

Age related interaction of dopamine and serotonin synthesis in the striatal synaptosomes

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Background and Aims: Tyrosine hydroxylase (TH) and tryptophan hydroxylase (TPH) are key rate limiting enzymes in the biosynthesis of dopamine and serotonin respectively. TH utilizes O₂ to oxidize the reduced pterin cofactor (BH₄), and is subjected to feedback inhibition by catecholamines. Similar studies on a possible serotonin/TPH feedback loop have been complicated, but both enzymes are tightly regulated by inhibitory feedback via autoreceptors. In addition, both catecholamines and serotonin inhibit TPH and TH activities respectively. Since both enzymes are active in striatum, and affected by age, this study was undertaken to investigate interaction between dopamine and serotonin synthesis in the brain striatal synaptosomes of aging rat.

Methods: Male Wistar rats (3 and 30 month old) were decapitated and the brains removed and dissected over ice. Six striatum were homogenized and synaptosomes were separated by ultracentrifugation at 4°C. The synaptosomes were incubated in the presence of added pargiline (monoamine oxidase inhibitor), tyrosine or tryptophan, and dopamine or serotonin synthesized during 25min. was measured by HPLC, employing an electrochemical detection.

Results: Dopamine synthesis in the synaptosomes prepared from young animals was markedly inhibited (30%) by addition of 5µM serotonin concentrations, and increasing serotonin concentrations upto 50µM caused only a relatively small additional inhibition. However, different concentrations of serotonin (5-50µM) had little effect on dopamine synthesis of the synaptosomes preparations from old animals. In case of serotonin synthesis, exogenously added dopamine inhibited serotonin synthesis in the synaptosomes of both ages by 40%, and addition of high concentration of dopamine was highly pronounced in the old rats as compared to that of young animals.

Conclusions: It is suggested that dopamine and serotonin cross reaction might be noteworthy, where long-term treatment with L-DOPA of patients suffering from Parkinson's disease, renders the drug less effective and that patients experience fluctuations in response and even psychiatric problems.

Keywords: Aging, Dopamine synthesis; Neurotransmitter; Serotonin synthesis; Parkinson's disease