

Neuroscience Translational Comp Question

Alzheimer's Disease (AD) is a disease of senescence, and the principal neurodegenerative disease. It is characterized by the presence of β -amyloid plaque, and neurofibrillary tangles. While neuronal loss occurs in a number of brain regions during AD, disruption of hippocampal function, especially episodic memory is an early and prominent sign. Hippocampal function is improved by enhancing the function of cholinergic synapses, especially those utilizing nicotinic type receptors. At present, the only therapeutic intervention approved for use in AD is inhibition of acetylcholinesterase, functionally enhancing cholinergic tone, but doing so nonspecifically. Considerable data suggest a role for nicotinic cholinergic receptors in the development of AD. Expression and function of specific subtypes of nicotinic receptors is impaired in brain of AD patients and in animal models of AD.

- 1.) Describe the structure, function and physiology of nicotinic receptors, comparing peripheral and central forms.
- 2.) Evaluate the evidence for and against the role of nicotinic receptors in the pathophysiology of Alzheimer's Disease. Pay attention to subtype-specific contributions.
- 3.) Describe a series of experiments to test the potential utility of a new nicotinic receptor agonist in AD. Your experiments should include whole animal preparations, as well as in vitro and/or in situ preparations. Be sure to include appropriate controls, and delineate expected side effects of your proposed therapeutic.
- 4.) Describe the peripheral and central effects which occur following acetylcholinesterase inhibition, and which of these effects would be expected to be eliminated by use of a specific nACh receptor agonist?