- 1 The authors present the results of a single center observational clinical study aimed to explore the performance in the walking trail making test (WTMT) performance in older people with white matter hyperintensities (WMH). The authors found that older adults with WMH showed poorer WTMT performance. WTMT could be a potential indicator for the cognitive and motor deficits in WMH patients. For a better presentation of the data, the following issues need to be clarified: 1. The authors should mention in the Introduction that signs of small vessel disease in conventional MRI include: recent subcortical lacunar infarcts (clinically symptomatic), white matter magnetic resonance hyperintensities, lacunes (clinically silent), prominent perivascular spaces, cerebral microbleeds and atrophy (Int J Mol Sci 2022; 23, 1497). See and include this supporting reference. Reply: Thank you for your recommendations. We have added this point and citation in revised manuscript.
- 2. Because cognitive impairment is an essential clinical feature of Binswanger's disease, I would suggest expanding the text in relation to the cognitive profile of white matter hyperintensities and neuropsychological features of subcortical vascular dementia (Expert Rev Neurother 2009; 9: 1201-1217). I suggest including it in the Discussion.

Reply: Thank you very much for your suggestion. As a matter of fact, in our study, we did not include patients with Binswanger's disease. Although we did not show in the manuscript the detailed data, there were few patients with typical pseudobulbar syndrome. Considering that the global cognitive function of the participants was almost unaffected (average MMSE score above 28.00), we could also conclude that we did not include patients with Binswanger's disease.

We totally agree with the reviewer's comments, and we believe that WTMT is suitable for evaluating cognitive function of white matter hyperintensities and neuropsychological features of subcortical vascular dementia. In the Discussion section, we have added new text describing our opinion about the future utility of the WTMT. In our next step, new studies would be launched to determine the performance of the WTMT in subcortical vascular dementia.

3. The authors should clearly point out in the text the relevance of clinically silent lacunes (as a major neuroimaging feature of cerebral small vessel disease) on cognitive performance. In a clinical study, more than half of the patients with a first-ever lacunar stroke had minor neuropsychological alterations. These minor alterations were mainly related to the presence of clinically silent lacunar infarcts on neuroimaging at this early stage of cerebral small vessel disease (see and add this reference BMC Neurol 2013; 13: 203). Did the authors consider in their study protocol the relevance of silent lacunes on cognitive performance?

Reply: Thank you for your comments. We agree with your opinion that clinically silent lacunes are a commonly found neuroimaging feature of CSVD. In addition, multiple lacunar infarcts are another potential cause of poor performance on the WTMT and other cognitive domains. In the current study, we only collected patients with pure WMH, and we did not recruit patients with silent lacunes. We have added this point in the MATERIALS and METHODS section.

Thank you once again. We would like to conduct another new study to determine the performance of the WTMT in patients with clinically silent lacunes.

4. A brief concluding comment on other possible lines of future research on the presented topic would be appreciated.

Reply: Thank you for your recommendation. We have added a new paragraph to discuss other possible lines of future research on the presented topic. Notably, the TMT has been modified in different ways by different research groups (e.g., WTMT, oral TMT<sup>[1]</sup>, driving TMT<sup>[2]</sup>), and, alternative evaluation systems for the TMT also have been reported (e.g., error analysis<sup>[3]</sup>, derived TMT indices<sup>[4,5]</sup>). From our point of view, delta TMT is a good indicator of executive function, which is commonly impaired in CSVD. Thus, delta WTMT might be another effective tool for detecting the cognitive profile of WMH and neuropsychological features of subcortical vascular dementia in the future.

## References:

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- 3. Mahurin RK, Velligan DI, Hazleton B, Mark Davis J, Eckert S, Miller AL. Trail making test errors and executive function in schizophrenia and depression. *Clin Neuropsychol* 2006; **20**: 271-288. [PMID: 16690547 DOI: 10.1080/13854040590947498]
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- 5. Hobert MA, Meyer SI, Hasmann SE, Metzger FG, Suenkel U, Eschweiler GW, Berg D, Maetzler W. Gait is associated with cognitive flexibility: a dual-tasking study in healthy older people. *Front Aging Neurosci.* 2017; **9**: 154. [PMID: 28596731. DOI: 10.3389/fnagi.2017.00154]