presence of sodium ions. Since these observations are not consistent and have been made using saturation binding methodology, we performed an autoradiography analysis using three different radioligands, i.e. [3H]spiperone, [3H]raclopride and [3H]quinpirole. Dopamine D2 receptor autoradiography was made on the naïve mouse brains. Mice were decapitated immediately after, as well as 3 days after forced swim test (FST). The highest binding was observed for [3H]spiperone in opposite to [3H]raclopride for which we observed only ~30% of specific binding as compared with [3H]spiperone. Only for [3H]raclopride and [3H]quinpirole we observed changes in specific binding immediately after FST. However, the character of changes was different for both radioligands. [3H]quiniprole revealed decrease, and [3H]raclopride – an increase in specific binding. Such result indicate the reduction of number of receptors in high affinity state upon acute stress. When experiments were made 3 days after FST, the specific binding returned to control level for both radioligands. Supported by grant DeMeTer (POIG.01.01.02-12-004/09; 3.6).

7. Synthesis and evaluation of new indole derivatives as aminergic GPCR ligands

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Aim: Developement of new series of indole and other priviledged structures derivatives as new aminergic GPCR ligands. Screening of active compounds towards 5-HT6 selectivity in the search of therapeutics and neuroimaging agents.
Methods:
Total synthesis, purity examination via LC-MS, NMR and elemental analysis. Structure determination via 1D and 2D NMR. Binding affinity measurement on a 96-well plate using appropriate GPCR-overexpressed HEK293 cells and specific radioligands. CNS screening for alpha-1 and alpha-2C adrenergic, dopamine D3, muscarinic M1 and M5, serotonine 5-HT2C and 5-HT3 done by CEREP.
Preliminary results:
Series 1:
Very high binding affinity for 5-HT6R (Ki = 2-14nM) and selectivity over D2, 5-HT1A, 5-HT7 in the range of 9 to 574 fold. Low affinity towards adrenergic and muscarinic receptors.
Series 2:
Compounds contain iodine atom which can be substituted with 127I; binding affinity for 5-HT6R Ki<50nM.
Acknowledgements:
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8. Acute and chronic administration of glucocorticoids affect expression of glucocorticoid receptor and target genes in astrocytes *in vitro*

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Chronic stress associated with glucocorticoid (GC) hormone release has been linked to development of mood disorders such as depression. Alterations in both astrocyte numbers and astrocytic genes' expression were reported in animal models of chronic stress and in brains of depressed patients. We have previously shown that astrocytes are a major target of acute GC action in the central nervous system through glucocorticoid receptor (GR)-mediated transcriptional response, while the effects of chronic stimulation remain unknown. Here we treated murine astrocytes with GR agonist, dexamethasone (DEX). Single short exposures to DEX (5-30 min) resulted in a rapid accumulation of GR protein, followed by upregulation of GR target gene proteins SGK1 and FKBP5 at longer times, corroborating earlier results of mRNA analysis. Repeated DEX treatments resulted in a significant attenuation of induction of GR targets, suggesting that chronic glucocorticoids may affect GR not only in neurons, but also in astrocytes, which could contribute to astrocytic alterations under chronic stress. [This work was supported by grant 2011/03/B/NZ3/01683 from National Science Centre].