

Dissertation thesis supervisor's report for Pascal Michel Samir Jorratt Callejas in Neuroscience doctoral study program

Thesis title: Effects of endogenous NMDA receptor modulators on neuronal morphology and synaptic plasticity

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In his thesis, Pascal Jorratt investigated the effect of NMDA receptor neuromodulators on synaptic plasticity in primary cell cultures and changes in the expression of key elements involved in the regulation of synaptic plasticity. Specifically, the neuromodulators Kynurenic acid, Pregnenolone sulfate, Spermidine and Zinc Chloride were tested. Their potential therapeutic effects were additionally tested in an animal model of depression, specifically the Chronic Despair model in mice. The student developed all experiments independently, partly in the NIMH laboratories, and partly as part of an internship at the University of Freiburg.

The thesis has the classic structure of a comprehensive research report. In the introduction, he describes the NMDA receptors and their role in the pathophysiology of selected mental disorders, then he describes in detail the different groups of neuromodulators and their potential relevance to the pathophysiology of mental disorders and possible therapeutic implications. Subsequently it delineates the main objectives and describes the methodological procedures in detail and with precision. The whole work is supplemented by detailed diagrams of the action of neuromodulators on the synapse with illustrations of the mechanisms that play a role in synaptic plasticity.

The main result of the study is the finding that of all the neuromodulators studied, pregnenolone sulfate appeared to be the most active in inducing synaptic plasticity at glutamatergic synapses, while the opposite effect was observed at inhibitory GABA neurons. In an animal model of depression, pregnenolone sulfate had a moderate anxiolytic effect, however, in other tests targeting both sociability and depression, the effect was not demonstrated.

The entire work is thoroughly researched, and documents the student's above-average abilities. I can state that it has been an honor to guide such an exceptionally talented student on his path of graduate study. As supervisor, I enthusiastically recommend his dissertation for the PhD degree in the Neuroscience PhD program.

In Klecany 21.03.2024

MUDr. Tomáš Páleníček, PhD.

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