P01-73 - **THE NOVEL ANTIDEPRESSANT AGOMELATINE NORMALIZES HIPPOCAMPAL NEURONAL ACTIVITY AND PROMOTES NEUROGENESIS IN CHRONICALLY STRESSED RATS**

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Agomelatine is a melatonergic (MT1/MT2) receptor agonist and 5-HT_{2C} receptor antagonist with demonstrated antidepressant properties in animal models and in clinical studies. Several preclinical studies report agomelatine-induced effects on brain plasticity, mainly under basal conditions. Yet, it is important to unravel agomelatine-mediated changes in the brain affected by psychopathology. Since stress is implicated in the etiology of depression, it is valid to investigate antidepressant-induced effects in animals subjected to chronic stress. Here, we determined changes in the brain (hippocampal neuronal activity and neurogenesis) after agomelatine treatment in chronically stressed rats. Adult male rats were injected with BrdU (300 mg/kg i.p.), and 4 days later subjected to daily footshock stress and agomelatine (40 mg/kg i.p.) or vehicle (1% HEC) treatment for 21 days. Blood samples were taken in order to assess plasma ACTH and corticosterone levels. One day after the last stress exposure and agomelatine treatment, brains were collected and processed for immunohistochemistry. Rats exposed to footshock stress showed robust increases in ACTH and corticosterone, which were not influenced by agomelatine treatment. Chronic agomelatine therapy normalized the reduced c-Fos expression in the hippocampal dentate gyrus observed after chronic stress exposure. Moreover, agomelatine enhanced hippocampal cell proliferation and survival in stressed but not in control rats. Furthermore, agomelatine reversed the stress-induced decrease in doublecortin (a marker of newly-born immature neurons) expression in the hippocampal dentate gyrus. Taken together, these data show a beneficial action of agomelatine in the stress-compromised brain, where it restores stress-affected hippocampal neuronal activity and promotes adult neurogenesis.

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