Imipramine prevents inhibitory effect of dexamethasone on SH-SY5Y cell proliferation

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Glucocorticoids have a significant role in neuronal cell death and an abnormal increase of glucocorticoid levels has been associated with atrophy of the hippocampus. On the other hand it has been shown that some antidepressant drugs could attenuate some glucocorticoid-induced changes in the central nervous system. The aim of the present study was to examine the effect of imipramine on dexamethasone (DEX)-induced changes in SH-SY5Y cell proliferation. The proliferation rates of the cells were measured using 3-[4,5 dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) and 5-bromo-2'-deoxyuridine (BrdU) assays. Imipramine was co-incubated with DEX (10 mM) in concentrations (0.1–5 mM) for 24 h. This antidepressant in low concentrations (0.1–1 mM) prevented inhibitory effect of dexamethasone on SH-SY5Y cell proliferation. To explore the putative intracellular signaling pathways implicated in the protective effect of imipramine we used protein kinase inhibitors: the mitogen-activated protein/extra-cellular signal-regulated kinase (MAPK/ERK1/2, PD98059 and U1026) and the phosphatidylinositol-3 kinase/Akt (PI3K/Akt, wortmannin). The inhibitory effect of imipramine on dexamethasone-induced decrease in cell proliferation was reversed by inhibitors of MAPK/ERK. Similarly, the western blot analysis showed that imipramine could prevent the decrease in active ERK1/2 kinase level evoked by dexamethasone.

In conclusion these results have shown that imipramine prevents the antiproliferative effect of dexamethasone in the SH-SY5Y cells. Moreover an involvement of MAPK/ERK1/2 in the effect of imipramine in the investigated cellular model has been demonstrated.

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The study of antinociceptive effect of 4-substituted derivatives of 5-(4-chlorophenyl)-2-(morpholin-4-ylmethyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione in mice

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In the present experiments the antinociceptive activity of 4-substituted derivatives of 5-(4-chlorophenyl)-2-(morpholin-4-ylmethyl)-2,4-dihydro-3H-1,2,4-triazole-3-thione was investigated. The difference in struc-
tures of obtained compounds is closely associated with the kind and/or number of halogens. Structures of the newly synthesized compounds were defined on the basis of the $^1$H NMR spectra. The antinociceptive activity was studied in mice in two behavioral tests: the hot plate test and writing test. Additionally other behavioral effects of animals, like locomotor activity and motor coordination were measured. We showed that all examined compounds possess antinociceptive activity without the impact on motor coordination. Two compounds significantly inhibited the locomotor activity of mice. The obtained results have shown that new compounds may possess a unique antinociceptive activity.

Lysophosphatidic acid analogues (LPA): oleoyl-sn-glycero-3-phosphate (L-$\alpha$-LPA) and 1-oleoyl-2-$\alpha$-methyl-rac-glycerophosphothionate (OMPT) affect uterine smooth muscle contractility of the pregnant pigs

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Experiments conducted on mice showed that the presence of lysosphosphatidic acid receptor (LPA$_3$) has an influence on the proper time of implantation and regular location of the embryos in the uterus. Increased expression of LPA$_3$ has also been observed in the porcine endometrium during perimplantation period and during pregnancy. The aim of the study was to define the role of the LPA and its receptor LPA$_3$ in the contractile activity of the porcine uterus during perimplantation period according to the presence of embryos in the uterine horns. The research was performed on pregnant gilts weighting 100–120 kg, in which one of the uterine horns was surgically closed to prevent the development of embryos in that horn. Myometrial tissue sections around 3–4 mm in length were collected from both (gravid and non-gravid) uterine horns. Sections were kept in 5 ml water bath with Krebs-Ringer fluid at 37°C saturated with carbon. After 60–90 min preincubation examined sections were stimulated with: a) OMPT – agonist of LPA$_3$ receptor in concentrations of: 68 nM, 136 nM and 680 nM, b) L-$\alpha$-LPA – agonist of LPA$_1$ and LPA$_2$ receptors in concentrations of $10^{-8}$ – $10^{-6}$ M. The contractile activity of the myometrium was assessed with the Hugo Sachs Elektronik equipment measuring the isometric contractions. It has been demonstrated that L-$\alpha$-LPA at a dose-dependent manner causes a significant increase of the myometrial tension of sections collected from the gravid uterine horn in the contrast to non-gravid horn, where these changes was not observed. Whereas, OMPT in used concentrations had a non-significant influence on the myometrial tension in the sections from gravid uterine horn and no influence on the myometrial tension in the sections from non-gravid uterine horn.