MRI patterns of atrophy associated with Parkinson's subtypes

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Target: Researchers interested in classification of subtypes of Parkinson's disease.

Introduction: Measures of gray matter (GM) such as cortical thickness and GM volume, has been used to track the progression of disease in people with neurodegenerative disorder (1), but it may also be informative for disease subtype classification (2), which is extremely important for guiding treatment and predict progression. Previous clinical studies (2-3) on subtypes of Parkinson's disease (PD) have shown the cognitive function degrades at a faster rate in postural instability and gait difficulty (PIGD) subgroup compared to tremor-dominant PD (TDPD). In addition, the former has a higher risk to develop dementia. Therefore, it is crucially important to classify the subtypes of Parkinson's. To our best knowledge, no investigation has been reported on automatic PD discrimination using cortical thickness of the whole brain yet.

Methods: 32 people with parkinson's (PwP) underwent a clinical assessment, including Unified Parkinson's Disease Rating Scale. We then calculated the mean global tremor score and an average global tremor score. 9 patients (mean age: 64 ±11.42 years) were classified as PIGD and the remaining 23 were assigned to TDPD subtype based on the ratio of these two average scores. To ensure the number of patients is matched, 18 TDPD (mean age: 65.05 ±9.31 years) subjects were randomly selected and further grouped into two divisions with 9 patients in each group. Disease durations were comparable among different subgroups. ***Cortical thickness***: High-resolution 1mm-isotropic 3D T1 weighted images were performed at 3-Tesla MR scanner (GE Discovery 750) using a 32-channel head coil and a clinical 3T MRI scanner (Achieva, Philips Healthcare, Best, Netherlands), 8-channel coil. To ensure that our results would not be confounded by the different scanning systems, we examined the volume differences in healthy volunteers and PwP by grouping them according to the vendors using voxel-based mophometry analysis. The result revealed that the scanner effect (bilateral thalamus Fig 3) is less significant than the group difference between PwP and HC (Fig 2). To further avoid the cross-scanner effect, we used the measure of cortical thickness. We then pooled the T1WI data across the two scanners. 74 regions of cortical sulco-gyral structure on each hemisphere were identified according to an automatic parcellation scheme and their mean cortical thicknesses (CTs) were measured using FreeSurfer software package (www.surfer.nmr.mgh.harvard.edu) for each subject as previously presented (5 and Fig 1 for pacellation image). ***Pattern classification analysis***: Similar procedures to our previous work were performed (6): Linear support vector machine (SVM) was applied to see whether PIGD could be separated from both of the TDPD groups after running the principle-component analysis (PCA) to reduce the dimension. Components that represent 90% variance of the data were fed into the SVM learning machine. For cross-validation, we used leave-one-out classification with 5 folds. To examine the robustness of discrimination, we also performed SVM on the two TDPD clusters (within-subtype: group1 and group2), presumably on which the classification should fail. Both procedures were statistically examined by comparing the outcome of the null distribution, which was generated by randomizing the labels 10000 permutations.

Results: Our results show that the classification performance is statistically significantly different from the chance level (50%) for both PIGD and TDPD-group1, and TDPD-group2 with an accuracy of 93% ($p < 0.05$) and 89% ($p < 0.05$); whereas accuracy of classification for the within-subtype was 53%, nearing the chance level.

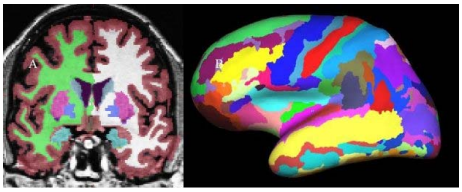

Fig 1. Automatic parcellation results displayed in 3-D (left) and surface images (right).

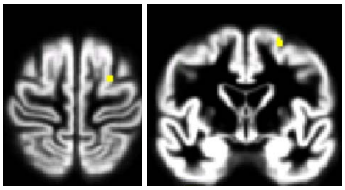

Fig 2. VBM result: region shows the main effect of groups marked in yellow after FWE corrected (p<0.05).

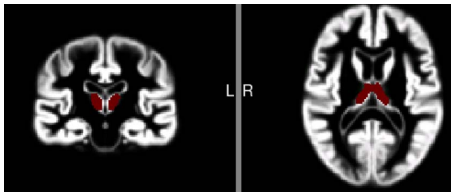

Fig 3. VBM result: region shows the main effect of scanners marked in red after FWE corrected (p<0.05).

Discussion: One previous study (4) suggests that PIGD is closely associated with the volume reduction of GM by focusing on the motor-related areas only. However, it is well know that other regions beyond motor network may also be engaged in the progression of Parkinson's. This is supported by our clinical UPDRS scores and the regions extracted by PCA, which indicate that the areas involving in cognitive function were also impaired. Furthermore, Our VBM analysis failed to find typical motor-related regions when comparing between PwP and HV. Therefore, different from this study, we also include other regions besides the typical motor-related areas. In addition, our results using metric of CT is complementary to their findings of GM reduction.

Conclusion: Despite the small sample size, our study suggests that the spatial pattern of gray matter loss in combination of multivariate pattern classification might be a sensitive approach for discriminating the two motor subtypes of Parkinson's disease.

Reference: 1. Whitwell et al., 2008; 2. Benninger et al., 2009; 3. Selikhova et al., 2009; 4. Rosenberg-Katz et al., 2013; 5. Yue et al., 2014; 6. Yue et al., 2013.

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