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Correspondence

Contribution of white matter lesions to cognitive decline in Parkinson's disease

In this prospective longitudinal study, the relationship between white matter lesions (WML), manually delineated on MRI, and cognitive decline over a two-year period was examined in 34 patients with Parkinson's disease (PD). WML was associated with clinically important cognitive impairment in PD, i.e. the transition from normal cognition to mild cognitive impairment (MCI).

Vascular pathology is considered to be the main underlying cause of WML. WML contribute to PD patient mortality [1]. In our recent review [2], we examined published evidence on the relationship between WML and cognition in PD. The conclusion is not clear. Some effect of WML on cognition was described in 8 articles; 3 articles found no relationship. Previous studies, even those that confirmed a link between WML and cognitive impairment, did not show whether this link was clinically important. In this longitudinal study, we focused on the clinically relevant transition from normal cognition to MCI [3].

We recruited a cohort of 47 patients who had been diagnosed with PD according to the UK Brain Bank Criteria. All patients underwent an MRI T2-FLAIR scan and clinical and psychological investigations at baseline and after two years. We performed various psychological tests, as well as blood tests and obtained the patients' clinical information, these are all included in the supplementary data tables. The images were acquired on a 1.5T MAGNETOM Avanto, with TR = 7250 ms, TE = 67 ms, FOV = 192 × 256mm, flip angle = 180°, voxel size = 1 × 1x3mm, slice thickness = 3 mm, and 54 transversal slices. The lesions were manually delineated using the freeware program Slicer (see Fig. 1). Each patients' baseline and follow-up brain scans were reviewed slice by slice (each brain scan was composed of 80 slices with 3.162 mm resolution), resulting in a slice-by-slice WML mask. The original T2 scans were segmented and normalized to MNI space. Using the ICBM DTI [4] atlas, we parcellated the lesions into 50 different regions of interest (ROI). We consolidated these ROIs into two super-areas: subcortical and periventricular. We calculated the total white matter volume and the total white matter lesion volume for each area. Relative WML load was calculated for each ROI, as well as for each super-area as the ratio between lesion volume and white matter volume.

We determined which patients were cognitively normal (CN) and which had mild cognitive impairment (MCI) according to the MDS criteria [3]. In this longitudinal study, 34 patients with normal cognition at baseline were included and divided into two groups: Patients in group 1 (23 patients, 14 male; age at baseline 50–72 years, median 63) were cognitively normal at the two-year follow-up visit. Patients in group 2 (11 patients, 7 male; age at baseline 58–82 years, median 65) had developed MCI at the two-year follow-up visit.

Using the Mann-Whitney test, we found that Group 2 had significantly higher values than Group 1 for periventricular WML at the follow-up visit ($p = 0.0136$, $median_1 = 0.2860$ ml, $median_2 = 1.5320$ ml), periventricular WML change ($p = 0.0468$, $median_1 = 0.0560$ ml, $median_2 = 0.4480$ ml), total WML at the follow-up visit ($p = 0.0194$, $median_1 = 0.2940$ ml, $median_2 = 1.5320$ ml), and total WML change ($p = 0.0468$, $median_1 = 0.0670$ ml, $median_2 = 0.5040$ ml) – this indicates an association between WML and cognitive decline. Baseline periventricular and baseline total WML volumes did not differ significantly among groups 1 and 2. Subcortical lesions had a very low volume, and they also did not differ significantly among groups 1 and 2 in either baseline, follow-up or their progression. The various measured

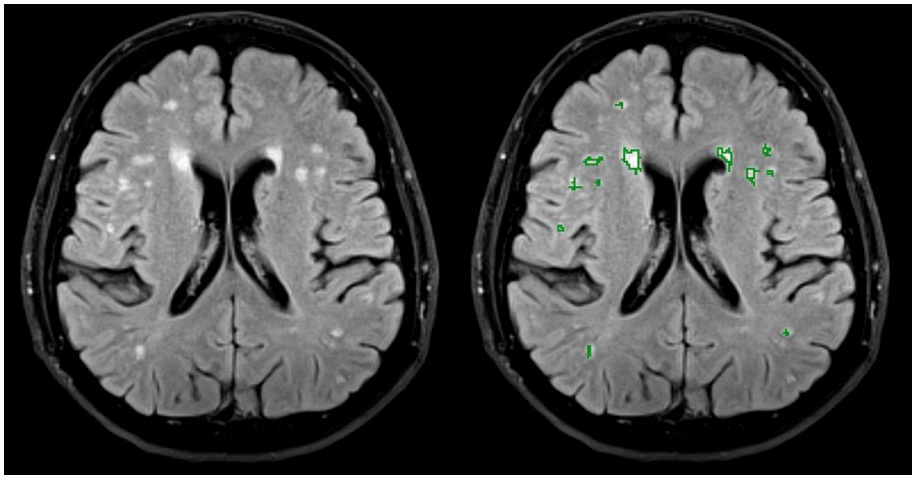

Fig. 1. On the left, one slice of the native T2-weighted FLAIR MRI brain scan. On the right, the same slice with white matter lesions manually delineated, using Slicer.

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biochemical markers, psychological test and other patient information did not vary among groups 1 and 2 (see supplementary tables).

The transition from normal cognition to MCI and the progression of WML were examined over a two-year period. Our study found evidence of association between WML and a clinically important cognitive decline in PD, i.e. transition from normal cognition to MCI. Although the progression of synucleinopathy-based neurodegeneration appears to be responsible for deteriorating cognitive functions in PD [5], other comorbidities may be also involved, and our study suggests that WML are relevant for cognitive decline in PD. However, due to the small number of patients and the lack of a multivariate analysis, this should only be considered a pilot study. Further studies on larger populations should be encouraged to confirm WML as a biomarker of cognitive deterioration toward MCI in PD. It is possible that by reducing the vascular risk factors underlying WML, cognitive decline in PD could be prevented or slowed.

Conflicts of interest

The authors report no conflicts of interest.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.parkreldis.2018.10.015.

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Michael Teodor Grey
Masaryk University, Central European Institute of Technology (CEITEC), Centre for Neuroscience, Brno, Czech Republic
Masaryk University, Faculty of Medicine, P-PooL Program, Brno, Czech Republic

Branislav Veselý*
Masaryk University, Central European Institute of Technology (CEITEC), Centre for Neuroscience, Brno, Czech Republic
Department of Neurology, Nitra Hospital, Slovak Republic
E-mail address: brano.vesely@yahoo.com (B. Veselý)

Martin Gajdoš
Masaryk University, Central European Institute of Technology (CEITEC), Centre for Neuroscience, Brno, Czech Republic

Patrícia Klobušiaková
Masaryk University, Central European Institute of Technology (CEITEC), Centre for Neuroscience, Brno, Czech Republic
Masaryk University, Faculty of Medicine, P-PooL Program, Brno, Czech Republic

Ivan Rektor
Department of Neurology, Nitra Hospital, Slovak Republic

* Corresponding author. Department of Neurology, Faculty Hospital Nitra, Nitra, Slovak Republic.