The report by Sheeler is a well-written and thought-provoking article suggesting that activation of nicotinic cholinergic alpha 7 receptors (nAChRα7) after traumatic brain injury cannot only be used to suppress peripheral inflammation as we described, but may also promote slow-wave sleep (i.e. deep sleep). The author reviews experimental evidence by Ni et al. (2016) which indicated that stimulation of nAChRα7 activates GABAergic neurons within the thalamic reticular nucleus leading to slow-wave sleep, and proposes a link to a report by Morawska et al. (2016) indicating that slow-wave sleep is neuroprotective after TBI. It is well known that the pro-inflammatory cytokines IL-1ß and TNFα play a role in sleep regulation, with the symptoms of sleep loss (i.e. fatigue, impaired cognition, sleepiness) being mimicked by central application of TNFα or IL1β. Interestingly, central and systemic injections of IL-1ß and TNFα increase the time spent in non-rapid eye movement sleep (NREMS), of which slow-wave sleep is a component. This suggests that treatment with nAChRα7 agonists to reduce peripheral inflammation (i.e. reducing TNFα and IL-1ß levels) could have the unintended consequence of also reducing slow-wave sleep. However, as pointed out by Sheeler, central actions of nAChRα7 agonists may compensate for this effect by directly acting on the thalamic reticular nucleus to induce slow-wave sleep. Additional experiments to determine if systemically administered nAChRα7 agonists (or positive allosteric modulators) can induce slow-wave sleep and reduce axonal damage after traumatic brain injury would provide strong support for this interesting premise. To expedite translation of this strategy to clinical testing, experiments using FDA approved cholinergic drugs (e.g. Galantamine, an acetylcholinesterase inhibitor) could be carried out in TBI animals. The authors congratulate Ms. Sheeler on her insightful review of the literature and for providing an interesting avenue for future study.

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