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MEETING ABSTRACT

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Changes in rat brain expression of calcyon, after chronic or acute imipramine treatment: evidence of time-dependent sensitization

Maciej KUŚMIDER*, Agata FARON-GÓRECKA, Joanna SOLICH, Paulina PABIAN, Dariusz ŻURAWEK, Magdalena KOLASA and Marta DZIEDZICKA-WASYLEWSKA

Department of Pharmacology, Institute of Pharmacology, Polish Academy of Sciences, Kraków, Poland

The current axiom in psychopharmacology states that repeated treatment with antidepressants lasting at least several weeks is required for clinical response. This axiom follows the so-called steady state paradigm: a psychoactive drug needs to saturate its target receptors to exert its activity in the brain. Some authors, among them members of our laboratory, have reported phenomena called time-dependent sensitization (TDS). It is a unique property of the central nervous system to respond to a single stressful event after a prolonged response-free time. In case of antidepressant drugs (ADS), it turned out to be true for some biochemical changes reported so far only after repeated treatment with ADS. Such data lead to the concllusion that at least some biochemical changes observed after chronic treatment with antidepressants may occur not due to repeated treatment, but because of time passing since the first drug exposure.

Calcyon is a cellular protein initially reported as one of the dopamine receptor-interacting proteins (DRIPs). Later it turned out that it interacts with distinct elements of the endosomal and synaptic scaffolding machinery. Electrophysiological and cell-biological studies indicate that its integration with the vesicle-trafficking system is required for synaptic plasticity, as well as for transcytosis and targeting of axonal cargos. Therefore it was interesting to investigate whether changes (in the TDS paradigm) are related only to dopamine receptors or to other elements of signaling pathway as well.

We examined the expression of calcyon after chronic and acute imipramine (IMI) treatment, as well as during 3 weeks of that treatment's discontinuation. Wistar male rats were treated with IMI (10 mg/kg, i.p.) or saline (2 ml/kg, i.p.) for 20 days. On the 21st day some animals, treated previously with saline, received an acute dose of IMI (10 mg/kg). Then, the 3 weeks discontinuation phase began, during which, at certain time points (3 h, 72 h, 7 days, 21 days), a number of animals were sacrificed and the tissue was collected. In these brains the expression of calcyon mRNA (*in situ* hybridization) was measured. Chronic IMI treatment increased the expression of calcyon in certain basal ganglia. Similar effects were observed at some time points during discontinuation. The results will be presented with detailed time and anatomical resolution.

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*Submitting author e-mail: *kusmider@if-pan.krakow.pl*

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