A NEW PHARMACOLOGICAL STEP: THE MELATONERGIC APPROACH

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A breakthrough has recently been made in antidepressant research with the development of agomelatine. Agomelatine has a distinct pharmacological profile compared with all other classes of clinically available antidepressants.
Agomelatine is a high-affinity agonist at both the melatonergic MT_1 and MT_2 receptor types, and, in addition, blocks 5-HT_{2C} receptors. Agomelatine did not significantly bind to any other site studied. In accordance with this profile, agomelatine resynchronized circadian rhythms and elicited a dose-dependent elevation in extracellular levels of noradrenaline and dopamine in the frontal cortex of freely moving rats while exerting no effect upon serotonin levels. The antidepressant actions of agomelatine has been described in several validated animal models: learned helplessness, forced swim, chronic mild stress, mice with impaired glucocorticoid receptors, isolated aggressive mice, and the marble burying test, with antidepressant-like effects being shown in all behavioural paradigms examined. Based on these results, the nocturnal sleep pattern of psychosocially stressed male tree shrews (a valid animal model for depression) was investigated: agomelatine resynchronized disrupted circadian rhythms and antagonized the effect of stress on the total amount of rapid eye movement (REM) sleep and on the fragmented sleep pattern. In conclusion, the antidepressant efficacy of agomelatine may be due to its receptor profile, and it is hypothesized that melatonergic and 5-HT_{2C} receptors may be acting in synergy, thus representing a novel approach to treating depression.