Short communication

Effect of lipopolysaccharide and antidepressant drugs on glucocorticoid receptor-mediated gene transcription

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Abstract:
It has been hypothesized that pro-inflammatory response and hyperactivity of hypothalamic-pituitary-adrenocortical axis (HPA) are involved in the pathogenesis of depression. Hyperactivity of HPA axis results probably from deregulation of glucocorticoid receptor function and impairment of the control mechanism of glucocorticoid secretion. Previously, we found that antidepressants inhibited glucocorticoid receptor (GR) function under the in vitro condition. In order to study a role of some mediators of pro-inflammatory response in this process, presently, we investigated the effect of lipopolysaccharide (LPS) on imipramine- or fluoxetine-induced inhibition of GR-mediated gene transcription in fibroblast cells, stably transfected with mouse mammary tumor virus promoter (LMCAT cells). Two days of incubation of the cells with imipramine (3–10 μM), fluoxetine (10 μM) or LPS (1 μg/ml) inhibited the corticosterone-induced gene transcription. Concomitant incubation of the cells with LPS and fluoxetine or imipramine had stronger inhibitory effect than that evoked by each compound alone. Moreover, we found that fluoxetine (10 μM) but not imipramine (3–10 μM) significantly inhibited the LPS-stimulated interleukin-6 (IL-6) production in these cells. These data suggest that pro-inflammatory agents facilitate antidepressant-induced inhibition of glucocorticoid receptor function.

Key words: glucocorticoid receptor, lipopolysaccharide, antidepressant drugs, interleukin-6