Investigation of Age-Dependent Changes in Hippocampal Long-Term Potentiation Related Tau Phosphorylation

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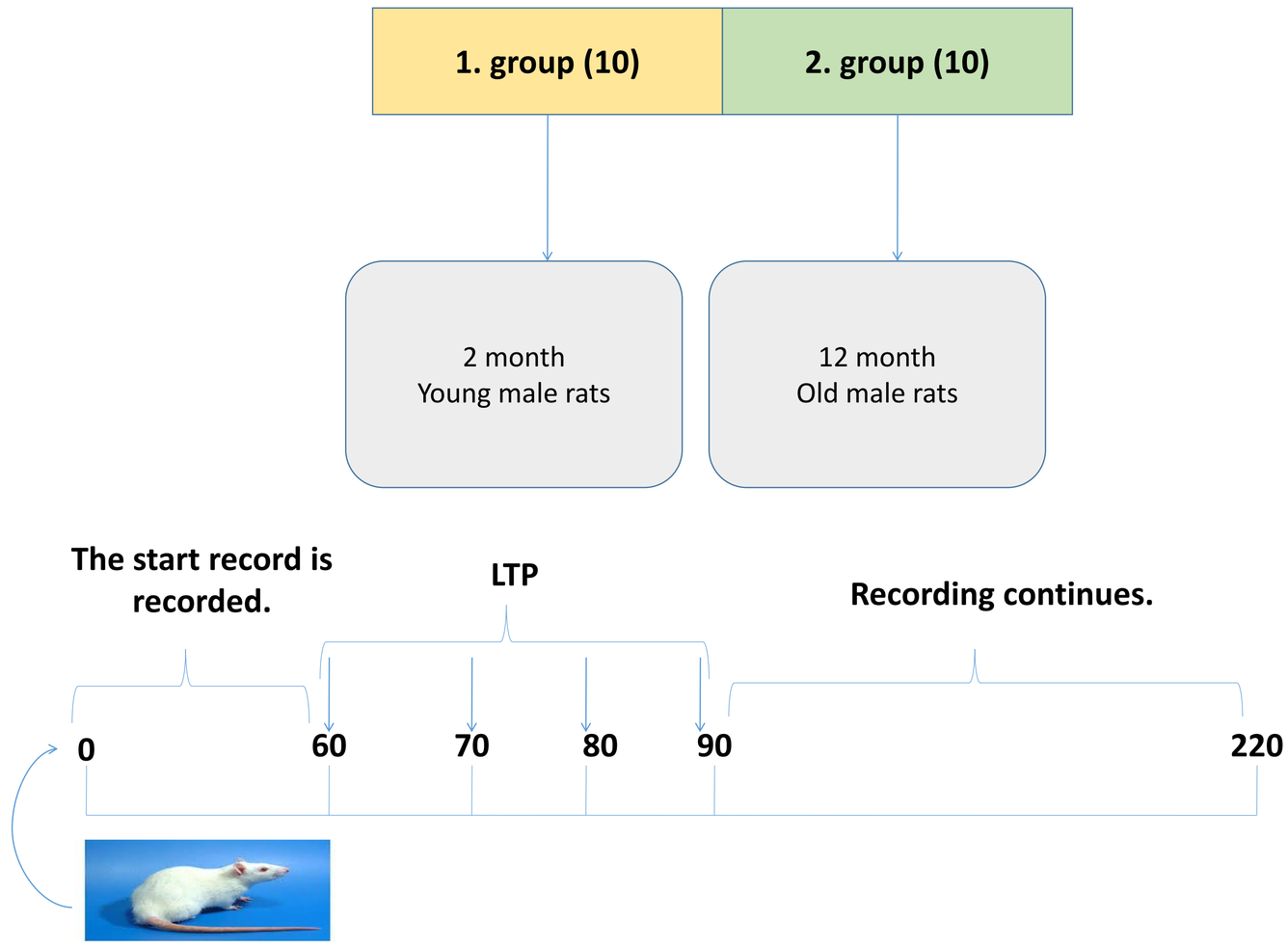
INTRODUCTION

Dementia is disruption of memory and other mental abilities with a severity that will affect daily life. 60-80% of diseases associated with dementia are Alzheimer's type dementia. Aging is an important factor in the formation of Alzheimer's disease, which is characterized by tau protein accumulation and tangle, especially in the cortex and hippocampus, since the majority of cases are 65 years old or older. The aim of this study is to investigate the effect of old age on hippocampal LTP and how the phosphorylation levels of different Tau epitopes are affected in stimulated hippocampus.

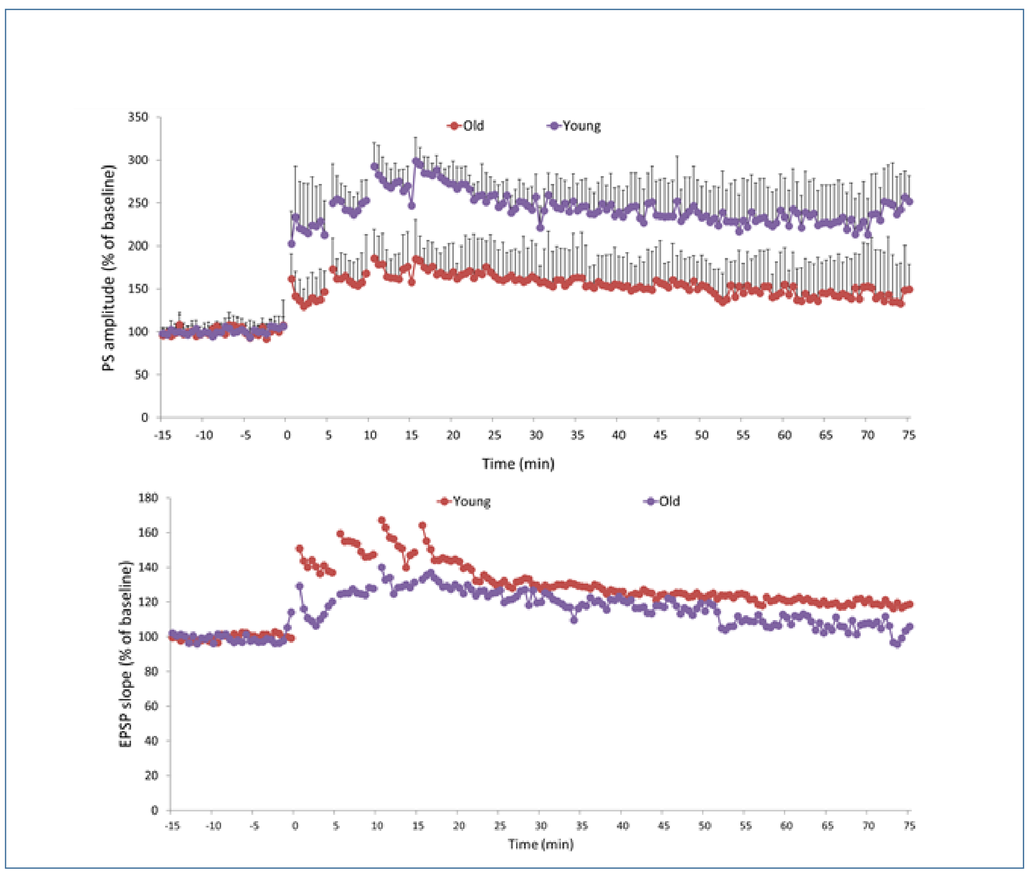
METHODS

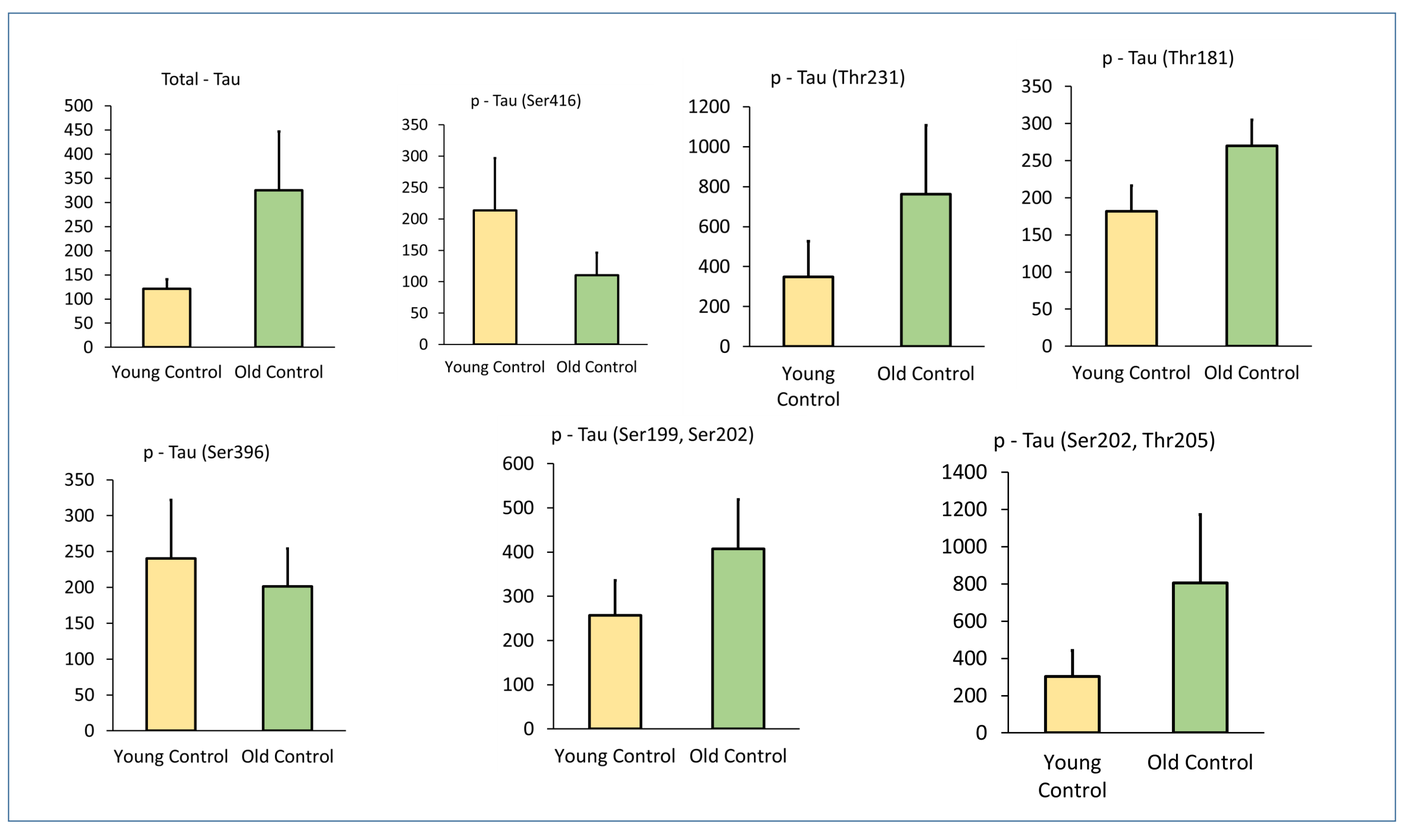
The study was carried out on 2-month and 12-month old (n=10/group) Wistar albino male rats. Potential changes occurring in the hippocampal dentate gyrus region were recorded by applying high frequency stimulation to the perforant pathway 4 times at 5-minute intervals to induce LTP. To evaluate LTP, EPSP slope and population spike amplitude were measured by taking the average of the first 5 minutes after the LTP induction and in the last 5 minute time interval. For protein analysis, hippocampus in which LTP is induced was used. Protein analyzes were performed by western blot method.

The data obtained were compared using Kruskal-Wallis and Man-Whitney U tests. One sample t test was used for LTP data.



RESULTS





The PS amplitudes decreased significantly with aging in the induction and maintenance periods without any change in the EPSP slopes ($p<0.05$). It was found in LTP-induced hippocampus that the total-Tau protein level and the p-TauThr181, p-TauThr231, p-TauSer199-Ser202, p-TauSer202-Thr205 epitopes were increased, while the p-TauSer416 epitope was decreased with aging.

CONCLUSION

Impaired LTP that occur with aging may be among the underlying causes of dementia that occurs in older ages. In addition, Tau epitopes known to play a role in the pathogenesis of Alzheimer's disease may support increased phosphorylation-impaired LTP responses with aging. These results may explain the causes of cognitive functions such as impaired learning and memory in old age.

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