PW01-22 - **AGOMELATINE TREATMENT REVERSES CHANGES IN NEUROPLASTICITY INDUCED BY PRENATAL STRESS IN RATS**

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The rat model of prenatal restraint stress (PRS) is particularly valuable to study the mechanisms involved in the pathophysiology of anxiety/depression since adult PRS rats show endocrine and behavioral abnormalities that are corrected by antidepressant medication. We have previously shown that agomelatine chronic treatment reversed the anxiety behaviour and decreased hippocampal neurogenesis observed in PRS. Here, we investigated the mechanisms that may contribute to the antidepressant activity of agomelatine, by assessing the effects of a chronic treatment with agomelatine on neurobiological markers of neuroplasticity in the rat hippocampus such as BDNF and its receptor, TrkB, the transcription factor pCREB and metabotrophic glutamate receptors (mGluRs). Adult SD control and PRS rats were treated chronically with agomelatine (40mg/kg ip) or vehicle. 16h after last drug administration, animals were sacrificed and hippocampus dissected for biochemical analysis.

PRS animals showed reduced levels of pCREB in the hippocampus and increased hippocampal BDNF, and TrkB receptor levels. Agomelatine reversed changes in pCREB and BDNF/TrkB levels in PRS rats, had no effect on pCREB in control rats, and, interestingly, increased BDNF and TrkB receptor levels in control rats. Moreover, agomelatine reversed the reduced expression (for mGluR5 and mGluR2/3 receptors) and function (for mgluR5 receptor) observed in the hippocampus of PRS rats.

In conclusion, we have shown that agomelatine treatment reversed all biochemical and cellular changes induced by PRS in rats. These changes, independently of their direction, are the expression of an enduring maladaptive form of neuroplasticity that may contribute to the depressive/anxious phenotype of PRS rats.

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