



Letter to the editor

Reply to Josef Finsterer's letter referring to "Connectivity on fMRI in the MELAS brain may strongly depend on heteroplasmy and extension or dynamics of stroke-like lesions"

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Dear Editor

We are grateful for Dr. Finsterer's comments on our article entitled "Connectivity on fMRI in the MELAS brain may strongly depend on heteroplasmy and extension or dynamics of stroke-like lesions" and would like to take the opportunity to answer his interesting comments.

1. fMRI is an imaging technique that indirectly reflecting the activity of neurons (Logothetis, 2008), which mainly associated with gray matter. Thus, regression of white matter signals is a standard data analysis step in fMRI studies to attenuate the interference of this nuisance variable to the BOLD signal of gray matter.
2. In our study, the MELAS patients at chronic stage (within 6–8 months after SLEs attack) were free from SLEs symptoms (Wang et al., 2020). Evaluated by radiologists and neurologists, the cortical SLLs at this period were stable without showing extension or dynamics. Thus, the distinction between acute and chronic SLLs is reasonable and our fMRI results are reliable as shown in our article.
3. In our article, we don't use "only" to claim that MELAS is due to the variant m.3243A>G in MT-TL1 and SLLs are characterized by cortical swelling, subcortical T2-hyperintensity, and cortical DWI hyperintensity.
4. Dr. Finsterer suggests that hearing impairment in MELAS is usually due to affection of the cochlea or the retro-cochlear acoustic nerve. In fact, the cause of hearing impairment in MELAS remains unknown. We think it is justified that hearing loss may be a manifestation of a

SLL, because it has been reported that lesions in the auditory cortex can lead to deafness (Gutschalk et al., 2015).

5. Other questions raised by Dr. Finsterer, such as the correlation between heteroplasmy rates, phenotypes and fMRI, the ability of rs-fMRI to delineate psychiatric disease from SLEs, the disturbed function of nodes improved upon NO- application and the comparison between expanding SLLs and regressing SLLs were interesting but beyond the scope of our present study. These questions will be addressed in future studies.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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<https://doi.org/10.1016/j.nicl.2021.102596>

Available online 15 February 2021

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