SS01-01 - **A NEW WAY TO MANAGE DEPRESSION SUCCESSFULLY: RESTORING CIRCADIAN RHYTHMS**

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Depression is a complex disorder characterized by a disruption of brain functions and altered intracellular mechanisms. However, it is evident that none of the current hypotheses of depression (monoamine, hypothalamo-pituitary adrenal, and neuroplasticity), can explain all the effects of antidepressants. On the other hand, there is no doubt that each of these hypotheses affords important insights into the pathophysiology of depression.

One hypothesis in particular is the object of an increasing body of evidence: the circadian rhythm hypothesis of depression is based on the fact that (i) depression is very often associated with a disruption of circadian rhythms, and (ii) the severity of depression is correlated with the disruption of circadian rhythms, suggesting that resetting the circadian rhythms may play a pivotal role in the treatment of depression.

Agomelatine is the first melatonergic antidepressant acting as an MT_1/MT_2 melatonergic agonist and as a $5\text{-}HT_{2C}$ antagonist whose efficacy has been proven in several animal models of depression and in patients with major depressive disorder. These receptors are mainly present in the suprachiasmatic nuclei, but also in the hippocampus, prefrontal cortex, and hypothalamus.

Given the action of agomelatine through these receptors, it was important to establish to what extent agomelatine works through modulation or via synergic interaction between MT_1/MT_2 and $5\text{-}HT_{2C}$ receptors. Recent data show that only agomelatine (not melatonin or a $5\text{-}HT_{2C}$ antagonist) modulates the expression of neuroplastic genes (BDNF and Arc), suggesting that the intracellular events can be regulated through synergic activity between both melatonergic and $5\text{-}HT_{2C}$ receptors.

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