to show its "inspiration" to investigate an obscure situation, as an undertaking inspires an in-numbered apprehension reaction.

Table 2: Table of dosage pattern given to Mice (n=25)

Drug	DOSING mg				
	1	2	3	4	5
Control	-	-	-	-	-
Nuxvomica	0.06	0.06	0.07	0.08	0.09
Reserpine	0.06	0.06	0.07	0.08	0.09
Anacardium	0.06	0.06	0.07	0.08	0.09
Chlorpromazine	0.06	0.06	0.07	0.08	0.09

Table 3: Effect of drugs on the home cage test (mean ±SEM) (n=5)

DRUG	0 min	2 min`	4 min	6 min	8 min	10 min	Mean+ S.E.M
Control	-	27	24	18	16	12	16.16+6.50
Nuxvomica	-	23	19	16	11	03	12.0+6.57
Reserpine	-	04	06	10	12	13	12.66+4.7
Anacardium	-	16	11	06	03	01	6.16+4.4
Chlorpromazine	-	14	10	07	04	02	6.16 + 3.7
Values are mean ±SEM (n=25) non-significant differences by student t-test P <0.05, P <0.1 as being compared to control.							

Table 4: Significant and non-significant effects of drugs on home cage, latencies, defecation and urination (n=25)

DRUG	CAGE-CROSSING	LETENCY NUMBER	DEFECATIONS	URINATION
Control	↓↓	Non-significant effect	Non-significant effect	Non-significant effect
Nuxvomica	↑↑	↑↑	↓↓	↑↑
Reserpine	Non-significant effect	↓↓	↓↓	↑↑
Anacardium	↓↓	↓↓	↓↓	↓↓
Chlorpromazine	↓↓	↓↓	↓↓	↑↑

Vertical bars represent mean ±SEM (n=5) significant differences by student t-test that is p<0.05 and p<0.01

Table 5: Effect of drugs on cage crossing the explanatory activity of mice (n=25)

Treatment	Cage-Crossing (Home Cage)
Control	108.6+ 5.84
Nux Vomica	103 + 90.8
Reserpine	107.8+92.4
Anacardium	86.6+61.8
Chlorpromazine	90.8+74.8
Values are mean ± SEM (n=5) non-significant differences by student t-test P <0.05, P <0.1 as being compared to control.	

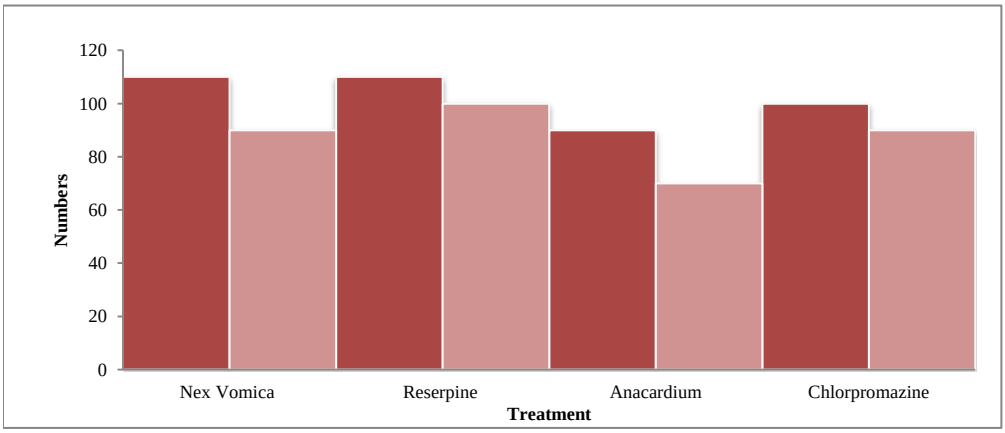

Fig. 1: Effect of herbal drugs on explaratory activity

Two recent cage-crossing studies have also provided evidence that cage-crossing by labyrinth reduces repeated exposure to the home cage apparatus if this behavior is a convincing measure of neophilia cage-crossing is additionally expected to be higher in the presence of objects than without articles (Renner *et al*., 1990). In our study, the results showed that the cage crossing was high during the first test and decreased further after the test, and remained generally stable in the rest of the test. Our results, consistent with the Prut and Belzing 2003 (Marin *et al*., 2007).

Study of the initial drop in the cage crossing following the first trial, may indicate a neophiliac reaction that declines as the animal has become memorable with the cage, i.e., the cage crossing (Home-cage) symbolizes a directed exploratory behavior that drops as the device loses its curiosity. On the other hand, if this understanding is correct, we would also foresee that cage-crossing would be more noteworthy in the presence of items, if, as may be the case, there was no confirmation of an increase in container-crossing behavior when articles were available below the enclosure. These results do not support the theory that the enclosure intersection is a significant measure of neophilia.

The second translation of the starting drop in the enclosure intersection could recur is that the boundary intersection could lead to a terrible, neophobic reaction, such that at the first exposure, the creature was effectively trying to discover the departure path of adult mice mazes showing an increase in the current levels of corticosteroids taking place after solitary exposure (Prut *et al*., 2003) Recommending that testing in this device is a distressing occasion. In the event that this understanding of the cage-crossing is correct, we would also anticipate that, as the cage-crossing behavior decays, the horror would also decrease for this translation while the confines of the initial few tests, the measurement of the locomotion in the cage-crossing (Home-Cage) and the time spent therein would significantly increase over these trials. In this way, as fear manifestly diminished, the border crossing further decreased in the event that we accept that the trepidation experienced when presenting a novel mechanical assembly can be compared to ordinary or state tension (Marquez *et al*., 2006), these results negate the suspicion that cage-crossing behavior is stifled by a nervousness such as a reaction, in which case we might have expected cage-crossing.

In a late study (Belzung *et al*., 2001), it was suggested that the effect of anxiolytic drugs on cage-crossing behavior is gently perplexed by changes in the general locomotive, regardless of where cage-crossing is inconsistent with the action of the locomotives. In our study, cage-crossing showed a decrease in recurrence at the end of the test after eight or more exposures to the mechanical assembly. Subsequently, we cannot rule out the likelihood that, as the subjects turned out to be extremely familiar with the device, they would be engaged in a higher level of visual investigation through the gaps. They explore the behavior of research Centre creatures with enthusiasm for different regions of behavioral pharmacology. On the other hand, how best to quantify exploratory behavior in mice and rats remains a hostile issue in numerous unconditioned tests, for example, the open field may jumble, as cage-crossing into the cage on the floor is thought to be a significant measure of subjects' fascination with curiosity. This trial is intended to evaluate behavioral changes caused by some herbs that are finally being scientifically investigated. There are two main areas of focus for this research. One is the examination and the other was the evaluation of the efficacy of some herbal extracts using the home cage assessment tool for brain and behavior. This research provides a scientific basis for comparing herbal remedies. The other direction for research is the search for newer drugs between known plants or new species of plants.

Psychopharmacological screening generally indicates simply the presence or lack of response. The basic elements of the drug

discovery program are therefore the bioassays used to detect biologically active substances (Kliethermes *et al*., 2006) (Ghosh *et al*., 1987) (Schatzberg *et al*., 2000. The CNS behavioral screening includes different parameters such as cage crossing, open field activity, head drop swimming induced depression and radial labyrinth. There was a group in which 06 mice per group and one group were kept under control. They were provided with ad-libitum food and water, and different CNS screening tests were performed. In the course of this study, the herbs Rauwolfia serpentine, *Strychnous nux-vomica* and Semecarpus anacardium were studied. In order to determine whether a cage crossing can be validated as an exploration measure, two criteria were suggested. First, it should reflect the novel features of the surrounding area; second, contact with the home cage (cage-crossing) would have an impact on the storage of information. Cage-crossing reflected curiosity was shown by the more drawn-out span of the crossings at the start of the presentation than the second exposure, the shorter the duration of the cage-crossing. Data stockpiling was shown by habituation on the re-presentation of the home cage. The critical positive relationship between the number of cage crossings was obtained from mice. This provides some backhanded evidence that the mice cage crossing in the "Home cage" also reflects exploration (Pawlak *et al*., 2008). Nux vomica, reserpine, anacardium and chlorpromazine have been tested in cage-crossing. Anacardium and chlorpromazine decreased and Nux vomica increased the frequency and duration of cross-screening of natural pharmaceutical drugs as psychotropic drugs has a strong tweaking effect on cerebrum and behavior. In this study, we assessed the adequacy of these drugs as psychotropic operators and the cage-crossing parameter. Among these *Strychnous nux-vomica*, has a strong cholinergic framework activity. The movement of the CNS is seen as a fact-finding behavior (Moncrieff *et al*., 2006). Chronic reserpine therapy has shown a non-significant effect on water intake. Previously, reserpine was reported to increase the intake of water during the light phase and the animal consumed less water during the dark phase. Other herbal drugs such as Nux vomica and anacardium did not produce a remarkable effect. Based on this information, the therapeutic significance of these herbs, our present study was designed to screen these herbs for CNS action on mice (Haq *et al*., 1993) (Stephen *et al*., 2004). This could not have been due to the non-particular size of the excitement and action due to the proximity of the medication given, on the grounds that the medication was presented, the animals spent a shorter or longer time at the cage crossing than the others.

The duration of the cage-crossing increased and decreased at the different crosses. Thus, the cage-crossing behavior of the animal mirrored the consideration given to the drug. It must be argued that the adjustment in the surrounding area should have resulted in increased or decreased cage-crossing. Though the creatures had been indicated habituation under this condition. It could be the case that the investigation of one cross was sufficient to gather the data. As a result, the results of the exploration in data storage have been fulfilled. Despite the fact that these are considered to be essential conditions for the demonstration of investigations, it is perceived that they are unlikely to be adequate. However, within these limits, the results suggest that the cage-crossing does reflect exploratory behavior. Motor activity involved in measuring cage-crossing only to the degree that the creature needs to move in the cage, but can do so gradually or with ataxia. The upside of the measure is that it does not depend on progress itself. The outcome recommends that the cage-crossing span should be the preferred impression of investigation over recurrence. All past chip away at the home cage used a recurrence measure, and it would be extremely difficult to quantify the span of the "Home cage" due to the high degree of exceptionally short crosses that occur. As well related action in the cage cross for the maze, it may be the case that the mouse cage cross is only a decent measure of motor activity (Shepard *et al*., 2008) (Gagliano *et al*., 2008).

CONCLUSION

Psychopharmacology can be a marker of disease burden rather than a direct cause of death. These drugs have been shown to have potent neuro-pharmacological and diuretic activates, etc. These facts indicate the scientific basis for the use of these drugs.

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