PEER-REVIEW REPORT 1

Name of journal: Neural Regeneration Research
Manuscript NO: NRR-D-18-00262
Title: Nanometer ultrastructural brain damage following low intensity primary blast wave exposure
Reviewer's Name: Ubaldo Armato
Reviewer's country: ITALY
Date sent for review: 2018-04-26
Date reviewed: 2018-05-09
Review time: 13 Days

Your peer review comments will be published as an open peer review report. Do you agree to have your name included with the published article?
Yes

COMMENTS TO AUTHORS

The paper is undoubtedly of interest and clearly written. The topic is hot given the warlike attitude of the human kind. Clarification of hidden and late human costs of using explosives of many kinds is critical particularly if brain damage is involved. I think the paper is to be published and have suggested some topics to be added to make its strength greater.
This is an interesting manuscript addressing a very actual topic given the several ongoing frank and hidden wars and the warlike behaviour of a lot of people. The standardised animal model is an achievement indeed and can reveal aspects of brain injury that have so far gone unnoticed though having later significant clinical consequences. However, they should also mention that the human brain is very different from the rodent one from several standpoints like dimensions, weight, extent of the cerebral cortex, cell types, cell numbers, different behaviour of astrocytes and neutrons when confronted with noxious physical or chemical agents, etc. Hence studies concerning the brains of those exposed to exploding devices are also very important and should be aimed at.
The authors should also consider some aspects they do not mention maybe because of space limitations: what might be the effects of the continuous use of firearms for training, for war or police actions, particularly big caliber automatic firearms (.357, .380, .450, .500, etc.)? And what about the use of explosives for civil purposes? And what about the effects of potentially or actually neurotoxic compounds released from explosives, be their amount small (bullets) or big (artillery shells, fragmentation bombs, rockets, etc)?
I appreciate the demonstration by TEM of actual explosive-induced damage of myelin sheaths and mitochondria. However, the authors should give a greater relevance to biochemical damages which are very likely to go beyond the release of ROS. The authors did not find any trace of necrosis in the animal brains. However, I ask: "did they look for cell apoptosis"? Apoptosis is very quick to be executed and hence leaves nearly no traces but requires hours to be prepared. Hence, apoptosis is easily missed if not looked for specifically. Neuronal apoptosis could be one of the causes of later appearing behavioural abnormalities. The damaged mitochondria are known to release apoptosis-promoting proteins like cytochrome C, AIF (apoptosis-inducing factor), Smac/Diablo, etc.