

Oponentský posudek na práci

Research on ghrelin mechanisms for the prevention of relapse in cannabinoid addiction

autora

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The thesis consists of three parts: introduction, theoretical part and experimental part. In the introduction and theoretical part, addictions are defined, then there are described endogenous and exogenous cannabinoids and their receptors, the problems associated with the use of natural and synthetic cannabinoid derivatives, the reward system in the brain, the role of ghrelin and the methodologies used (IVSA and CPP).

This part of the thesis has some formal shortcomings, in particular repetition of information, skipping from one topic to another, limiting the text mostly to statements without attempting to explain the issues in depth, not progressing from general to detailed, from the known to the new, etc.

The core section of the thesis can be found in the third, experimental part. The hypotheses are stated at the beginning and then we find the traditional structure of a research paper: methodology, results, discussion and conclusion. In the results we learn the unique and promising results: i) the systemic pretreatment with the JMV2959 reduced the WIN55,212-2 intravenous self-administration and the tendency to relapse/ drug-seeking behavior, ii) systemic pretreatment with acyl-ghrelin enhanced the WIN55,212-2 induced IVSA and seeking behaviors, iii) co-administration of JMV2959 together with acyl-ghrelin reduces the ghrelin antagonism effects on the WIN55,212-2 induced IVSA, iv) WIN55,212-2 intravenous self-administration model confirmed the cannabinoid reinforcement effects in comparison to the saline self-administering group of rats, v) the JMV2959 pretreatments during the IVSA experiment did not significantly influence the body weight and vi) the GHS-R1A antagonist JMV2959 reduced the tetrahydrocannabinol (THC)-induced conditioned place preference expression as well as development.

The experimental part of the work, on contrary to introduction, passes the criteria of the strictest evaluation of scientific work. All the information presented is relevant, well-structured and well written, the methodology is detailed, supplemented with diagrams, the results are well written and documented with graphs, the discussion interprets and compares all the results obtained. From a formal point of view, it might have been useful to link the results more closely to the hypotheses or to replace the significance markers in the graphs with lines.

The thesis is written in English, I do not dare to evaluate the level of the text, but I dare to say that the text has not been revised by a native speaker. The text contains a minimum of typos.

Questions to the author:

1. Explain the comparison of the body-weight between the food-limited groups when both groups ate everything without rest? Could this have affected the results given the role of ghrelin in food intake and addiction?
2. Based on what work can it be argued that JMV2959 shares a receptor with acyl ghrelin? Further, is there any physiological rationale for a pro-addictive function of ghrelin?

Conclusion:

The paper is based on one large publication, which contains many results from long-term research, and seven other publications by the author on the subject of addiction and its treatment. All of these papers have been published in prestigious journals and demonstrate the scientific erudition of the author. Since my complaints concern only the formal treatment of the introductory part of the thesis and the experimental part is written at a high scientific level, I clearly recommend the thesis for defence.

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