Comment to the article N. Dahmardeh et al. **Fingolimod attenuates harmaline-induced passive avoidance memory and motor impairments in a rat model of essential tremor**

I have read, with great interest, the article entitled "Fingolimod attenuates harmalineinduced passive avoidance memory and motor impairments in a rat model of essential tremor".

In this study, the authors constructed a harmaline-induced tremor model in rats, which has been extensively used as an animal model for essential tremor (ET) [1]. Interestingly, the authors have also found that harmaline can cause cognitive disturbances by using passive avoidance test. Therefore, it is indeed an ideal model to study the effect of fingolimod on cognitive deficits associated with ET. The authors' results demonstrated that pretreatment with fingolimod could ameliorate harmaline induced tremor, motor dysfunction as well as cognitive impairment, which is exciting. The authors should be congratulated for their laboratory findings on a topic not fully explored.

However, there are two main limitations noted in this article. Although the authors documented that fingolimod was administered (1 mg/kg) intraperitoneally 24 h before harmaline injection, it was not clear how the authors had decided the dosage. Using different doses would better determine the efficacy of fingolimod on ET-associated cognitive deficits. Another issue would be that tremor intensity. motor impairment and passive avoidance memory were evaluated at only one time point (30 min after harmaline injection). It would be of particular interest to know how long the positive effect of fingolimod on harmaline induced tremor and cognitive impairment would last. As shown in other articles, efficacy of specific treatments on

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harmaline induced tremor was tested at multiple time points [2,3].

Literatura

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3. Nahab FB, Handforth A, Brown T et al. Octanoic acid suppresses harmaline-induced tremor in mouse model of essential tremor. Neurotherapeutics 2012; 9(3): 635–638. doi: 10.1007/s13311-012-0121-1.