Dear Sir or Madam,

Thank you very much for your review and the comments, which were very valuable to us for the revision. We have tried our best to revise the text according to the suggestions and indicated the issues we addressed with red font in the body of the article. Please find more detailed answers to your questions below, together with an extended list of references. We hope that the revisions are satisfactory.

Reviewer 1

QUESTION 1. Astrocytes in the central nervous system and their roles in health and disease: a review, by Lidija Gradisnik, Tomaz Velnar. The authors review a topic of increasing relevance: astrocytes, and the growing evidence of their new functions in both physiological and pathological conditions. The chosen subtopics are appropriate and the references are consistent with the review.

ANSWER 1. Thank you for this review.

QUESTION 2. Major concern. Despite the correct review, it is superficial and there are no suggestions and/or discussion on the edge of current knowledge of each subtopic. As an example of this point of view, they should delve into the pathophysiology of astrocytes under conditions of hyperammonemia. As P. Souto et al., WJG, 2016, reviewed hyperammonemia hepatic encephalopathy, astrocytes are the target cells. They induce severe changes such as: cell death, cell damage, changes in energy metabolism, neurosteroid synthesis/peripheral-type benzodiazepine receptor, neutrophil activation, changes in membrane potential, increased intracranial pressure, pH change, NMDA/cGMP, astrocyte morphology, inflammation, changes in the release of neurotransmitter systems, receptors and transporters, oxidative/nitrosative stress, altered intracellular calcium signalling, modification of cerebral blood flow, changes in mRNA and protein expression, mitochondrial dysfunction. Type II astrocytes (Type II Alzheimer's) was Noremberg's first description in humans, and a wealth of data has since become available on this interesting and challenging topic involving astrocytes.

The whole point of this reviewer is please authors dig deeper into this amazing topic, you need to review current astrocyte data to be aware of what's going on.

ANSWER 2. Thank you for this suggestion. We have supplemented and revised the parts of the article with the subject of hyperammonemia and cited the recommended work. We have also added the astrocyte types, their main differences and functions, as well as the differences between adult and neonatal astrocytes, so we went deeply into the topic, as advised in the review report.

In addition to trauma per se (i.e., brain injury), various nervous system disorders such as metabolic disorders (hyperammonemia and hypoglycemia), ischemia, hypoxia, and epileptic seizures are associated with astrocyte swelling. In particular, hyperammonemia is of great interest with regard to astrocytes [64]. Hepatic encephalopathy, which occurs as the main complication of acute or chronic liver failure, is the clinical consequence of increased ammonia concentrations in the brain leading to cerebral dysfunction [65, 66]. In clinical practise, it is recognised as a spectrum of neuropsychiatric and neurologic symptoms ranging from minimal abnormalities such as attention and memory deficits to seizures, cerebral edema, intracranial hypertension, coma, and death. Hyperammonemia in the brain is associated with disturbances in cerebral metabolism and leads to a cascade of secondary effects and encephalopathy. An important morphological feature of hyperammonemia is Alzheimer-type astrocytes II [64-66].

Hyperammonemia, like other traumatic and metabolic disorders of the nervous system, is an uncontrollable condition. These patients may experience marked alterations in extracellular ion concentrations, including decreases in Na+, C1-, and Ca2+, increased K+ concentration, decreased extracellular pH, and accumulation of excitatory neurotransmitters. This can lead to various changes in astrocyte function, protein expression, and morphology [2, 53]. Reactive astrocytes in the adult brain, which are generated in response to injury and then plated in culture, re-express some markers of developing astrocytes, including genes for DNA binding, apoptosis, cell cycle regulation, cell adhesion, cytoskeleton and extracellular matrix formation, and genes for signal transduction. Normally, adult astrocytes express more genes for metabolic enzymes than neonatal astrocytes [1, 18]. The most striking morphological change is the swelling of astrocytes, which is reversible, and the morphology changes as soon as the cells are placed in culture [2, 7, 42, 53].

Corrections, The response of astrocytes in various central nervous system insults, page 11:

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Reviewer 2

QUESTION 1. An interesting manuscript, but it does not correspond to the mini-review format because it has a small amount of information (40 references).

ANSWER 1. The references have been added.

QUESTION 2. I consider it necessary to add modern material on the topic of genetic polymorphism astrocytes - their role in pathology. After revision and updating, the manuscript can be recommended for publication in this journal in the format of a mini-review.

ANSWER 2. Thank you. The text was revised. The references were added, as well as the questions raised by reviewers. These additions are marked in red font in the body of the article.