Reviewer's report

Title: Associations of genetic variation in CASP3 gene with noise-induced hearing loss in a Chinese population: a case-control study

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Reviewer: Xiangrong Xu

Reviewer's report:

Comment 1: I suggest to check plagiarism and revise the sentences in all the text, especially in the abstract, method and conclusion.

Comment 2: Please specify if there is a quality criterion for genotyping error rate per patient and per SNP?

Comment 3: Some remarks to subjects recruitment. As usually, the noise-exposed subjects with average of binaural HL in high frequency > 40dB indicates hearing loss, which is a precondition of diagnosis of occupational noise-induced hearing deafness. So, why this study use the definitions of case as "the average of binaural HL in high frequency > 25dB"?

Comment 4: Control have normal hearing. I suppose, that low frequency hearing loss in study group was excluded? I suppose that non-occupational reasons of hearing loss (mainly in high frequency) were also excludes (e.g. tumors, autoimmunological diseases and others). But the author take some non-occupational reasons (listen to music, telephone using and sleeping later) as the risk factors of NIHL, it is not reasonable. Please explain it.

Comment 5: The Chinese Diagnostic Criteria of Occupational NIHL (GBZ49-2007) was abolished and the newset is GBZ49-2014. Please note it.

Comment 6: In the part "SNP selection and genotyping", the author selected SNPs according to "reported in previous studies", please cited the references.
Comment 7: The author was suggested to performed Bonferroni correction to control for multiple testing.

Comment 8: Table 1. Noise intensity means noise Lex8h measured during the experiment? Dose CNE was calculated using this value and years of employment? But if the worker was employed at several workplaces which varied with the exposure during the whole-life? It is not clear to the reader how cumulative noise exposure is defined, please add the calculation method of CNE in the method.

Comment 9: For noise is the most frequent cause of NIHL, I suggest to conduct stratified analysis by noise intensity and CNE.

Comment 10: In order to further analyze, the authors are suggested to analyze the effects of haplotypes of associated SNPs on NIHL and/or the interactions between SNPs.

Comment 11: The discussion is too long. Particularly, the paragraphs on the function of the candidate genes should be shortened, or at least move parts of it to the introduction.

Comment 12: Please explain all abbreviations in the text and in the abstract.

Comment 13: Replication of the results is needed and could be included in this section.

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Please indicate how interesting you found the manuscript:

- An article of limited interest

**Quality of written English**

Please indicate the quality of language in the manuscript:

- Not suitable for publication unless extensively edited
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