Reviewer's report

Title: Evidence for Synergistic Effects of PRNP and ATP7B Mutations in Severe Neuropsychiatric Deterioration.

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Reviewer: Grazyna Gromadzka

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Authors present results of their observations on distinct phenotypic features of Wilson’s disease among siblings with the same genotype of ATP7B, but different genotype of PRNP. Carriership of the PRNP c.160G>A variant allele seems to be related to severe neuropsychiatric decline.

Authors propose that synergism may occur between at least some allelic variants of ATP7B and PRNP, possibly exerted through effects on cellular copper metabolism.

It is a very interesting hypothesis. The manuscript is well written. Unfortunately, drawing conclusions based on observations of only two family members is difficult. In most previous studies different WD phenotype was observed among patients possessing the same mutations of ATP7B, including family members and even monozygotic twins. Authors should acknowledge it as a limitation of their study.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: No, the manuscript does not need to be seen by a statistician.

Declaration of competing interests:

I declare that I have no competing interests