Effects of some new antidepressant drugs on the glucocorticoid receptor-mediated gene transcription in fibroblast cells

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Abstract:
Antidepressant drugs are thought to counteract effects of hypercortisolemia, frequently associated with depression, by lowering cortisol level and by modifying the function of glucocorticoid receptors (GR). Indeed, classical antidepressants inhibit corticosteroid-induced gene transcription in cell cultures. The aim of the present study was to investigate effects of new generation antidepressant drugs on GR function in mouse fibroblast cells (L929), stably transfected with mouse mammary tumor virus-chloramphenicol acetyltransferase (MMTV-CAT) plasmid (LMCAT cells). It has been found that reboxetine (at 10 and 30 µM), venlafaxine, citalopram and mirtazapine (at 30 µM), but not milnacipran, in statistically significant manner inhibited corticosterone-induced gene transcription. However, the effects of new generation antidepressant drugs were weaker than those evoked by imipramine, which was active already at 3 µM concentration. Further studies on the mechanism of antidepressant action on GR function revealed that protein kinase C, but not mitogen-activated protein kinases (MAPK), glycogen synthase kinase (GSK-3) and protein kinase B (PKB, Akt) play a role in this phenomenon.

Key words:
antidepressant drugs, glucocorticoid receptor-mediated gene transcription, protein kinase C