OPEN PEER REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-19-00051
Title: Modulating neuronal plasticity with choline
Reviewer's Name: Giacinto Bagetta
Reviewer's country: Italy
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COMMENTS TO AUTHORS

The long description of the list of biochemical and neurochemical effects of choline on phospholipis and neutransmitter metabolism, neuronal membrane structure and function as well as preclinical evidence of cognitive improvements seem to guide the Author to conclude for enclosure of "choline as a non-invasive and inexpensive means to modulate neuronal plasticity for the improvement of cognitive function, or in the treatment of neurological disorders". This conclusion is misleading for the reader; in addition, it is representative of a simplistic approach to the problem the Authors have used. In fact, they omit the most important question of the use of choline that is: Is there clinical evidence for efficacy and security of choline use in the therapy of neurological disorders characterized by cognitive dysfunction? The answer is no. Actually, the evidence accumulated since the last 40 years indicate that choline for up to 16 g per day for two or more weeks does not affect normal or pathological cognition. Accordingly, this referee would like to suggest for the Authors to incorporate clinical negative evidence in their article to make it clear that the use of choline is out of an evidence based medical use, cannot be found in any therapeutic guidance and it is unlikely to produce a measurable cognitive improvement even when assumed as nutraceutical.