

# Resting-state fMRI in Parkinson's disease patients with cognitive Impairment

Citation for published version (APA):

Wolters, A. F., van de Weijer, S. C. F., Leentjens, A. F. G., Duits, A. A., Jacobs, H. I. L., & Kuijf, M. L. (2019). Resting-state fMRI in Parkinson's disease patients with cognitive Impairment: A meta-analysis: Answer to Wang and colleagues. *Parkinsonism & Related Disorders*, 66, 253-254. <https://doi.org/10.1016/j.parkreldis.2019.07.014>

## Document status and date:

Published: 01/09/2019

## DOI:

[10.1016/j.parkreldis.2019.07.014](https://doi.org/10.1016/j.parkreldis.2019.07.014)

## Document Version:

Publisher's PDF, also known as Version of record

## Document license:

Taverne

## Please check the document version of this publication:

- A submitted manuscript is the version of the article upon submission and before peer-review. There can be important differences between the submitted version and the official published version of record. People interested in the research are advised to contact the author for the final version of the publication, or visit the DOI to the publisher's website.
- The final author version and the galley proof are versions of the publication after peer review.
- The final published version features the final layout of the paper including the volume, issue and page numbers.

[Link to publication](#)

## General rights

Copyright and moral rights for the publications made accessible in the public portal are retained by the authors and/or other copyright owners and it is a condition of accessing publications that users recognise and abide by the legal requirements associated with these rights.

- Users may download and print one copy of any publication from the public portal for the purpose of private study or research.
- You may not further distribute the material or use it for any profit-making activity or commercial gain
- You may freely distribute the URL identifying the publication in the public portal.

If the publication is distributed under the terms of Article 25fa of the Dutch Copyright Act, indicated by the "Taverne" license above, please follow below link for the End User Agreement:

[www.umlib.nl/taverne-license](http://www.umlib.nl/taverne-license)

## Take down policy

If you believe that this document breaches copyright please contact us at:

[repository@maastrichtuniversity.nl](mailto:repository@maastrichtuniversity.nl)

providing details and we will investigate your claim.



## Correspondence

**“Resting-state fMRI in Parkinson's disease patients with cognitive impairment: A meta-analysis”:  
Answer to Wang and colleagues**


## ARTICLE INFO

## Keywords:

Parkinson's disease  
Functional MRI  
Cognitive impairment  
Functional connectivity  
Resting-state network

## Dear Editor

We would like to thank dr. Wang and his colleagues for their interest in our study. While the authors address important measures to assess the validity of a meta-analysis such as heterogeneity between studies, the pooling of Parkinson's disease (PD) patients with mild cognitive impairment (PD-MCI) and patients with dementia (PDD) and the ON or OFF state during scanning, it is important to recognize the need for sufficient power when performing subgroup analyses.

In this meta-analysis an extensive assessment of the quality of the included studies has been carried out. Furthermore, the anisotropic effect-size version of the signed differential mapping method (AES-SDM) was applied, which takes into account the effect sizes of the individual studies [1,2]. When performing a meta-analysis with fMRI studies, there is always a trade-off between study heterogeneity and the number of experiments that can be included [3]. An increased power is reached with the inclusion of a higher number of studies, but on the other hand one wants to aim for the highest homogeneity possible. A clear statement about the minimum amount of studies necessary for an fMRI meta-analysis is currently lacking and depends on several factors such as the sample size of the individual experiments and the expected effect size. However, some authors recommend to include at least 17–20 experiments [4]. Since our meta-analysis consists of a relatively limited amount of studies, with rather small patient groups, we chose to accept a certain level of heterogeneity between studies in order to prevent the sample size and the power from becoming too small to draw any reliable conclusions. Performing meta-regression and subgroup analysis for the discrimination of different cognitive profiles and the ON and OFF medication groups was considered while executing this meta-analysis. While the performance of a meta-regression analyses is important to confirm the clinical relevance of the results, the homogeneity of the outcome measures of the individual experiments was insufficient for this meta-analysis. Furthermore, we again argued that when performing subgroup analyses, the subgroups would become too small to draw any reliable conclusions. In fact, only 7 studies included patients with PDD and those patient groups were separately analysed from PD-MCI in only 5 experiments. In addition, 11 studies that compared healthy controls (HC) with PD patients with cognitive impairment (PD-

CI) have performed the fMRI while ON medication and 3 experiments carried out the fMRI while OFF medication. Only 4 experiments while ON medication and 2 studies in OFF medication states were carried out for the comparison of PD with and without cognitive impairment. It is of course well known that the use of dopaminergic medication influences the functional connectivity patterns of the brain [5]. Moreover, compensatory mechanisms and different pathophysiological substrates may indeed give rise to connectivity changes that are different for mild cognitive impairment and more progressed states of cognitive impairment [6,7]. In this study, no conclusions were drawn for connectivity changes in mild cognitive impairment as a clinical entity and the validity of our meta-analysis has been discussed. Future studies with methodologically homogenous data sets and larger sample sizes are important in order to map differences in functional connectivity. This meta-analysis indicates that the default mode network might be of significant interest in cognitive impairment in PD, which may be relevant for future studies on this topic.

## Declarations of interest

None.

## Funding sources for study

None.

## References

- [1] 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 : J. Assoc. Eur. Psychiatrists* 27 (8) (2012) 605–611.
- [2] J. Radua, D. Mataix-Cols, Meta-analytic methods for neuroimaging data explained, *Biol. Mood Anxiety Disord.* 2 (2012) 6.
- [3] V.I. Müller, E.C. Cieslik, A.R. Laird, P.T. Fox, J. Radua, D. Mataix-Cols, C.R. Tench, T. Yarkoni, T.E. Nichols, P.E. Turkeltaub, T.D. Wager, S.B. Eickhoff, Ten simple rules for neuroimaging meta-analysis, *Neurosci. Biobehav. Rev.* 84 (2018 Jan) 151–161.
- [4] S.B. Eickhoff, T.E. Nichols, A.R. Laird, F. Hoffstaedter, K. Amunts, P.T. Fox, D. Bzdok, C.R. Eickhoff, Behavior, sensitivity, and power of activation likelihood estimation characterized by massive empirical simulation, *Neuroimage* 137 (2016 Aug 15) 70–85.
- [5] D.M. Cole, C.F. Beckmann, N.Y. Oei, S. Both, J.M. van Gerven, S.A. Rombouts,

<https://doi.org/10.1016/j.parkreldis.2019.07.014>

Received 4 July 2019; Accepted 12 July 2019

1353-8020/© 2019 Elsevier Ltd. All rights reserved.

- Differential and distributed effects of dopamine neuromodulations on resting-state network connectivity, *Neuroimage* 78 (2013) 59–67.
- [6] A.A. Kehagia, R.A. Barker, T.W. Robbins, Cognitive impairment in Parkinson's disease: the dual syndrome hypothesis, *Neurodegener. Dis.* 11 (2) (2013) 79–92.
- [7] Z.W. Zhan, L.Z. Lin, E.H. Yu, J.W. Xin, L. Lin, H.L. Lin, Q.Y. Ye, X.C. Chen, X.D. Pan, Abnormal resting-state functional connectivity in posterior cingulate cortex of Parkinson's disease with mild cognitive impairment and dementia, *CNS Neurosci. Ther.* 24 (10) (2018 Oct) 897–905.

Amée F. Wolters\*

*Department of Neurology, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands*  
*E-mail address: amee.wolters@mumc.nl.*

Sjors C.F. van de Weijer

*Department of Neurology, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands*

Albert F.G. Leentjens

*Department of Psychiatry, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands*

*Department of Neuropsychology, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands*

Annellen A. Duits

*Department of Neuropsychology, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands*

Heidi I.L. Jacobs

*School for Mental Health and Neuroscience, Alzheimer Center Limburg, Maastricht University, P.O. Box 616, 6200, MD, Maastricht, the Netherlands*

*Department of Radiology, Division of Nuclear Medicine and Molecular Imaging, Massachusetts General Hospital and Harvard Medical School, 55 Fruit Street Boston, MA, 02114, Massachusetts, USA*

Mark L. Kuijf

*Department of Neurology, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands*

\* Corresponding author. Department of Neurology, Maastricht University Medical Centre, P.O. Box 5800, 6202, AZ, Maastricht, the Netherlands.