Cholinergic involvement and manipulation approaches in multiple system disorders

By soreq
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By soreq June 4, 2013


Abstract:

Within the autonomic system, acetylcholine signaling contributes simultaneously and interactively to cognitive, behavioral, muscle and immune functions. Therefore, manipulating cholinergic parameters such as the activities of the acetylcholine hydrolyzing enzymes in body fluids or the corresponding transcript levels in blood leukocytes can change the global status of the autonomic system in treated individuals. Specifically, cholinesterase activities are subject to rapid and effective changes. The enzyme activity baseline increases with age and body mass index and depends on gender and ethnic origin. Also, the corresponding DNA (for detecting mutations) and RNA (for measuring specific mRNA transcripts) of cholinergic genes present individual variability. In leukocytes, acetylcholine inhibits the production of pro-inflammatory cytokines, suggesting relevance of cholinergic parameters to both the basal levels and to disease-induced inflammation. Inversely, acetylcholine levels increase under various stress stimuli, inducing changes in autonomic system molecules (e.g., pro-inflammatory cytokines) which can penetrate the brain; therefore, manipulating these levels can also effect brain reactions, mainly of anxiety, depression and pain. Additionally, neurodegenerative diseases often involve exacerbated inflammation, depression and anxiety, providing a focus interest group for cholinergic manipulations. In Alzheimer’s disease, the systemic cholinergic impairments reflect premature death of cholinergic neurons. The decline of cholinesterases in the serum of Parkinson’s disease and post-stroke patients, discovery of the relevant microRNAs and the growing range of use of anticholinesterase medications all call for critical re-inspection of established and novel approaches for manipulating cholinergic parameters.

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