

# Effects of Acute Ethanolic Extract of Cannabis sativa on Learning and Memory in Albino Mice: A Comparative Study Using Novel Object Recognition and T-Maze Models

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## Abstract

The effects of marijuana on cognitive function remain controversial, particularly regarding its impact on different memory systems. This study aimed to evaluate learning and memory in albino mice following acute exposure to ethanolic extract of Cannabis sativa using the NORT and T-maze paradigms. Adult albino mice were administered 2 mg/kg of ethanolic extract of Cannabis sativa and cognitive performance was assessed at different time points following administration. Recognition memory was assessed using NORT by assessing exploration time, discrimination index and recognition index, while spatial working memory was evaluated using the T-maze through latency and correct arm choice performance. Data were expressed as mean  $\pm$  SEM and analyzed using one-way ANOVA, with significance set at  $p < 0.05$ . Results showed a time-dependent effect on recognition memory. At 1-hour after treatment, recognition memory was impaired (novel object exploration and discrimination index). However, at 2 hours, a significant enhancement was seen with maximum values reached for all NORT measures. A return to normal was observed at 3 and 4 hours. On the other hand, there were no significant differences in the T-maze task for any treatment ( $p > 0.05$ ), suggesting that spatial working memory is not impaired. In conclusion, acute exposure to ethanolic extract of marijuana has selective, reversible effects on memory. Recognition memory is particularly vulnerable to cannabinoid effects, while spatial working memory is preserved at low doses of cannabinoids.

**Keywords:** Cannabis Sativa; Learning and Memory; Novel Object Recognition; T-Maze; Albino Mice; Cannabinoids; Cognitive Function

## 1. Introduction

Learning and memory are critical brain functions that enable the acquisition, storage and recall of information necessary for survival. These functions rely on integrated activity of critical brain structures, including the hippocampus, prefrontal cortex, and amygdala [2]. Impairment of these brain regions can result in cognitive dysfunction, which is often experimentally studied in animals for improved control [3].

Albino mice are widely used in neurobehavioral studies because they are easy to handle and produce consistent behavioral responses [4]. Among the available behavioral models, the Novel Object Recognition (NOR) test and the T-maze are commonly used to assess different aspects of memory [5]. The NOR test evaluates recognition memory based on the natural tendency of rodents to explore new objects, while the T-maze assesses spatial and working memory through alternation behavior [6].

Cannabis sativa (marijuana) has multiple active components such as  $\Delta^9$ -tetrahydrocannabinol (THC) and cannabidiol (CBD) that interact with the endocannabinoid system [7]. These compounds predominantly act on cannabinoid

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receptors (CB<sub>1</sub> and CB<sub>2</sub>), which are highly expressed in brain regions of interest for learning and memory [8]. These interactions affect the release of neurotransmitters, synaptic plasticity, and cognitive processes [8].

Despite the growing recreational and therapeutic use of marijuana, the impact on cognition is still unclear [9]. There is evidence of memory deficits, as well as limited or even positive effects, depending on the dose, duration and model used [10, 11]. A potential limitation of some previous studies was the use of only one behavioural test, which may not reflect the full range of memory processes [12].

The aim of our study was to compare the effects of ethanolic extract of marijuana on learning and memory processes in albino mice using the novel object recognition (NOR) and T-maze tests. This will enable a broader assessment of the effects of marijuana on multiple aspects of memory within the same testing environment.

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## **2. Materials and Methods**

### **2.1. Experimental Animals**

Adult albino mice weighing 20-30 g were used in this study. They were obtained and maintained in a conventional laboratory environment, with ad libitum access to food and water. The animals were kept at a 12-hour light/dark cycle and were left to acclimatize for two weeks.

### **2.2. Ethical Approval**

All experiments were performed according to the guidelines for the care and use of laboratory animals. This study was approved by the Ethics Committee of the Faculty of Basic Medical Sciences, College of Health Sciences, Niger Delta University, Wilberforce Island, Bayelsa State, Nigeria.

### **2.3. Preparation of Ethanolic Extract of Cannabis sativa**

Dried marijuana leaves were collected and grounded into a fine powder. The powdered material was soaked in ethanol for extraction. The mixture was filtered and the filtrate was concentrated by evaporating the solvent to obtain the ethanolic extract.

### **2.4. Experimental Design**

The animals were randomly divided into two groups (control and treatment group). The treatment group received 2 mg/kg body weight of the ethanolic extract of marijuana, and the control group received distilled water. The extract was administered orally using an oral gavage.

### **2.5. Novel Object Recognition Test (NOR)**

The Novel Object Recognition test was used to assess recognition memory. Animals were first habituated to the arena. In the object training phase, two identical objects were introduced to the arena and the mice were allowed to explore. During the test phase, one of the objects was replaced with a new object. Exploration of the objects was measured.

### **2.6. T-Maze Test**

A T-maze was used to assess spatial learning and working memory. The maze had a start arm and two goal arms. Mice were allowed to explore the maze and their performance in choosing the correct arm was measured. The animals' latency to enter the correct arm and the percentage of correct choices were recorded.

### **2.7. Behavioral Parameters**

The following parameters were recorded: Exploration time (seconds), Discrimination index (DI), Recognition index (%), Latency to correct arm (seconds) and Percentage of correct arm choices

### **2.8. Statistical Analysis**

All data were expressed as mean  $\pm$  standard error of mean (SEM). Statistical analysis was performed using one-way analysis of variance (ANOVA). Differences between groups were considered statistically significant at  $p < 0.05$ .

### 3. Results

#### 3.1. Novel Object Recognition Test

##### 3.1.1. Exploration Time

Table 1 shows time of exploration of the familiar and novel objects. In control rats, exploration time of the novel object (29.0 s) was greater than the familiar object (24.6 s), demonstrating intact recognition memory

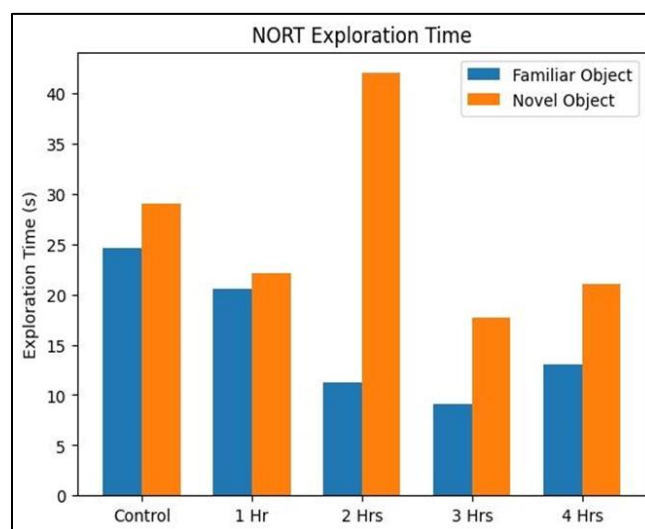
At 1-hour post-treatment, the time spent exploring the novel object shortened (22.1 s), indicating a short-lived memory impairment. Exploration of the novel object significantly increased (42.0 s) at 2-hours post-treatment and was the highest among all groups. This suggests an enhancement of recognition memory.

At 3- and 4-hours post-treatment, exploration of the novel object declined to 17.7 s and 21.0 s, respectively, although values remained higher than those for the familiar object.

**Table 1** Exploration time for familiar and novel objects in the Novel Object Recognition Test

| Group                  | Familiar Object (s) | Novel Object (s) |
|------------------------|---------------------|------------------|
| Control                | 24.6                | 29.0             |
| 1 Hour Post-Treatment  | 20.5                | 22.1             |
| 2 Hours Post-Treatment | 11.3                | 42.0             |
| 3 Hours Post-Treatment | 9.1                 | 17.7             |
| 4 Hours Post-Treatment | 13.0                | 21.0             |

Note: Values represent mean exploration time (seconds)



**Figure 1** Exploration time for familiar and novel objects in the Novel Object Recognition Test

Bar chart showing mean exploration time (seconds) for familiar and novel objects across experimental groups.

##### 3.1.2. Discrimination Index (DI)

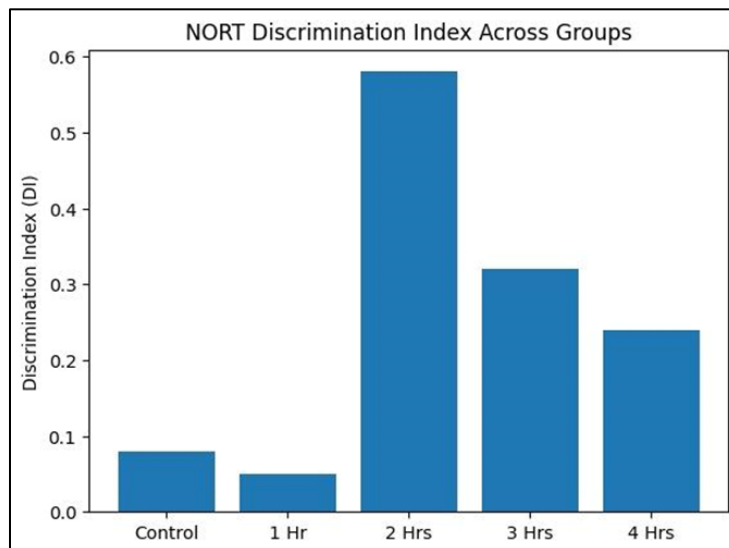
The discrimination index is presented in Table 2. The DI value for control animals was 0.08. DI values at 1-hour post-treatment were 0.05, representing a decline in recognition memory.

The DI was highest (0.58) at 2 hours post-treatment, suggesting improved recognition memory. At 3 and 4 hours after treatment, the DI values were 0.32 and 0.24, respectively, which were still positive, showing that the mice still preferred the novel object.

**Table 2** Discrimination index in the Novel Object Recognition Test

| Group                  | Discrimination Index (DI) |
|------------------------|---------------------------|
| Control                | 0.08                      |
| 1 Hour Post-Treatment  | 0.05                      |
| 2 Hours Post-Treatment | 0.58                      |
| 3 Hours Post-Treatment | 0.32                      |
| 4 Hours Post-Treatment | 0.24                      |

Note: Discrimination Index (DI) = (Novel – Familiar) / (Novel + Familiar)

**Figure 2** Discrimination index in the Novel Object Recognition Test

Bar chart showing discrimination index (DI) across experimental groups, indicating preference for novel objects.

### 3.1.3. Recognition Index (%)

Values for the recognition index are shown in Table 3. In the control group, animals had a recognition index of 54%.

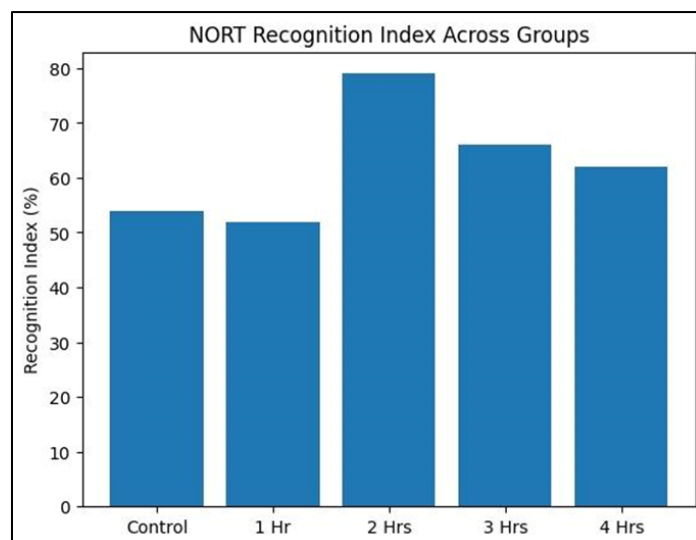
At 1-hour post-treatment, the recognition index slightly dropped to 52%. At 2 hours post-treatment, the recognition index significantly increased to 79%, which was the highest index.

The recognition index returned to lower at 3- and 4-hours post-treatment (66% and 62%) showing a return to baseline.

**Table 3** Recognition index (%) in the Novel Object Recognition Test

| Group                  | Recognition Index (%) |
|------------------------|-----------------------|
| Control                | 54                    |
| 1 Hour Post-Treatment  | 52                    |
| 2 Hours Post-Treatment | 79                    |
| 3 Hours Post-Treatment | 66                    |
| 4 Hours Post-Treatment | 62                    |

Note: Recognition Index (%) = [Novel / (Novel + Familiar)] × 100.



**Figure 3** Recognition index (%) in the Novel Object Recognition Test

Bar chart showing percentage recognition index across experimental groups.

### 3.2. T-Maze Test

#### 3.2.1. Latency to Reach Correct Arm

Mean latency values are presented in Table 4. Control animals showed a latency of  $8.2 \pm 0.5$  s.

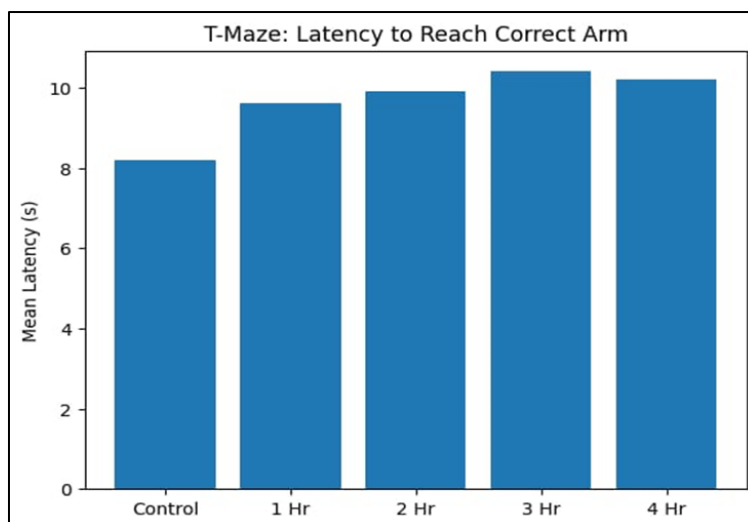
Following treatment, latency increased slightly across all time points, with values of  $9.6 \pm 0.7$  s (1 hour),  $9.9 \pm 0.6$  s (2 hours),  $10.4 \pm 0.8$  s (3 hours) and  $10.2 \pm 0.9$  s (4 hours).

But one-way ANOVA revealed no significant difference between groups ( $F = 0.71$ ,  $p > 0.05$ ), suggesting that the extract did not have an effect on spatial learning.

**Table 4** Latency to reach the correct arm in the T-maze

| Group                  | Mean Latency (s) |
|------------------------|------------------|
| Control                | $8.2 \pm 0.5$    |
| 1 Hour Post-Treatment  | $9.6 \pm 0.7$    |
| 2 Hours Post-Treatment | $9.9 \pm 0.6$    |
| 3 Hours Post-Treatment | $10.4 \pm 0.8$   |
| 4 Hours Post-Treatment | $10.2 \pm 0.9$   |

Note: No significant difference among groups ( $F = 0.71$ ,  $p > 0.05$ ).



**Figure 4** Latency to reach the correct arm in the T-maze

Bar chart showing mean latency (seconds) across experimental groups. No significant differences were observed ( $p > 0.05$ ).

### 3.2.2. Correct Arm Choice Performance

The percentage of correct arm choices is shown in Table 5. Control animals showed  $92 \pm 3\%$  correct choices.

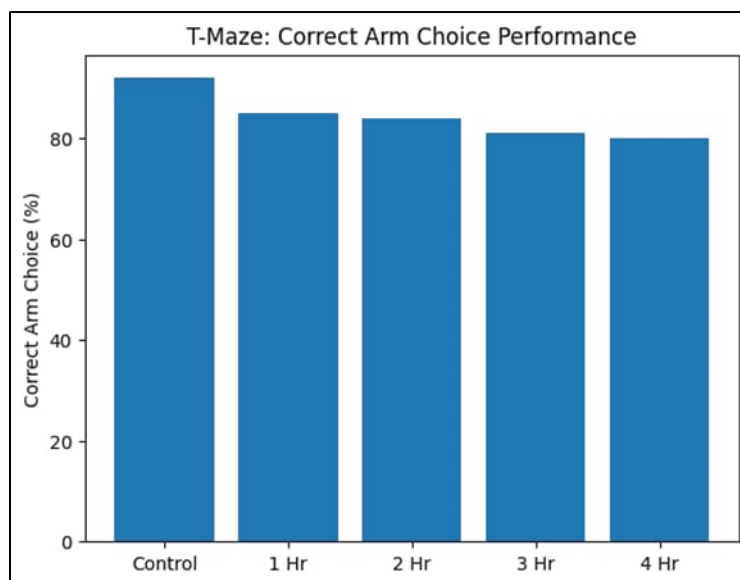
Following treatment, a slight reduction was observed:  $85 \pm 4\%$  (1 hour),  $84 \pm 5\%$  (2 hours),  $81 \pm 6\%$  (3 hours) and  $80 \pm 6\%$  (4 hours).

There was no significant difference between groups ( $F = 1.33$ ,  $p > 0.05$ ), suggesting that working memory was not seriously affected.

**Table 5** Percentage of correct arm choices in the T-maze

| Group                  | Correct Arm Choice (%) |
|------------------------|------------------------|
| Control                | $92 \pm 3$             |
| 1 Hour Post-Treatment  | $85 \pm 4$             |
| 2 Hours Post-Treatment | $84 \pm 5$             |
| 3 Hours Post-Treatment | $81 \pm 6$             |
| 4 Hours Post-Treatment | $80 \pm 6$             |

Note: No significant difference among groups ( $F = 1.33$ ,  $p > 0.05$ ).



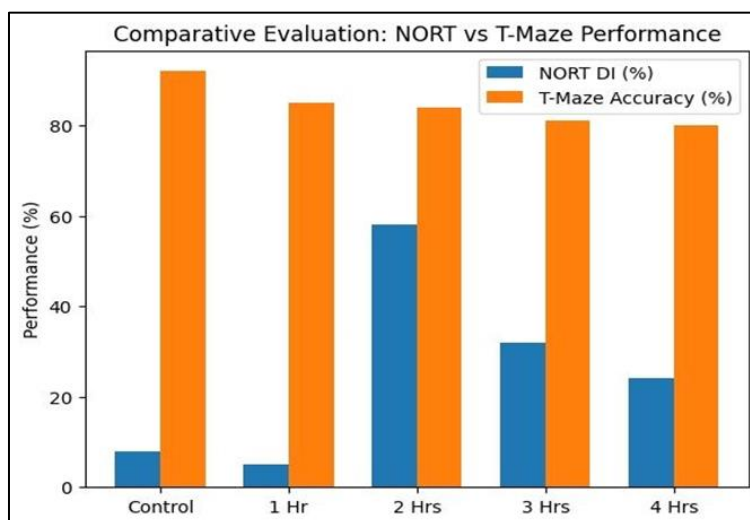
**Figure 5** Percentage of correct arm choices in the T-maze

Bar chart showing mean percentage of correct arm choices across groups. No significant differences were observed ( $p > 0.05$ ).

### 3.3. Comparative Analysis

A comparison of the two behavioural paradigms showed that recognition memory exhibited time-dependent changes following marijuana administration, with an initial decrease at 1-hour, peak performance at 2 hours and gradual normalization by 4 hours.

However, spatial working memory (T-maze) performance was maintained with no significant difference between the time points ( $p > 0.05$ ).



**Figure 6** Comparative evaluation of NORT and T-maze performance

Graph showing comparative trends in recognition memory and spatial memory performance across time points following marijuana administration.

#### 4. Discussion

This study evaluated the effects of acute administration of 2 mg/kg ethanolic extract of *Cannabis sativa* on learning and memory in albino mice using two behavioral models: NOR and the T-maze. These models assess different domains of memory, allowing a broader understanding of how marijuana influences cognitive function.

The results of the NORT demonstrated time-dependent effects on recognition memory. 1-hour after marijuana administration, there was a decrease in time spent exploring the new object, reduced discrimination index and recognition index. This implies an early transient decrease in recognition memory following cannabinoid treatment. This may be related to the initial activation of CB<sub>1</sub> receptors in the hippocampus, which could temporarily alter synaptic plasticity and decrease exploration [13, 14].

At 2 hours after treatment, recognition memory was significantly improved. This was demonstrated by the greatest exploration time, discrimination index and recognition index of all groups. This may reflect a transient improvement or rebounds effect after the initial impairment. This could be due to the fact that low levels of cannabinoid stimulation may temporarily affect neurotransmitters such as glutamate and GABA, which may increase synaptic plasticity in the short term [15, 16].

At 3- and 4-hours post-treatment, recognition memory gradually declined from the peak observed at 2 hours but remained above baseline levels. This indicates that the effects of marijuana on recognition memory are dynamic, reversible and not persistently damaging at the administered dose [17, 18]. The NORT results show that recognition memory is highly sensitive to acute cannabinoid exposure and responds in a time-dependent manner.

This is in contrast to the T-maze results, which indicate no impairment in spatial learning and working memory. While there were modest increases in latency and slight decreases in the number of correct arm choices made, these results were not statistically significant ( $p > 0.05$ ). This supports the hypothesis that the circuits underlying spatial working memory may not be as easily affected by low doses of cannabinoids [19].

The discrepancy between the results of the NORT and T-maze tasks suggests an important feature of memory: it is not a unified memory system, but several different systems. Recognition memory, which relies heavily on the hippocampus and perirhinal cortex, seems to be more affected by cannabinoids [13]. In contrast, spatial working memory, which is supported by the hippocampus and prefrontal cortex, was less affected in these conditions [21, 22].

These results are in line with other studies that have shown cannabinoids can cause hippocampal dysfunction and interfere with long-term potentiation (LTP), a process essential for memory formation [13, 14, 23]. But the lack of impairment in the T-maze suggests that the degree of cognitive impairment depends on the dose and duration of exposure [24].

This study's comparative nature adds to its importance. The use of both NORT and T-maze paradigms allowed us to demonstrate that marijuana has no global impact on memory. Rather, effects are task-specific, time-limited and selective [21].

The findings indicate that acute administration of ethanolic extract of marijuana results in temporary modulation recognition memory, whereas spatial working memory is relatively intact at low doses.

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#### 5. Conclusion

This study demonstrates that acute administration of ethanolic extract of *Cannabis sativa* produces a task-dependent and time-dependent effects on learning and memory in albino mice. Object recognition memory, measured by the Novel Object Recognition Test, initially impaired at 1 hour, reached a maximum level at 2-hours, and then declined to normal levels by 4-hours after treatment. On the other hand, spatial working memory, indicated by the T-maze, is unaffected. The results suggest marijuana does not have a general negative effect on all learning and memory, but rather has a selective effect on some memory systems in a reversible fashion.

## Compliance with ethical standards

### *Disclosure of conflict of interest*

The Authors declared no competing interests exist.

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