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ALPHA1-ADRENOCEPTOR ANTAGONIST AMELIORATES MEMORY IMPAIRMENT IN THE ELDERLY WITH LUTS? A STUDY ABOUT THE INFLUENCE OF TAMSULOSIN ON THE MEMORY IMPAIRMENT THROUGH ENHANCEMENT OF ALPHA1A-ADRENOCEPTOR IN THE HIPPOCAMPUS OF OLD-AGED RATS

Hypothesis / aims of study
Voiding dysfunction is a common problem in the elderly, and therefore medications such as alpha1-adrenoceptor antagonist (α1-AR antagonist) have been used very widely. In addition, elderly people with voiding problem often show aging-induced memory impairment at the same time because deterioration of noradrenaline system may also contribute to the impairments of learning and memory during aging. Recently, tamsulosin, α1-AR antagonist, is reported to access to the brain and affect the neuronal activity. Therefore, we investigated the effect of tamsulosin on the memory in old-aged rats.

Study design, materials and methods
In order to evaluate short-term memory, Step-down avoidance tasks were conducted, and spatial learning ability was evaluated by performing radial 8-arm maze tasks in old-aged rats. Terminal deoxynucleotidyltransferase-mediated dUTP nick end labeling (TUNEL) assays were performed for the evaluation of the effect of tamsulosin on the level of apoptosis in the hippocampal dentate gyrus. The expression of α1-AR, phospho-protein kinase C alpha (p-PKCα), phospho-cAMP-responsive element binding protein (p-CREB), brain-derived neurotrophic factor (BDNF), TrkB, phospho-phosphatidylinositol (p-PI) 3-kinase p85α and phospho-Akt (p-Akt), Bax and caspase-3 were analyzed in the hippocampus.

Results
Expressions of p-PKCα, p-CREB, BDNF, TrkB, p-PI 3-kinase p85α and p-Akt in the hippocampus of old-aged rats significantly decreased, and expressions of Bax and caspase-3 significantly increased, resulting in decrease of BrdU-positive cells and increase of TUNEL-positive cells in the hippocampal dentate gyrus of old-aged rats. Consequently, old-aged rats exhibited significant impairment of short-term and spatial learning memory. On the other hand, tamsulosin dose-dependently facilitated the activation of p-PKCα and p-CREB, and increased the levels of BDNF and TrkB, contributing to enhancement of hippocampal neurogenesis in old-aged rats. Moreover, it significantly enhanced the expressions of VEGF and Bcl-2, and decreased Bax expression, resulting in significant suppression of neuronal cell death in the hippocampus of old-aged rats.

Interpretation of results
Findings reflected the decreased neurogenesis and increased apoptosis of the hippocampus were correlated with the functional impairment in the old-aged rats. The enhancement of hippocampal neurogenesis after administration with tamsulosin presented the protective effect of α1-AR antagonist on the memory impairment in the elderly.

Concluding message
Tamsulosin can be used for the elderly patient with memory impairment as well as Lower urinary tract symptoms (LUTS) by the neuroprotective effects through enhancing neurogenesis and suppressing apoptosis in the old-aged hippocampus. Therefore, tamsulosin may be the safer α1-AR antagonist for the elderly who have cognitive impairment and LUTS.

References
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