Review of: "The α7 Nicotinic Acetylcholine Receptor: a Key Molecule in Post-COVID Syndrome?"

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Potential competing interests: No potential competing interests to declare.

This is an interesting minireview that summarizes published as well as unpublished evidence in support of a role the alpha7 nicotinic acetylcholine receptors (alpha7 nAChR) in Post-COVID Syndrome. The hypothesis is not novel and has been previously supported (as well as confuted) by other researchers. On the other hand, a new idea proposed by the author, based on the identification of anti-alpha7 nAChRs in mice immunized with a Spike peptide that has been shown to interact with these receptors is that alpha7 nAChR ligands could arise as antidiotypic antibodies that, by binding the alpha7 nAChRs, could contribute to long COVID. Unfortunately, one of the two reports by the author in support of this notion is not published yet. I think that posting it on a pre-print server would strengthen the author's argument. The same applies to the identification of anti-alpha7 nAChR antibodies in the blood of long-COVID patients (here no reference is provided, is this finding part of the submitted report?). Finally, the author should cite the report by Godellas et al (PNAS 2022) that experimentally tests and confutes the nicotinic hypothesis of COVID-19. Additionally, the report by O'Brien et al (J Biol Chem 2023), showing that the neurotoxin-like region of Spike can both activate and inhibit the alpha7 nAChRs depending on the subtypes should be discussed, as it has important implications for defining the role of these receptors in disease pathogenesis and for the proposed therapeutic targeting of the cholinergic system in long COVID.