

# Effects of Lamotrigine in open-field, water maze and step-through tests in rats

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## Introduction

Lamotrigine was introduced in clinical practice for monotherapy or adjunctive therapy of partial, generalized tonic-clonic and absence seizures. It has also been approved for use in treatment-resistant depressive disorders and bipolar disorder [1]. These are chronic diseases demanding long-term treatment and it is very important for Lamotrigine to be not only efficient but safe [2].

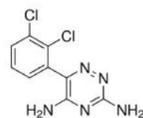
## Aim

The aim was to study the effects of Lamotrigine on exploratory activity, spatial memory and passive learning in rats, using open-field, Morris water maze (MWM) and step-through tests.

## Material and Methods

### Lamotrigine:

6-(2,3-dichlorophenyl)-1,2,4 triazine-3,5-diamine (Lamictal tablets, GlaxoSmithKline)



**Rats:** Male Wistar, 180 – 220 g b.w., 9 per group [9 per cage, 08.00 – 20.00 light, food and water at lib] were treated once daily:

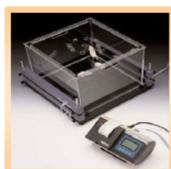
### Groups:

- A: distilled water 0.1 ml/100 g body weight p.o. (controls)
- B: Lamotrigine 10 mg/kg p.o.
- C: Lamotrigine 20 mg/kg p.o.

The tests were performed 60 min after drug application.

### I. Open-field test

**Apparatus** – automatic set-up with infrared photo-sensors (Ugo Basile, Italy). The number of horizontal and vertical movements in relative units for 5 minutes per rat were recorded on the 1<sup>st</sup> and 15<sup>th</sup> day of the experiment.



### II. Step-through passive avoidance test

**Apparatus** – automatic set-up for passive avoidance "step-through" (Ugo Basile, Italy). Parameters: door delay – 6 s, open door for 12 s, followed within 9 s 0.4 mA foot shock. Step-through passive avoidance test was performed in a two-day learning session, followed by short-term memory retention test after 24 h and long-term memory retention test on the 7<sup>th</sup> day. Every test consists of 3 trials 60 minutes between each.



**Learning criterion:** latency of reactions maximal time of 3 minutes (180 ± 2 seconds), resting in the light compartment of the apparatus.

### III. Moris water maze test (MWM)

The animals were trained to find hidden under the water surface platform. Learning sessions consisted of 3 trials per day for 5 consecutive days. Memory retention was tested on day 7.



**Learning criterion:** the latency to reach the hidden platform for less than 60 sec on the memory retention test.

## Statistical analysis

It was used InStat computer program for analysis of variance. The mean and standard error of mean (SEM) for each group was calculated. A two-way ANOVA for repeated measurements was used to compare different groups with the respective controls. A p-value of  $P < 0.05$  was considered representative of a significant difference.

## Results

**In open-field tests** on the first day of testing the rats treated with 10 mg/kg Lamotrigine significantly increased the number of relative units in vertical activity ( $p < 0.05$ ), compared to the controls. In the second testing on the 15<sup>th</sup> day, the animals receiving the higher dose Lamotrigine significantly increased the number of relative units in both horizontal ( $p < 0.05$ ) and vertical ( $p < 0.05$ ) movements. (Fig. 1a, 1b)

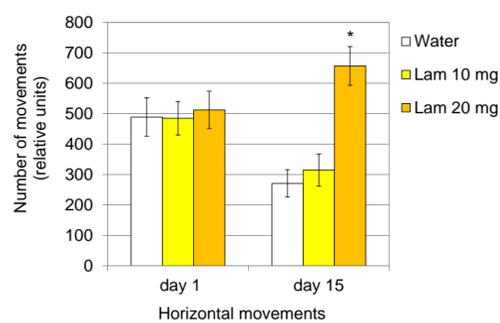


Fig. 1a. Effects of Lamotrigine on Locomotor activity in rats (horizontal movements)

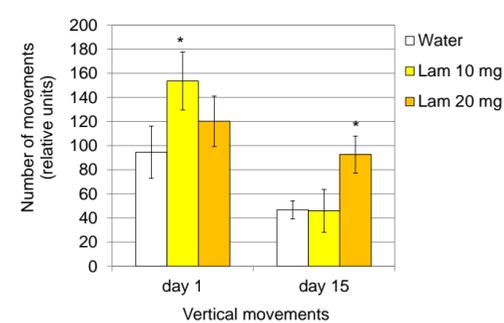


Fig. 1b. Effects of Lamotrigine on Locomotor activity in rats (vertical movements)

**In step-through test** the control rats increased the latency of reactions ( $p < 0.05$ ) on 2<sup>nd</sup> day learning, short and long memory test, compared to the first day. The rats treated with Lamotrigine in both doses significantly increased the time spent in the light chamber in the 1<sup>st</sup> day of learning session ( $p < 0.05$ ) compared to control group but did not keep it in the memory tests. (Fig. 2)

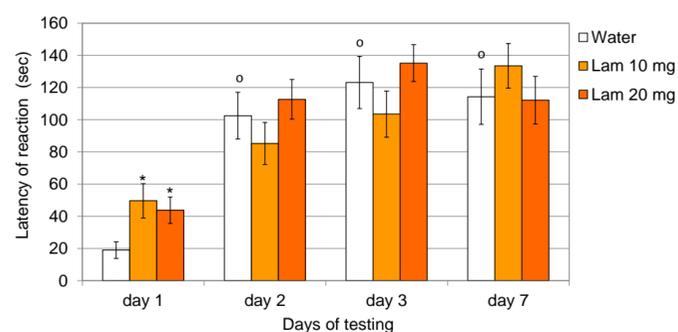


Fig. 2. Effects of Lamotrigine on step-through passive avoidance test

**In MWM test** the controls decreased the escape latency in all days of learning session and in memory retention test, compared to the first day ( $p < 0.05$ ). The animals treated with 10 mg/kg Lamotrigine significantly decreased the escape latency on day 3 and 4 of learning session ( $p < 0.05$ ), compared to the same day control group. The rats treated with 20 mg/kg Lamotrigine decreased the latency on day 4 and 5 of learning session ( $p < 0.05$ ). Both experimental groups significantly decreased ( $p < 0.05$ ) the time to reach the platform on memory retention test in comparison with rats treated with the same day controls. (Fig. 3)

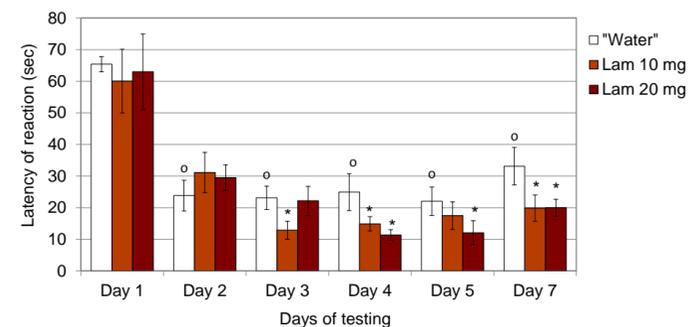


Fig. 3. Effects of Lamotrigine on MWM test

## Conclusion

Lamotrigine improves the exploratory activity of rats after repeated treatment with the higher dose. In step-through passive avoidance test Lamotrigine improves acquisition but does not affect memory consolidation. In MWM test Lamotrigine improves spatial learning and memory in both used doses. Some data show a cognition-protective effect of Lamotrigine in rats with cerebral ischemia [3] and our findings also suggest that Lamotrigine does not deteriorate learning and memory in rats. Furthermore, it presents beneficial effects on the cognitive functions.

## References

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