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Comment on “resting-state fMRI in Parkinson's disease patients with cognitive impairment: A meta-analysis”

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Dear Editor,

We have read with great interest the article in press in Parkinsonism and Related Disorders written by Wolters et al., entitled “Resting-state fMRI in Parkinson's disease patients with cognitive impairment: A meta-analysis” [1]. Resting-state functional magnetic resonance imaging (fMRI), a promising imaging technique to investigate brain functional reorganization, has been widely used in Parkinson's disease (PD) that has improved the current knowledge about the mechanisms underlying motor and non-motor symptoms [2]. One meta-analysis identified resting-state functional connectivity alterations within the corticobasal ganglia-thalamocortical motor network in PD [3]. However, functional connectivity alterations in cognitively impaired patients with Parkinson's disease (PD-CI) were not conclusive. For the first time, using the anisotropic effect size version of signed differential mapping (AES-SDM), Wolters et al. performed a voxel-based meta-analysis of 17 resting-state fMRI studies that investigated the resting-state functional connectivity alterations in patients with PD-CI compared with cognitively unimpaired patients with PD (PD-CU) or healthy controls [1]. This meta-analysis showed that cognitive impairment in PD was associated with brain functional connectivity alterations, predominantly in the default mode network [1]. We appreciate their work that contributes to understanding the neural basis of cognitive impairment in PD from the brain network level. However, some concerns could threaten the validity of their conclusions in this meta-analysis.

An important advantage of the AES-SDM approach is that it can perform several complementary analyses, such as sensitivity analyses, heterogeneity analyses, and publication bias analyses, to test the robustness of the results just like a standard meta-analysis [4]. However, Wolters et al. only conducted sensitivity analyses and publication bias analyses in their AES-SDM meta-analysis. Such analyses were not comprehensive. Heterogeneity analysis is crucial in any meta-analysis. Significant between-study heterogeneity cannot draw firm conclusion. We wondered whether significant heterogeneity existed in their meta-analysis. In case of significant heterogeneity, subgroup analyses and meta-regression analyses should be performed to explore its source among the included studies.

The meta-analysis by Wolters et al. investigated resting-state functional connectivity alterations in patients with PD-CI that included both PD with mild cognitive impairment (PD-MCI) and PD with dementia (PDD). It may be not an optimal way to pool PD-MCI and PDD studies directly as a whole for the meta-analysis. PD-MCI has been identified as a risk for PDD. However, not all patients with PD-MCI would progress finally to PDD. PD-MCI and PDD exhibit different degrees of cognitive impairment. Different pathophysiological substrates may underlie them. This meta-analysis would benefit from further conducting a subgroup analysis to determine the differences in functional connectivity between PD-MCI and PDD. If not, this meta-analysis should perform a meta-regression analysis to examine the effect of severity of cognitive impairment on functional connectivity alterations.

Previous resting-state fMRI investigations have suggested that brain functional patterns could be modulated by the medication states (ON and OFF) [5]. In the meta-analysis by Wolters et al., most of the included studies obtained brain MRI scans during the ON time, whereas some other studies during the OFF time. Hence, we suggest a subgroup analysis based on the medication states. In addition, Wolters et al. noticed variations in demographics and clinical characteristics across studies in their meta-analysis, such as age, severity of motor signs, and levodopa equivalent daily dose, as well as gender and disease duration that the authors did not mention. Further meta-regression analyses should be performed to examine such moderators’ effects on brain functional connectivity alterations.

In conclusion, as suggested by Wolters et al., their results are exploratory [1]. We brought to attention a few possible improvements to this meta-analysis that may strengthen the conclusions of the resting-state functional connectivity alterations in PD-CI.

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References

[1] A.F. Wolters, S.C.F. van de Weijer, A.F.G. Leentjens, A.A. Duits, H.I.L. Jacobs, M.L. Kuijf, Resting-state fMRI in Parkinson's disease patients with cognitive impairment: a meta-analysis, Park. Relat. Disord. 62 (2019 May) 16–27.
[2] M. Filippi, E. Sarasso, F. Agosta, Resting-state functional MRI in parkinsonian syndromes, Mov. Disord. Clin. Pract. 6 (2) (2019) 104–117.
[3] G.J. Ji, P. Hu, T.T. Liu, Y. Li, X. Chen, C. Zhu, Y. Tian, X. Chen, K. Wang, Functional connectivity of the corticobasal ganglia-thalamocortical network in Parkinson disease: a systematic review and meta-analysis with cross-validation, Radiology 287 (3) (2018) 973–982.
[4] J. Radua, D. Mataix-Cols, M.L. Phillips, W. El-Hage, D.M. Kronhaus, N. Cardoner, S. Surguladze, A new meta-analytic method for neuroimaging studies that combines reported peak coordinates and statistical parametric maps, Eur. Psychiatry 27 (8) (2012) 605–611.
[5] M. Tahmasian, L.M. Bettray, T. van Eimeren, A. Drzezga, L. Timmermann, C.R. Eickhoff, S.B. Eickhoff, C. Eggers, A systematic review on the applications of resting-state fMRI in Parkinson's disease: does dopamine replacement therapy play a role? Cortex 73 (2015) 80–105.

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