Neurophysiological mechanisms of aging: novel view of old concepts

ABSTRACT:

Age-dependent memory deterioration has been well documented and yet an increase in rat hippocampal LTP upon aging has been reported. This poses the question of whether the enhanced LTP is a cause or an attempt to compensate the memory deficits described in aged rats.

Hippocampal slices from young, adult and aged Wistar rats were pre-incubated, with an NMDA receptor (NMDAR) antagonist, memantine (1 μM, 4hours), and hippocampal LTP was evaluated. The results show that memantine significantly decreases the larger LTP magnitude recorded in hippocampal slices from aged rats without compromising LTP recorded in slices from young and adult animals.

To unveil the impact of *in vivo* administration of memantine, different doses (1,5 and 10 mg/kg/day) or saline vehicle solution were intraperitoneally administered, for 15-20 days, to both young and aged animals. Memantine did not significantly affect neither the place learning of young animals, evaluated by Morris Water Maze, nor LTP recorded from hippocampal slices from the same group of animals. However, memantine (5 and 10 mg/kg/day) significantly decreased the large LTP recorded in hippocampal slices from aged animals. Moreover, aged animals treated with memantine (10 mg/Kg/day) showed a significantly compromised place learning when compared to aged control animals.

Overall, these results suggest that the larger LTP observed in aged animals is a compensatory phenomenon, rather than pathological. The finding that age-dependent blockade of LTP by a NMDAR antagonist leads to learning deficits, implies that the increased LTP observed upon aging may be playing an important role in the learning process.

Keywords
Synaptic plasticity, Aging, Hippocampus, Memory, NMDA receptors

Published Work:

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