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Evaluation of the Effect of *Rauwolfia vomitoria* on Visuospatial and Cognitive Functions in Mice

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Abstract

Background: Due to the detrimental and adverse effect intense oxidative stress has on the brain resulting in cognitive function impairment. Hence, this study to evaluate the effect of *Rauwolfia vomitoria* on visuospatial and cognitive function in mice. **Methods:** Thirty (30) Swiss male albino mice weighing 19 to 35g were randomly assigned into three groups (A to C) ten mice each and treated as follows: Group A served as the control, Group B received 3-NP 20mg/kg via intraperitoneally for 5 days, Group C received 3-NP 20mg/kg intraperitoneally and *Rauwolfia vomitoria* 15mg/kg orally. Treatment was for 21 days and thereafter, neurobehavioral studies for visuospatial learning and memory was assayed using the Morris water maze test while cognition was evaluated using the novel object recognition test. IBM SPSS statistical software version 20, was used to analyze the data (P-value=<0.05) **Results:** 3-NP 20mg/kg significantly impaired cognition, as evidenced by decreased total exploration time, decreased index of habituation and decreased index of discrimination in the novel object recognition test. And also 3-NP caused impairment in visuospatial learning as evidenced by decreased retention quadrant duration, decreased annulus acquisition duration and decreased

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annulus reversal. *Rauwolfia vomitoria* treated group significantly ameliorated the visuospatial and cognitive impairments induced by 3-NP. **Conclusions:** It is based on these results, we draw the conclusion that *R. vomitoria* may possess memory enhancing property that resulted in the reversal of the visuospatial and cognitive decline in the *Rauwolfia vomitoria* (15mg/kg) treated group.

Keywords: Evaluation, *Rauwolfia vomitoria,* Visuospatial, Cognitive, Functions, Mice

INTRODUCTION

The exposure of one to high concentrations of reactive oxygen species should be controlled because it can result in the modification of cell components (Marnett 1999). And also an imbalance between the production of the reactive oxygen species and antioxidant defenses will result in excessive accumulation of the reactive oxygen species resulting in a condition such as oxidative stress (Dasuri et al, 2013; Ray et al, 2012).

Intense oxidative stress related processes in the brain are one of the main causal factors involved in the impairment in cognitive functions in the brain and this is through two critical changes in the brain. First occurs by a decrease in the neurotransmitters essential for memory and learning functions, such as acetylcholine (Ach), and secondly by a decrease in level of natural anti-oxidant in the brain thereby activating microglia, a source of reactive oxygen species (Calabrese & Field 2003; Kopelman, 2002).

In recent times, research has actually increased concern on these areas and herbal remedy may be of help in ameliorating these cognitive deformities and one of such plant is *R* vomitoria.

Rauwolfia vomitoria is a species of flowering plant and belong to the family of Apocynaceae. It is commonly known as African Serpent Wood, African Snakeroot and Swizzle Stick. In Nigeria local languages, it is called Asofeyeje (Yoruba), Akata (Bini), Ira (Igbo), Eto mmoneba/utoenyin (Efik and Ibibio) and Wadda (Hausa) respectively (Ehiagbonare 2007).

It has been documented that *R vomitori*a has been used to treat psychosis and schizophrenia (Eteng *et al.,* 2009; Amole *et al.,* 2009). *R. vomitoria* is also used in insanity, anxiety and stimulant to the central nervous system (James *et al* 2008)

Bisong, et al. [2013] ascertained that the aqueous root bark extract of *R. vomitoria* at 0.0, 0.25, 1.0, 2.0, 4.0 mg/kg body weight has a high potential as an antipsychotic than chlorpromazine.

Three nitropropionic acid replicates most of the clinical and pathological hallmarks of Alzheimer's and Huntington's diseases. 3-NPis a natural toxin synthesized by fungi (Aspergilllus flavus; Astragulus, Arthrinium) and plants (Indigofera endecapylla) and it inhibits succinate dehydrogenase in the mitochondrial respiratory chain and tricarboxylic acid cycle (Alexi *et al*., 1998). 3-NP produces lesions in basal ganglia (striatum), cortex, and hippocampus selectively and also produces dystonia in human [Beal 2012; Maya-López 2017].

METHODOLOGY

Procurement of Test Substances

Chemicals: The 3-Nitropropionic acid (3-NP) was purchased from Sigma- Aldrich Limited, Canada. All reagents and chemicals used for this study were of analytical grade.

Extraction of the root bark of *Rauwolfia vomitoria*: *Rauwolfia vomitoria* roots were obtained from the botanical garden, University of Calabar, Calabar. A botanist authenticated a sample of the plant (Voucher number - Bot/Herb/UCC/0576). The roots were thoroughly washed under clean running water and made free from dirt and sand and the dead cells which covered the roots were removed and the succulent part of the root bark was removed carefully and later sun-dried. The sun-dried root bark was powdered in an electric blender and 700g of the root bark powdered plant material was obtained. Seven hundred grams (700g) of the powdered root bark were mixed in a liter of water and allowed to sit for at least 2 hours. After 2 hours, the mixture was filtered using Whatman filter paper and the filtrate was evaporated using a rotatory evaporator and a thick paste obtained was then preserved in the refrigerator and also prevented from having direct exposure to sunlight until needed for administration (Labotech International Co., Ltd, Tokyo, Japan) at a temperature of 60 ^{0}C. Method used as described by Bisong *et al.,* (2013).

Laboratory Animals: Thirty (30) swiss male mice of 10 weeks weighing 19 to 35g were used for this study. The animals were housed in the Department of Physiology Animal House, University of Calabar, Nigeria. Standard animal cages (435 x 290 x150mm) with

wood shavings as bedding were used in housing the animals (5 mice per cage). They were given *ad libitum* access to feed (Flourmill Calabar, Cross River State, Nigeria) and fresh water, and exposed to 12/12-hr light/dark phase. The animals were acclimatized for a period of one week and kept in line with laid - down ethics for animal care approved by the National Committee for Research Ethics in Science and Technology (NENT), 2018. Before the commencement of this research, ethical approval was obtained from the University of Calabar animal ethics committee, which aligned with the standard guidelines for the use of laboratory animals outlined by the World Health Organization. The study was permitted with ethical clearance with approval number (Approval No.FARE C/PA/ [UC/050]/181PHY123)

Experimental Design and Administration of three nitropropionic acid (3 N-P) and *Rauwolfia vomitoria*.

The animals were randomly allotted into 3 different groups (n=10). At the expiration of the one week of acclimatization, 3 Nitropropionic acid 20mg/kg was administered intraperitoneally to induce oxidative stress in treatment groups B and C. Thereafter, *Rauwolfia vomitoria* 15mg/kg was given through oral means using gavage (dose per mice outlined in Table 1), once daily, to animals in treatment groups B and C using the doses outlined in Table 1. Whereas the control group was given feed and 0.5ml normal saline as a vehicle throughout the experimental duration. 3- Nitropropionic acid was administered for just 5 days, thereafter, Rauwolfia *vomitoria* administration continued through the period which lasted for about 21 days. Thereafter, the animals were subjected to behavioral testing to assess behavioral changes at the expiration of the treatment.

Table 1. Study Design and Drug and Extract administration

Groups	**No. of mice**	**Treatment**
Group A **(Control)**	10	Feed + 0.5ml of normal saline as a vehicle throughout the experimental period
Group B	10	20mg/kg bw of 3 - Nitropropinioic acid
Group C	10	20mg/kg bw of 3 - Nitropropinioic acid + 15mg/kg bw of *Rauwolfia vomitoria*

Behavioral, learning and memory Assessment.

The Cognitive Memory Assessment

The novel object recognition (novel object preference task NORT) capitalized on the findings of Berlne 1950 that rodents prefer to explore objects that they have not previously encountered over objects that are familiar. Preferences to explore the various objects are recorded and a tendency to explore the novel object over the familiar sample is interpreted as evidence of memory for the training exposure (Ennaceur and Delacour 1988). Object recognition experiments were performed in a locally constructed white wooden box of 60 x 40 x 30cm dimension. Objects to be discriminated were of about the same size, made of plastic, deferring in shape and color. Prior to testing, all mice were allowed to familiarize with the apparatus twice for 5 minutes in order to acclimatize. On the testing day, each mouse was placed in the box for 5 minutes and left to explore the objects freely. For this test, two pairs of identical objects are needed (01 and 02) and two trials (acquisition and recognition) are carried out on the same day, separated by a retention period of 15 minutes. During the first trial, two identical objects (01 and 02) were placed in diagonal corners opposite each other in the open field. Objects were secured to the floor of the apparatus with reusable adhesive. The mouse was scooped up from its home cage and placed in the middle of the open field arena. Each mouse was allowed to explore the arena and objects for 5 minutes. At the end of the trial the mouse is removed from the apparatus and returned to its home cage. After 15 minutes of inter-trial interval (retention period) the mouse was returned to the test apparatus (trial 2). The arena now contains the familiar object (01 or 02 from trial 1) in one of the two locations in trial 1 and a new object (N) that replaces 01 or 02. The procedure was repeated for 2 trials, and timing and recording were done accordingly.

The performance of the animals were video-taped and the following behavioral parameters were evaluated

1. Time spent by the mice in exploring the objects during either 01 or 02
2. Novel object recognition: this is obtained by calculating the percentage of the time spent in exploring the new object with respect to the total amount of time spent in exploring the two objects during 02; and
3. The discrimination-ratio was the duration of exploration of the novel object, divided by the total exploration duration of both objects during the test phase.

The Visuo-Spatial Memory Assessment

The visuo-spatial memory assessment was done using the Morris water maze. The Morris water maze (MWM) consists of a circular pool filled with opaque water. Mice were trained to use extra-maze visual cues to locate an escape platform hidden just below the surface of the opaque water (Morris, 1984). The hidden-platform version of the MWM is a test of visuo-spatial learning and memory, and its performance is impaired by lesions in the hippocampus (McDonald and White, 2004). The water maze was made out of a circular polypropylene pool measuring 110-cm in diameter and 20-cm in depth. The pool was filled to a depth of 14-cm (0.5-cm over the platform) with room-temperature tap water, which is made opaque by adding smoothly grinded non-toxic white chalk. The water was left to sit overnight in order to reach room temperature 25 ± 2°C). The pool is divided into four quadrants: Northwest, Northeast, Southwest and Southeast. The boundaries of these quadrants are marked on the edges of the pool with masking tape and labelled: North, South, East and West. A cylindrical cement block (13.75 cm x 9 cm diameter) was used as the escape platform in the maze. The platform has a removable red and yellow striped top (3 cm x 9 cm in diameter) with a colorful flag erected in the center. For visible platform tests the level of the water in the pool is adjusted to 0.5-cm below the surface of the striped top, thus creating a visible escape platform, or to 0.5-cm above the white cylinder (with the striped top removed), creating a hidden escape platform.

Procedure:

The Morris water maze test lasted for about 8 days:

Day 1: Acquisition day 1

Day 2: Acquisition day 2

Day 3: Acquisition day 3

Day 4: Reversal day 1

Day 5: Reversal day 2

Day 6: Reversal day 3

Day 7: Probe trial

Day 8: Visible-platform day

Acquisition and reversal training were with the hidden platform (water is 0.5-cm above platform). During reversal, the platform was moved to the opposite side of the maze. During the probe trial, there was no escape platform so that visuo-spatial memory can be assessed.

On the visible-platform day, the platform was moved to another quadrant of the pool and the visible top was added to the platform. This assessed basic visual ability and motivation to locate the platform.

On each day of the test, the mouse was removed from its home cage and was placed in a clean holding cage without wood shave bedding. Paper towel was torn into strips and placed in the bottom of the holding cages to allow the mice to dry more quickly and was replaced at intervals when wet. The mice were run in squads of 4-6 with 5-minutes between each trial (inter-trial interval) for each mouse.

During acquisition training, the platform was placed in the center of the Northeast quadrant. Each mouse receives 4 trials per day. In each trial, the mouse was given a maximum of 60-sec to locate the escape platform.

The starting positions of the mice were predetermined using a Latin square design, which prevented the repetition of starting location sequences on back-to-back test days. Possible start positions were at the boundaries of the quadrants (e.g. West, North, East or South). For each trial, each mouse was removed from its holding cage using a small, clean 500-mL plastic container to minimize handling stress. The animal was then placed into the water at the appropriate start position. It is worthy to note that care should be taken to prevent the immersion of the mouse's head underwater. This is because some of the mice will experience a "dive reflex" and drop to the bottom of the pool if their heads goes underwater. If this happened the mouse was taken out of the water, held it on the hand and pressed gently on its stomach in pulses – artificial respiration – and put it back in its home cage and retested as the last mouse.

At each trial, the mouse was permitted to explore the pool and to search for the hidden escape platform for 60-sec. When the animal locates the platform, the timer was stopped (manually) and the mouse allowed to stay on the platform. Once on the platform, the mice were permitted to view the extra-maze environment for 10-sec, at which point the mouse was picked up the in the plastic container and returned to the appropriate holding cage. It is important to only remove the mouse after it is on the platform so that it associates the

platform with escape. If the mouse did not find the platform during the allotted time, the animal was guided onto the platform using the back of the plastic container. And once on the platform it was allowed 10 second to view extra maze cues. The next mouse was then placed in the pool and the same procedure followed. Each animal completed 4 trials per day over 3 days, for 12 trials of acquisition training, each trial from a different one of the 4 start locations.

Reversal training began on day 4. The invisible platform is moved to the opposite quadrant (Southwest quadrant), and mice were again assigned to appropriate start positions. The same procedures as in acquisition training were carried out during reversal training. Each of the animals completed 4 trials per day for 3 days for a total of 12 trials of reversal training.

A probe trial was conducted on day 7 to assess visuospatial memory. At this time, there is no escape platform in the maze. Each mouse was placed in the pool from one of the four possible start positions and allowed to explore the pool for 60-sec, during which the time spent in each quadrant of the maze was recorded. When the 60-sec was completed, the mouse was scooped up using the container which was placed in a holding cage to dry before being returned to its home cage.

The visible platform task was conducted on the 8th day. The visible platform was placed in a new location within the Northwest quadrant of the pool. The same procedures as in acquisition and reversal trainings are carried out and mice complete 4 trials.

The behavior scored during the Morris water maze test included:

1. Swim latency - the time it took the mouse to locate the hidden platform during the acquisition and reversal training (these were charted against the days of training both for acquisition and reversal training), and visible platform task.

2. Quadrant duration – the amount of time spent in each quadrant during the probe trial

3. Annulus acquisition crossing – number of time the animal crossed the position of the platform at the acquisition training during the probe trial.

4. Annulus reversal crossing – number of times the animal crossed the position of the platform at the reversal training during the probe trial (Wong and Brown 2007)

Statistical Analysis

Data obtained were expressed as Mean ± Standard Error of Mean (M ± S.E.M). The result was analyzed using one-way Analysis of variance (ANOVA) followed by post-hoc multiple comparison test to compare level of significance between other groups and the control. SPSS version 20 and Microsoft Excel were used for the analysis. The level of significance was set at $P< 0.05$.

RESULTS

Comparison of total exploration time in NORT for short term memory in control and other experimental groups.

Novel Object Recognition Task in 3NP-induced oxidative stressed mice between the control, 3NP OS and RV+ 3NP OS groups of mice

The time spent in exploring objects by the control, 3NP and 3NP + RV groups of mice for short term memory is presented in Figure 1.

The result below shows that the 3NP + RV spent a longer time in exploring objects when compared to the control and 3NP-induced oxidative stress groups of mice

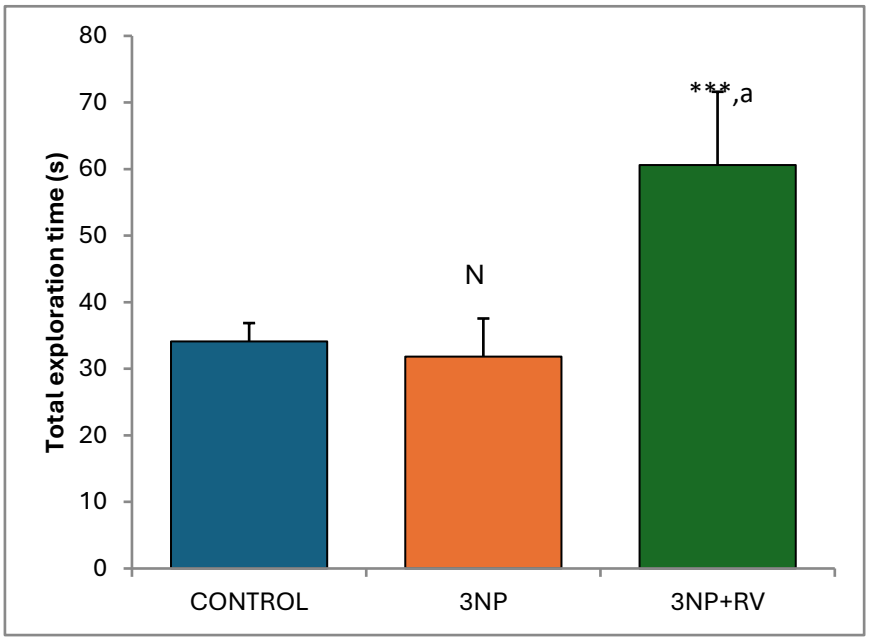


Fig 1. Comparison of total exploration time in the novel object recognition task (NORT) for short term memory in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

NS-Not significant; ***-significant at p< 0.001 vs control; a – p<0.05 as least level of significance vs 3NP group

Comparison of index of habituation in NORT for short term memory in control and other experimental groups.

The comparison of habituation index by the control, 3NP and 3NP + RV groups of mice for short term memory is presented in Figure 2.

The result below shows that the 3NP + RV had a better habituation index when compared to the control and 3NP-induced oxidative stress groups of mice

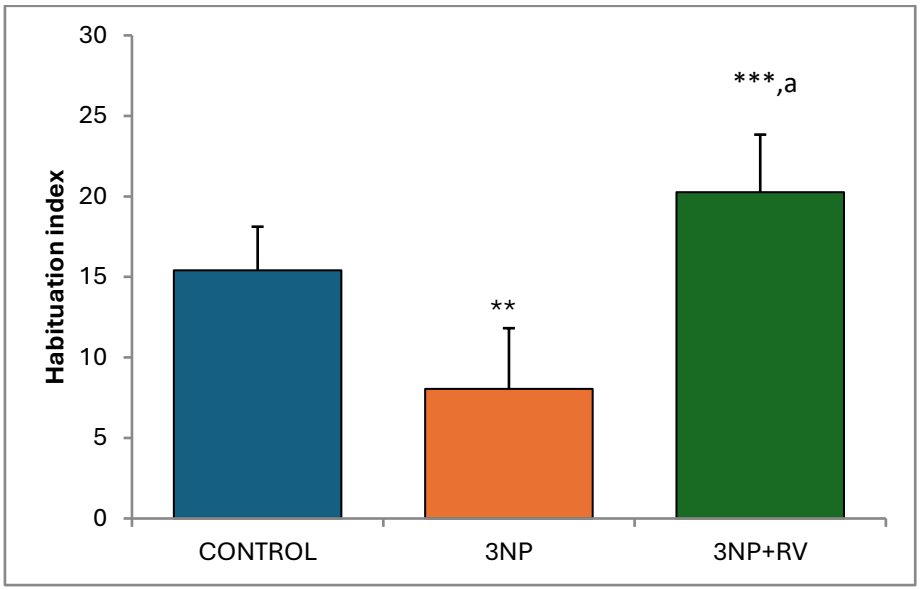


Fig 2. Comparison of index of habituation in the novel object recognition task (NORT) for short term memory in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

** - significant at p< 0.01 vs control; ***-significant at p< 0.001 vs control; a – p<0.05 as least level of significance vs 3NP group.

Comparison of index of discrimination in NORT for short term memory in control and other experimental groups.

The comparison of index of discrimination by the control, 3NP and 3NP + RV groups of mice for short term memory is presented in Figure 3.

The result below shows that the 3NP + RV showed preference for the novel object than the familiar object when compared to the control and 3NP-induced oxidative stress groups of mice

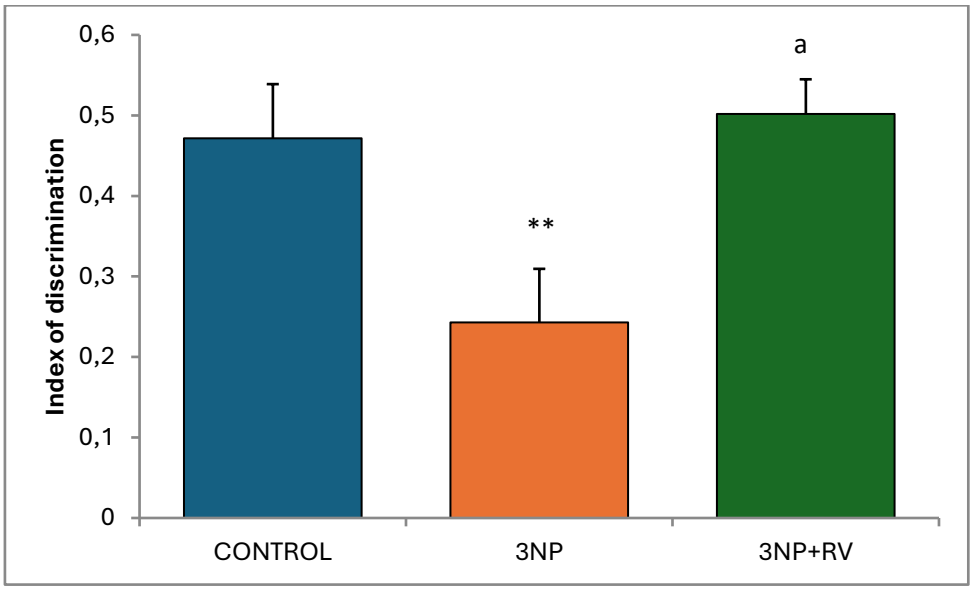


Fig 3. Comparison of index of discrimination in the novel object recognition task (NORT) for short term memory in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

** - significant at p< 0.01 vs control; ***-significant at p< 0.001 vs control; a – p<0.05 as least level of significance vs 3NP group.

Comparison of total exploration time in NORT for long term memory in control and other experimental groups.

The time spent in exploring objects by the control, 3NP and 3NP + RV groups of mice for long term memory is presented in Figure 4.

The result below shows that the 3NP + RV spent a longer time in exploring objects when compared to the control and 3NP-induced oxidative stress groups of mice

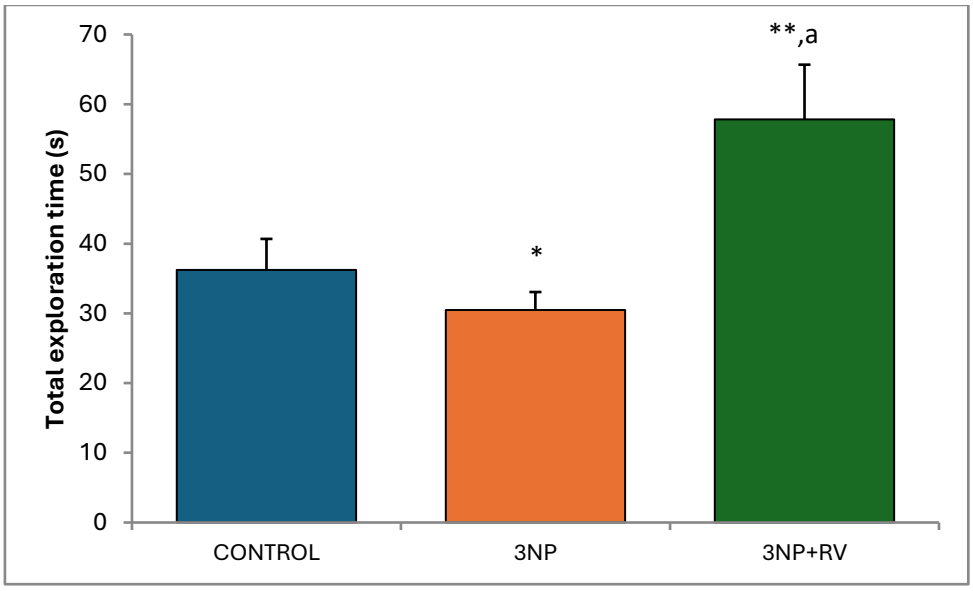


Fig 4. Comparison of total exploration time in the novel object recognition task (NORT) for long term memory in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

* - significant at p< 0.05 vs control; **-significant at p< 0.01 vs control; a – p<0.05 as least level of significance vs 3NP group

Comparison of index of habituation in NORT for long term memory in control and other experimental groups

The comparison of habituation index by the control, 3NP and 3NP + RV groups of mice for long term memory is presented in Figure 5.

The result below shows that the 3NP + RV had a better habituation index when compared to the control and 3NP-induced oxidative stress groups of mice

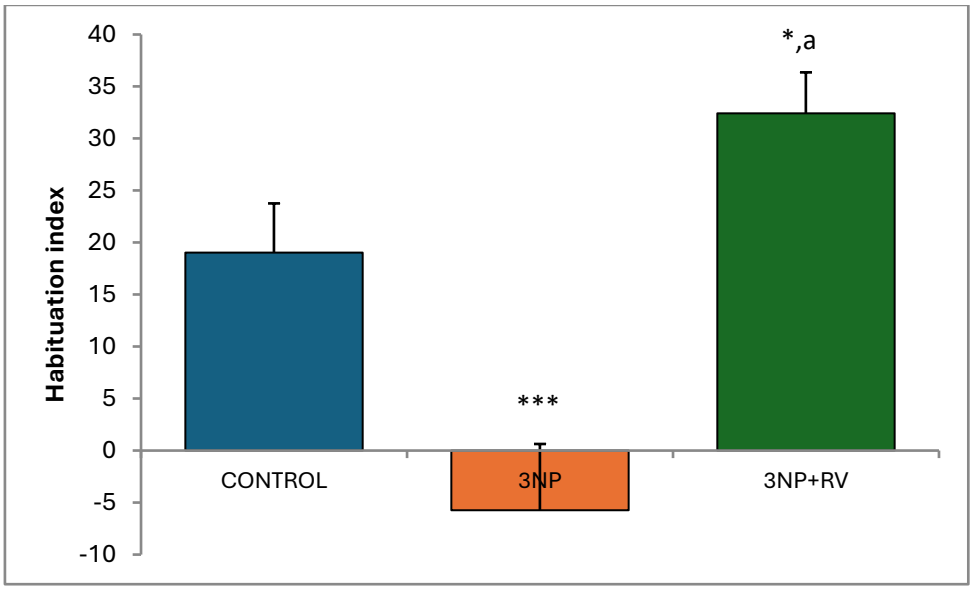


Fig 5. Comparison of index of habituation in the novel object recognition task (NORT) for long term memory in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

* - significant at p< 0.05 vs control; ***-significant at p< 0.001 vs control; a – p<0.05 as least level of significance vs 3NP group

Comparison of index of discrimination in NORT for long term memory in control and other experimental groups

The comparison of index of discrimination by the control, 3NP and 3NP + RV groups of mice for long term memory is presented in Figure 6.

The result below shows that the 3NP + RV showed preference for the novel object than the familiar object when compared to the control and 3NP-induced oxidative stress groups of mice

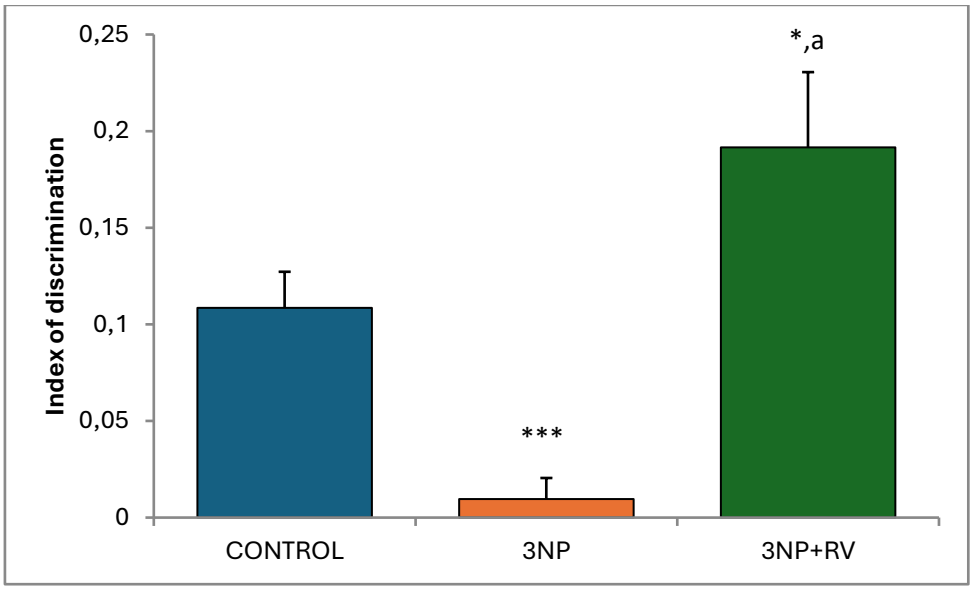


Fig 6. Comparison of index of discrimination in the novel object recognition task (NORT) for long term memory in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

* - significant at p< 0.05 vs control; ***-significant at p< 0.001 vs control; a – p<0.05 as least level of significance vs 3NP group

Comparison of the effect of R.vomitoria on swim latency during the acquisition training of the Morris water maze task in 3-NP induced oxidative stressed mice (day 1, 2 and 3) between the control and other experimental groups.

The swim latency (the time it takes for the mice to swim and locate the hidden platform) during the acquisition training of the Morris water maze task is shown in Figure 7. It is also referred to as the learning curve.

The result below shows no significant (P<0.05) swim latencies particularly for days 2 and 3 of the acquisition training in the 3NP-induced oxidative stress group of mice when compared to the control and 3NP + RV groups.

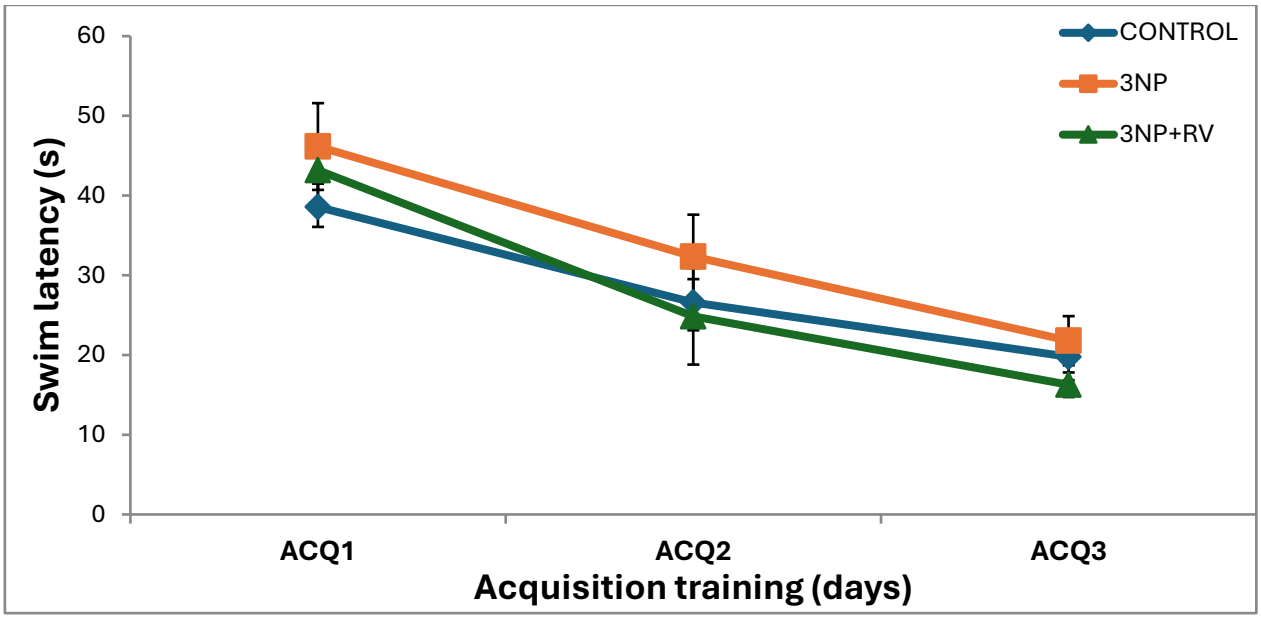


Fig 7. Swim latency during the acquisition training periods (days 1, 2 and 3) of the different experimental groups using Morris water maze test.

Values are expressed as mean ± SEM, n=10.

Comparison of the effect of R.vomitoria on swim latency during reversal training of the Morris water maze task in 3-NP induced oxidative stressed mice (day 4, 5 and 6) between the control and other experimental groups.

The swim latency (the time it takes for the mice to swim and locate the hidden platform) during the reversal training of the Morris water maze task is shown in Figure 8. It is also referred to as the learning curve

The result below shows no significant ($P<0.05$) swim latencies particularly for days 4, 5 and 6 of the reversal training in the 3NP-induced oxidative stress group of mice when compared to the control and 3NP + RV groups.

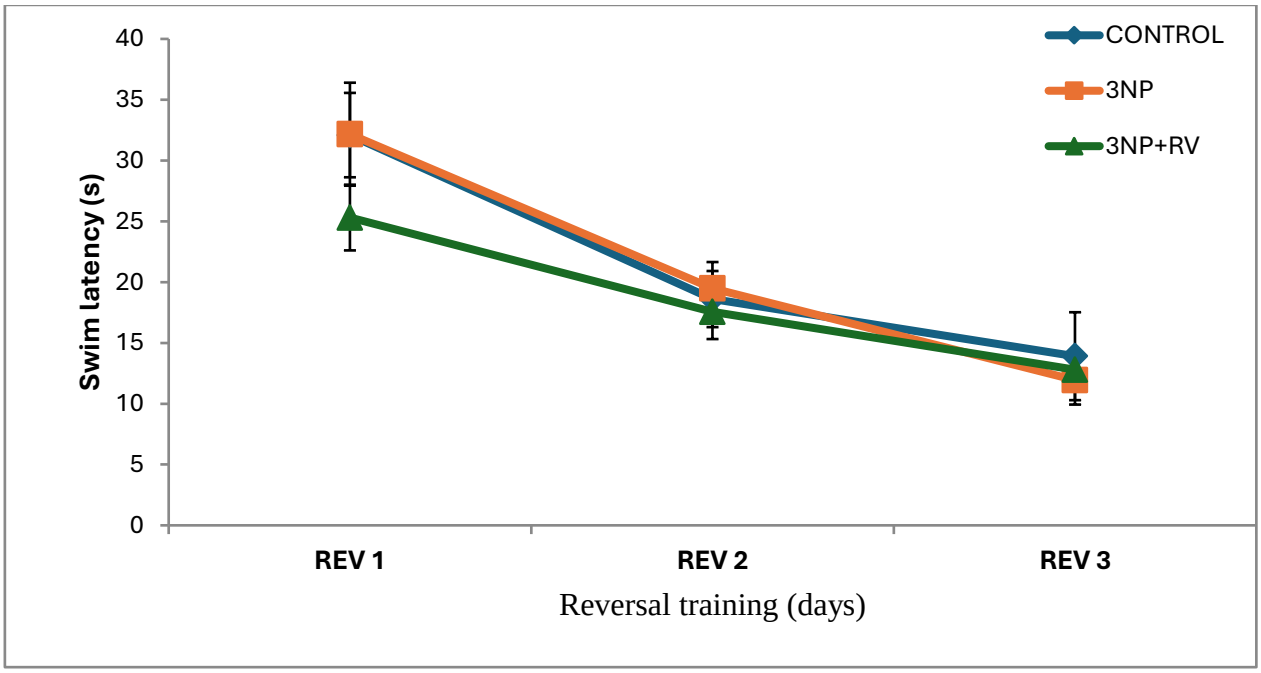


Fig 8. Swim latency during the reversal training periods (days 4, 5 and 6) of the different experimental groups using Morris water maze test.

Values are expressed as mean ± SEM, n=10.

Comparison of acquisition retention quadrant duration at the probe trial of Morris water maze in 3NP-induced oxidative stressed mice (day 7) between the control, 3NP and 3NP + RV groups of mice

The swim latency (the time it takes for the mice to swim and locate the hidden platform) during the retention quadrant duration training of the Morris water maze task is shown in Figure 9. It is also referred to as the learning curve.

The retention quadrant duration was significantly reduced in the 3-NP ($p<0.01$) when compared to the control and 3-NP +RV groups.

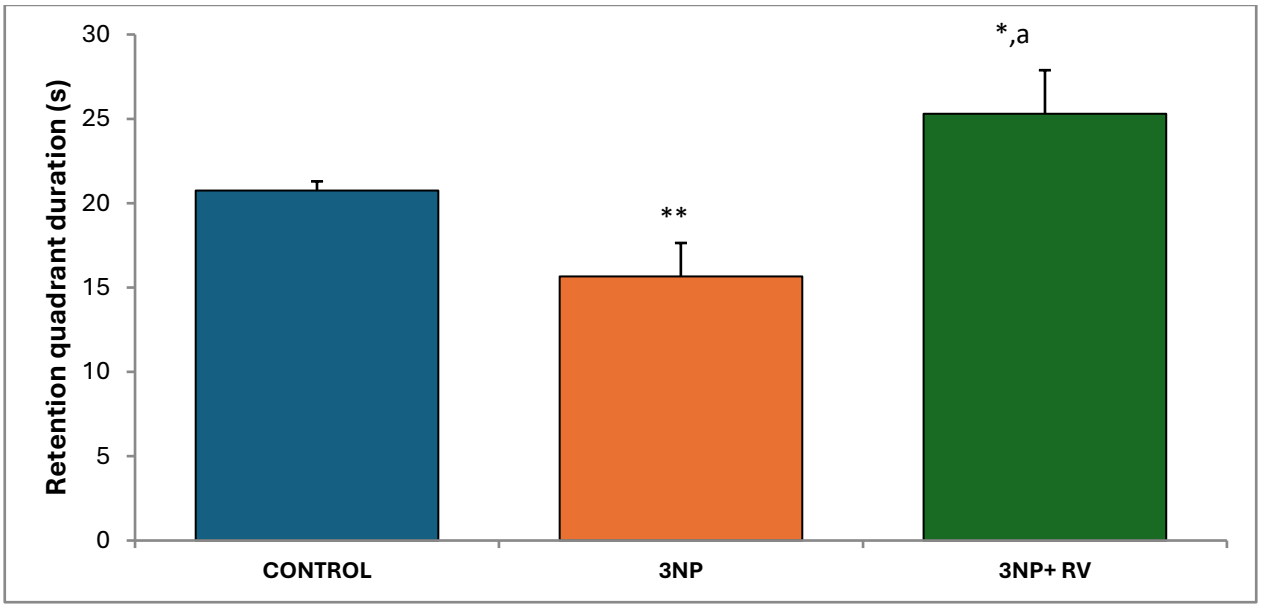


Fig 9: Comparison of retention quadrant duration at the probe trial of the Morris water maze in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

*- significant at p< 0.05 vs control; **-significant at p< 0.01 vs control; a – p<0.05 as least level of significance vs 3NP group

Comparison of Annulus acquisition in control and other experimental groups for visuospatial learning and memory.

The swim latency (the time it takes for the mice to swim and locate the hidden platform) during the acquisition training of the Morris water maze task is shown in Figure 10. It is also referred to as the learning curve.

The annulus acquisition was significantly reduced in the 3-NP ($p<0.01$) when compared to the control and 3-NP + RV groups

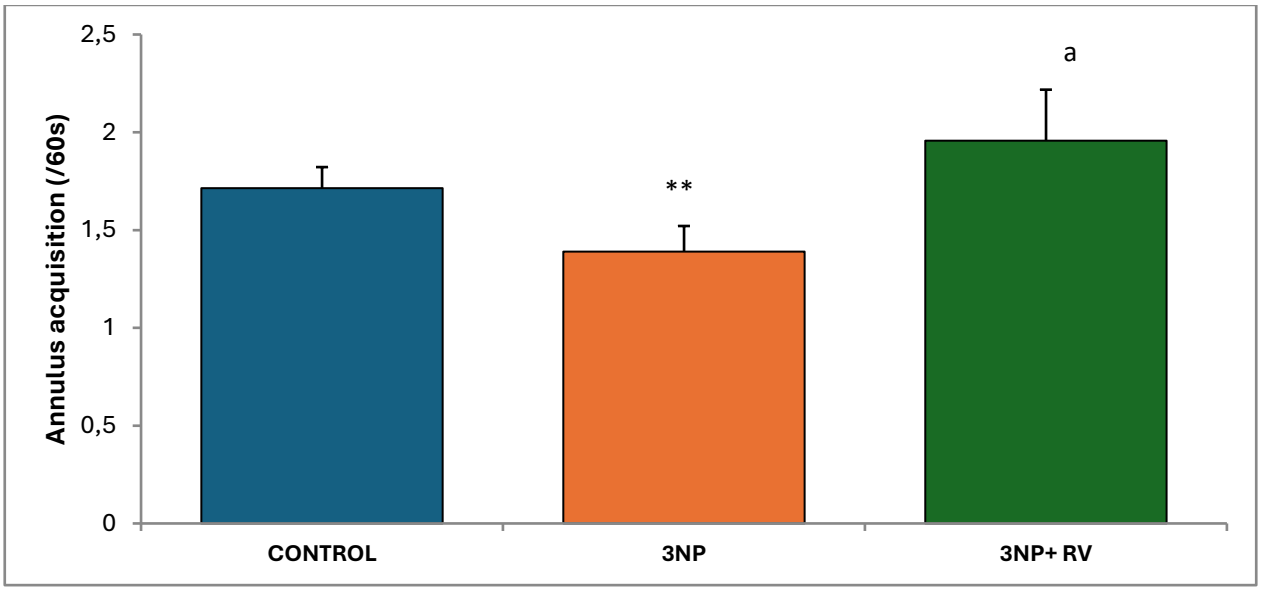


Fig. 10: Comparison of annulus acquisition duration at the probe trial of the Morris water maze in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

- Significant at p< 0.05 vs control; **-significant at p< 0.01 vs control; a – p<0.05 as least level of significance vs 3NP group

Comparison of Annulus reversals in control and other experimental groups for visuospatial learning and memory.

The swim latency (the time it takes for the mice to swim and locate the hidden platform) during the annulus reversal training of the Morris water maze task is shown in Figure 11.

The annulus reversal was significantly reduced in the 3-NP ($p<0.01$) compared to the control and significantly increased ($p<0.05$) compared to the 3-NP + RV

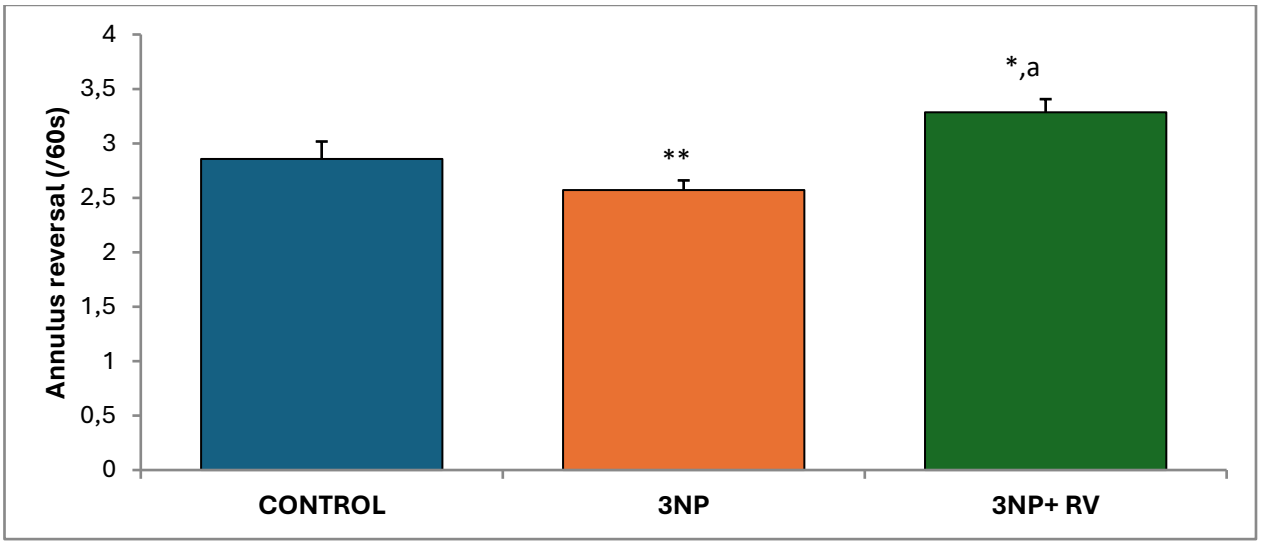


Fig. 11: Comparison of annulus reversals at the probe trial of the Morris water maze in mice treated with 3-nitropropionic acid (3NP) and R. vomitoria (RV).

- Significant at p< 0.05 vs control; **-significant at p< 0.01 vs control; a – p<0.05 as least Level of significance vs 3NP group

DISCUSSION

The research work was aimed at investigating the effect of *Rauwolfia vomitoria* on visuospatial and Cognitive functions in 3- NP oxidative stressed mice using Morris water maze and novel object recognition task.

Novel object recognition task is widely used for evaluating non-spatial working memory (cognition) in rodents (Ennaceur and Delacour 1988). This test is based on the spontaneous tendency of rodents to spend more time exploring a novel object than a familiar one. The choice to explore the novel object reflects the use of learning and recognition memory.

In this study, it is observed that the 3-NP + RV group showed preference for the novel objects than the familiar objects which is an indication of memory of the earlier exposure with the other object. This encouragement of cognitive memory is corroborated in Figs. 1, 2 and 3 for short term memory and also in Figs. 4, 5 and 6 for long term memory as observed in the increase in the total exploration time, index of habituation and index of

discrimination when compared to the control and 3-NP groups. This performance was as expected of mice with intact memory for the animals.

Morris water maze test is a test of visuo-spatial learning and memory. Here, the animals learned how to locate the hidden platform using a unique intra-maze cue. During the acquisition and reversal training, the swim latency was assessed and it is the time the mice swims to locate the hidden platform. Animals with longer swim latency are not able to learn fast to locate the hidden platform as quickly as those with shorter swim latency

[Acosta *et al,* 2010].

Results obtained from the acquisition training and reversal training which lasted for 3 days each; showed that the learning curves had no significant difference between the test groups and control indicating that animals in all the groups learned the location of the escape platform. This was found in the uniform decrease in swim latencies during the three days acquisition and reversal training. However, it was observed that the 3-NP +RV group learned faster compared to the group treated with 3-NP and the control groups. This result suggests improved learning ability.

For the probe trial day, with no hidden platform, the quadrant duration was measured. Quadrant duration is the amount of time spent in each quadrant during the probe trial

The quadrant that has the hidden platform during the reversal training is referred to as the retention quadrant. Here, an animal that has memory of the hidden platform will spend much time swimming around the quadrant that has the hidden platform during the reversal which means the animal has learnt well [Tambuyzer *et al*, 2009; Ihl *et al* 2012].

In this study, it was observed that upon induction of oxidative stress in mice with 3-NP, the quadrant durations both in acquisition quadrant and retention quadrant and annulus reversal were significantly decreased in the oxidative stressed (3NP) group compared to the control and 3-NP groups.

This is an indication that memory impairment occurred upon induction of oxidative stress in mice. This corroborates the fact that oxidative stress can result in impairment in memory evident in Alzheimer's disease [Bertram *et al*., 2010; Chaitanya *et al,* 2010**].**

On treatment with the root bark extract of *R. vomitoria*, there was a reversal of the impairment of memory. This was shown in the increased quadrants durations, both in the

acquisition and reversal or retention quadrants and also in the annulus reversal [Ekong *et al*, 2015].

The root extract of *R. vomitoria* seemed to have great ameliorating effect in decreasing the memory impairment induced by 3-NP. Therefore, these results is an indication that *R. vomitoria* reversed memory impairment induced by oxidative stress in both visuospatial and cognitive memory.

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