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Study of Cognitive Function Enhancing Effect of Nimodipine by using Morris Water Maze Test

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ABSTRACT

Objective: To study effect of nimodipine on the cognitive function by using morris water maze test.
Materials and Method: The effect of nimodipine on the cognitive function was studied using morris water maze test in albino mice. Albino mice of both sex were divided into three groups *viz.* young control group (n=10), old control group (n=10) and nimodipine treated old mice group (n=10). The first two groups were treated with normal saline whereas last group was treated with nimodipine (2mg/kg I.P. [Intraperitoneal]) for 10 days. The animals were tested on 1st, 5th, 9th and 10th day of the trial. vehicle and nimodipine were given half an hour before the test.
Results: In Morris water maze test the mice has to search the hidden platform. Young mice were competent from the beginning in learning and memory and their performance further increased with the training, as evident by significant decrease in latency to find the platform and increasing number of crossing over the platform area. On the contrary aged mice did not show significant performance in any parameter. However treatment with nimodipine in another group of aged mice showed significant improvement in all the parameters of the water maze test but did not reach the performance of young mice.
Conclusion: The study suggestions that nimodopine enhances cognitive function in mice.

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Calcium regulates variety of signaling pathways (Carafoli, 2002; Clampham, 1995 and Grrenberg, 1995). Acute uncontrolled calcium influx can cause neuronal death by overstimulation of N- methyl D asparate (NMDA) type glutamate receptors (Lee *et al.,* 1999; Rothman and Olnay, 1987). These observations indicate that elevation of L-type channel activity causes neuronal dysfunction during aging .Influx of calcium through L- type calcium channel is robustly increased in old rodents (Disterhoft *et al.,* 1994). Elevated L-type channel activity during aging responsible for up regulation of afterhyperpolarization in hippocampal CA1 neurons which may contribute to age related deficit in learning and memory (Norris *et al.,* 1998; Thibault *et al.,* 2001).

Calcium channel blockers apart from having action on cardiovascular system are also known to have effect on central nervous system. Nimodipine is highly lipophilic dihydropyridine (DHP) calcium channel blocker. It has selective DHP binding sites in the limbic system *i.e.* hippocampus, olfactory bulb, amygdala and frontal cortex (Cortex *et al.,* 1984; Schoemaker and Langer *et al.,* 1985). Hippocampus is crucial for learning and memory. Nimodipine may prevent in part of the damage of neuronal cell resulting from disrupted regulation of calcium homeostasis.

In the present study, the effect of nimodipine on cognitive function by using water maze test in young and old mice was examined. Old mice like humans exhibit accelerated forgetting under appropriate testing conditions (Zometzer *et al.,* 1982) and show deficits in spatial learning (Gallagher and Pelleymounter *et al.,* 1988).

MATERIALS AND METHODS

Animals:

Albino mice with average weight (15-25 gm) of either sex were used throughout the study. They were kept under standard 12 hour light dark cycle and fed with food ad libitum. Approval of institutional animal ethics committee was obtained. The experiments were performed between 9 A.M. to 12 noon in an experimental room. Animals were divided into three groups.