

### **Editor's Comment:**

My recommendation is rejection.

Although authors responded correctly the referees' queries, the manuscript still need a lot of reflection and work. Inclusively, the manuscript contains some typewriting mistakes and there are very long paragraphs that do not contain any bibliographic reference.

The main problem with this manuscript is the discussion section. It is true that the rationality of the study, the experimental design, the analysis of data are very well conducted. However, the interpretation of data is poorly supported by existing data; consequently, the conclusions seem very weak and poorly supported by their own data and even by the existing bibliography.

The core problem is the model used. Reserpine acts not only in monoamines and catecholamine depletion, but in other systems (e.g. adenosine). Reserpine was largely used to the treatment of arterial hypertension and as a major tranquilizer, later discontinued in many countries due to its collateral actions, mainly depression. It is true, but also is true that reserpine exerts many other actions not considered by authors which should discuss in order to support the validity of the model used.

For example, the high dose used by authors implies the control of other cardiovascular variables, for example, since it is not clear the exact reason of the behavioral actions reported by authors. Other authors use reserpine as a model of Parkinson disease; also, reserpine may produce a hyper reactivity of dopamine system, probably related with its dyskinesia-like actions. In summary, reserpine exerts many actions, but in no manner it may be considered as a pure model of depression. These aspects should be discussed in the manuscript.

Finally, looking carefully the graphics and the corresponding texts, it is clear that in no one case the pharmacological interactions of reserpine with the other treatments are comparable with the non-treated control group. It does with reserpine, representing solely a reduction of actions of reserpine, but not any clear antidepressant action.

It should be better to assume that the treatments reduce the actions of reserpine but in no manner represent some antidepressant action.

### **Editor's Details:**

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