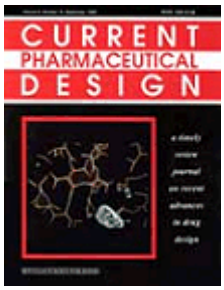

Role of Proinflammatory Cytokines in Dopaminergic System Disturbances, Implications for Anhedonic Features of MDD

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Anhedonia, characterized by a loss of interest and/or pleasure in previously enjoyable activities, is an important diagnostic criterion of Major Depressive Disorder (MDD). Converging evidence implicates a causal relationship between proinflammatory cytokines and behavioural disturbances that characterize anhedonia in the context of MDD. Additionally, anhedonia has been implicated in disturbances of key central dopaminergic modulatory pathways. Emerging research into the roles of tetrahydrobiopterin, a cytokine-targeted co-enzyme in the synthesis of dopamine, and kynurenine, a product of inflammation-sensitive breakdown of tryptophan via indoleamine 2, 3-dioxygenase, have shed new light into the role of inflammation in mediating anhedonic behaviours. The following narrative review is not meant to be comprehensive, but highlights the roles of both tetrahydrobiopterin and kynurenine pathways in anhedonia, and discusses a potential mechanism of action via oxidative stress and excitotoxicity. Treatment implications are discussed, with an emphasis on anti-inflammatories as complements to current treatments of anhedonia and MDD.

Keywords: Anhedonia; Major Depressive Disorder (MDD); cytokines; inflammation; kynurenine pathway; oxidative stress; tetrahydrobiopterin; treatment implications

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