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Cognitive impairment in Alzheimer's disease and central noradrenergic system: A review

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The Alzheimer's disease (AD) is a looming crisis in aged society. It is an urgent need to develop a new remedy to delay or prevent symptoms of AD. Accumulated knowledge suggest that the degeneration of noradrenergic (NAergic) forebrain projection neurons is an early feature of AD. A review of NAergic system and AD (587 publications) has been made by referencing basic researches in the visual cortical plasticity. Previous studies correlating NAergic cell loss with increased AD pathology in locus coeruleus projection sites suggest that NA is neuroprotective. NAergic system plays important roles in the regulation of plasticity in the brain. We have shown that the pharmacological inhibition of NAergic system resulted in a reduction of ocular dominance plasticity in some animal models. It is also demonstrated that the activation of central NAergic system enhanced ocular dominance plasticity in aplastic visual cortex of adult and/or pharmacologically treated animals with lower level of plasticity. These function are mediated by modifying $ß_1$-adrenergic receptors. While activation $alpha_1$ adrenoceptors was shown to sharpen thalmocortical propagation by inhibiting horizontal connection in the cerebral cortex. Microglia respond to cell death via extension of their processes toward ATP released at the site of neuronal lesion. It has also reported that NA induced process retraction in resting and activated microglia through $ß_2$ and $alpha_{2A}$ receptors, respectively. The molecular and cellular mechanisms of the plasticity provide some clues to understand the cognitive impairments in Alzheimer's disease: deterioration of i) activity dependent plasticity, ii) clearance of Aß by microglial cells, iii) astrocytic functions, and iv) decrease in release of neurotrophic factors. We have first demonstrated that the administration of L-threo, DOPS, an amino-acid precursor of NA restored ocular dominance plasticity in aplastic visual cortex. The possible administration of DOPS for reversing pathogenesis of AD should be discussed.