Reviewer's report

Title: Changes of tau profiles in brains of the hamsters infected with scrapie strains 263K or 139A possibly associated with the alteration of phosphate kinases

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Reviewer: Giorgio Giaccone

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Despite intensive research, the cellular and molecular mechanisms by which tau builds up in the neurons in some neurodegenerative conditions remain uncertain. This paper from Wang et al demonstrates an increase of total tau and changes of profiles of phosphorylated tau in the brain of scrapie-infected hamsters. This is an intriguing observation that could suggest that tau abnormalities are more common than previously thought in prion diseases. However, there are parts of the manuscript that are not very accurate and I may suggest some points that should be addressed to improve the paper.

Minor essential revisions
First page of background: “Aggregation of tau ......(AD) patients [5]. This sentence is not well formulated.
Two lines below: remove “probably”
Following pages; line 6: Shelton et al should be converted to a number
Last page of background: regarding the sentence “In the brain tissue of GSS........mouse model of vCJD [16]”, a more appropriate reference for tau pathology in GSS brain is Ghetti et al (Brain Pathology 1996;6:127-145).

In the material and methods, it appears that infected animals were analyzed at 20, 40, 50, 60, 70 days. Is this true also for 139A infected hamsters that have incubation time of 395 days?
The numbers of the animals studied (different groups and different ages) should be specified.
In the Real time reverse transcription PCR section, sence and antisence must be corrected
The manuscript can be shortened: for example, in the results section, parts of the methods are reiterated.
In the paragraph “Lower level of GSK3.....” I would substitute “obviously” with “clearly”, if this is the meaning.

At the beginning of the discussion, a reference should be provide for the Amyloid cascade hypothesis and it should be reminded that it is an hypothesis, even if the most widely accepted at present.
Again, the reference about NFT in GSS is not the most appropriate and the above mentioned one should be added.

What the authors intend stating that tau is an “ubiquitous expressed protein”? Should it be possible to complete with immunohistochemistry, at least in a subset of animals? If not, it must be acknowledged in the test that this is a limitation of the study.

And to verify whether tau in scrapie has some of the pathologic characteristics of tau in AD (insolubility, protease resistance)? Again, if not, it must be acknowledged in the test that this is a limitation of the study.

Discretionally revisions and comments

More appropriate control animals would have been hamsters intra-cerebrally inoculated with normal brain homogenate.

The authors should make an attempt to provide some hypotheses about the possible link between prion pathology and the derangement of tau phosphorylation.

I would also try to find a more attractive title.

**Level of interest:** An article of importance in its field

**Quality of written English:** Needs some language corrections before being published

**Statistical review:** Yes, but I do not feel adequately qualified to assess the statistics.

**Declaration of competing interests:**

I declare that I have no competing interests