

Serotonergic Modulation of Cognition in Prefrontal Cortical Circuits in Major Depression

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Abstract

Cognitive processes are altered in depression patients, and their neuromodulation by serotonergic treatments may depend on the specific pathophysiology of the disease. Here, we addressed this question in a computational model that included two mutually inhibiting network hubs in the ventral anterior cingulate (vACC) and dorsolateral prefrontal cortices, and one additional cognitive area involved in spatial working memory in the parietal cortex. We modeled two different network alterations that give rise to depression-like symptoms: glutamate re-uptake impairment in vACC, and reduced serotonin levels network-wide. We find that these two disease mechanisms have different implications in terms of cognitive behavioral deficits and serotonergic treatment outcome. We propose that these differences, and others revealed by additional computational efforts, will contribute to a classification of depression subtypes that directly address the possible heterogeneity of mechanisms in this disease.

Keywords (5-10 keywords)

Anterior cingulate cortex, glutamate, working memory, prefrontal cortex, selective serotonin re-uptake inhibitors (SSRI)

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