



Preclinical Studies of Serotonin and Nitric Oxide in Affective Disorders

Gregers Wegener

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Affective disorders are among the most common mental disorders. In a society comparable to the Danish, it is estimated that 3-7% of the population at any given time meets the diagnostic criteria of affective disorders. The physician treating these diseases faces several problems, apart from diagnostic difficulties and side effects of the drugs. One serious problem is delayed clinical efficacy of pharmacological therapy. The period between the direct pharmacological effect and the clinical effects seems to characterize all known antidepressants to some extent. Another major problem is the partial response. Patients with both anxiety and depression respond differently and unpredictably to treatment. Only 60-70% of patients starting a pharmacological treatment will respond, and 5-10% will continue to be ill, despite of many different interventions. This underlines the need to understand the causal relationships in psychiatric disease so as to develop alternative strategies that are more universally effective. Fortunately, new possible disease mechanisms, and consequently possible therapies for neuropsychiatric disorders have been in focus in recent years. One of these areas deals with the signaling molecule Nitric Oxide (NO). Thus, compounds inhibiting the NO synthase enzyme (NOS) and which have been used as antidepressant treatment on an experimental basis. Concurrently, animal studies have suggested potent anxiolytic, antidepressant, and antipsychotic effects of selective inhibitors of NOS. As serotonin (5-HT) plays a central role in the existing treatment of affective disorders, we have in the present work examined some aspects of the possible interactions of NO with 5-HT, and the potential involvement of the NO signaling cascade in already established treatments.

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