Role of NO synthase inhibition on passive avoidance performance after cold stress in rat

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Background and aims: Nitric oxide (NO) is a modulator of neuronal function and serves as an early signal for the acquisition of new information and in the consolidation of long-term potentiation (LTP). Nonselective NO synthase (NOS) inhibitors such as N^G-nitro-L-arginine methyl ester (L-NAME), impair learning and memory, as evidenced by impairment in passive avoidance and elevated plus-maze memory performance in rats. Also, stress is a potent modulator of cognitive function in general, and more precisely, of learning and memory. Stress increases serum corticosterone levels in rats. The hippocampus contains one of the highest concentrations of receptors for glucocorticoids in the brain which suggests that the hippocampus is sensitive to changes in glucocorticoid levels and that glucocorticoids may significantly impact hippocampal function. It has been reported that restraint stress combined with cold water immersion (for 60 min) increased latencies to enter the dark compartment before shock delivery, and decreased retention latencies in passive avoidance in rats. In contrast, recently it was showed that acute cold exposure (-15 ºC, for 2 hours) and subsequent rewarming resulted in enhanced performance of spatial learning and memory rats. Aim of the present work is evaluating effects of inhibition of NO production on passive avoidance performance in rats after cold exposure.

Methods: *Animals*: Adult male Wistar rats weighing 270-320 g were used in this study. The study consisted of experiment I and experiment II. In experiment I, rats had free access to standard pellet food and water. Animal were housed in temperature controlled room (21±2 ºC) on a 12-h dark/12-h light cycle for at least 1 week before experimentation. In experiment II, all conditions were similar with experiment I, except for overnight low temperature of animal room as cold stress, before training trial (12±2 ºC, between 19.00 and 7.00 h). Adaptation, training and testing were performed between 9.00 and 15.00 h.
Treatment: Each experiment consisted of two groups: L-NAME-pretreated and saline-pretreated. So, rats received an injection of L-NAME, 30mg/kg (was dissolved in isotonic saline) or saline, intra-peritoneally 30 min before training trial.
Apparatus: A shuttle-box consists of two communicating compartments of equal size (40×15×25 cm), separated by a guillotine door.

Procedure: Passive avoidance was conducted as following. After two days of adaptation of rat to apparatus, each 5 min; on training day (third day), rats were pretreated with L-NAME or saline, as was mentioned previously. Thirty minutes later, rat was placed in the light compartment and 60 seconds later the guillotine door was opened. Once the rat entered the dark compartment, the guillotine door was closed and an electric footshock (0.8 mA for 2 s) was delivered through the grid floor. The retention trial was carried out 24 h later. The rat was put in the light compartment and the time taken to enter the dark compartment was recorded as step-through latency (STL). A cutoff point of 300s was considered.

Results: In experiment I, pre-training L-NAME did not change initial latency, but significantly shortened STL ($p < 0.05$). In experiment II, with overnight cold stress, the results were different. Activity of rat was very low. Averages of initial latency in both L-NAME- and saline-pretreated rats were significantly prolonged compared with related values in same groups in experiment I ($p<0.05$). In addition, mean of STL in L-NAME-pretreated group was not different with saline-pretreated group in this experiment or saline-pretreated group in experiment I, and all were 300 s.

Conclusions: According to findings, it is suggested that probably short-term cold exposure blunted impairing effect of NOS inhibitor, L-NAME on memory consolidation of passive avoidance in rats.

Key words: Memory, Nitric oxide, Cold stress, Passive avoidance