Review of Ph.D. thesis THE ROLE OF STRIATAL CHOLINERGIC SIGNALING IN CONTROL OF BEHAVIOUR by Alice Abbondanza

The Ph.D. thesis results from a collaboration between the Institute of Physiology of the CAS and the Sorbonne University. The support of two scientific teams and the supervision of two renowned scientists made it possible to carry out an ambitious and methodologically diverse project, leading to numerous interesting findings.

First of all, I have to mention that I have reviewed the thesis for an internal defense held at the Institute of Physiology CAS. Thus, my work now was to check whether my previous concerns have been addressed and double-check if I have not missed any other potential shortcomings. In addition, part of the thesis (aimed at striatal nicotinic acetylcholine receptors) has already been published in a high-rank journal and thus underwent a rigorous peer-reviewing process.

Formally, the work is classically structured. It includes an Introduction, Aims, Methods, Results, Discussion, and Conclusion. The introductory section captures all the essential aspects needed to understand the work. I appreciate the inclusion of eight illustrative pictures, mostly pertaining to neuroanatomy, making the complex topic of the cholinergic system more accessible.

The thesis includes a clearly stated General aim and a general hypothesis that is further elaborated into five specifically defined objectives. Three of them are related to the striatum, and two of them to the prefrontal cortex. In the point 1.c, I would prefer to add in which context the c-Fos expression was measured (amphetamine challenge).

Methods and results are described in sufficient detail. I have just a few minor comments. Figure II-2 seems to be a graphic work done by the author. If not, then a citation needs to be included. When describing the elevated plus maze paradigm, the size of the apparatus and height of the walls should be indicated, as these parameters largely affect animal anxiety.

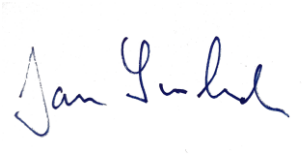
I am satisfied that all concerns related to the length and content of the Discussion were addressed after the first revision of the thesis.

As I have already concluded in the internal defense review, I was impressed by the amount of work and complexity of the approach. I appreciate that it honestly describes not only numerous results but also a few failures or constraints that were encountered. I find the thesis to be at a high scientific level, providing important insight into the function of nicotinic receptors in the brain. Alice Abbondanza fully proved her competence to independently perform state-of-art methods and discuss the results in a comprehensive way. I am genuinely glad I can recommend awarding her a Ph.D.

I have the following questions:

1) In auditory cortex, it has been described that number of NPY-positive neurons is increasing during aging. Is similar phenomenon observed in the prefrontal cortex?
2) Fig III-7. Please could you comment on the regional specificity of the spreading of the AAV-Cre-GFP virus? It seems there are few extrastriatal sites expressing GFP.
3) What results presented in the thesis do you find the most unexpected?

Prague, May 22, 2023



RNDr. Jan Svoboda, Ph.D.
Department of Neurophysiology of Memory, Institute of Physiology CAS