Modulatory activity of chronic treatment with the antidepressant agomelatine on LPS-induced inflammatory response in the rat ventral hippocampus: a genome wide analysis.

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Abstract

Given the large body of clinical and preclinical evidence suggesting that the activation of the inflammatory/immune system may contribute to depression pathogenesis, several studies reported that antidepressant drugs have immunoregulatory effects. Accordingly, the aim of the present work was to assess the anti-inflammatory properties of chronic agomelatine treatment with an unbiased genome-wide approach by using the well-established microarray technique. Adult male Sprague-Dawley rats received agomelatine or vehicle for 21 days before being challenged with an acute injection of LPS or saline 16h after the last drug administration. Animals were sacrificed 2h after the immune challenge and the ventral hippocampus was dissected and processed for microarray analysis.
The administration of LPS induced the transcription of genes mainly associated with the inflammatory response. Conversely, chronic treatment with agomelatine modulated 105 transcripts belonging to different signaling pathways such as the one of the phospholipase C and the pathway of the chemokine receptor CXCR4, which may contribute to potential neuroprotective effects of the antidepressant. From the transcripts found significantly modulated in the animals treated with agomelatine and challenged with LPS, the antidepressant was able to prevent the LPS-induced modulation of 91 genes with respect to the control group and of 52 genes with respect to animals treated only with LPS. An intersection analysis showed that some transcripts induced by LPS on which the pre-treatment with agomelatine has a large effect of normalization. In summary, we have highlighted the transcriptional profile of a chronic treatment with agomelatine in the rat ventral hippocampus both in basal condition and in condition of acute inflammation, identifying genes and pathways associated to its anti-inflammatory properties that might represent potential new targets for pharmacological intervention of depression associated to inflammation.