Common and specific subregional pathology in the striatum for Schizophrenia and Parkinson's disease

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Introduction:

The striatum is well known for its pivotal role in goal-directed behavior and a broad set of cognitive

functions (Pauli et al., 2016). Likewise, it has been implicated in the pathophysiology of two highly prevalent disorders, Parkinson's disease (PD) and schizophrenia (SCZ) (Schlagenhauf et al., 2014, Singh et al., 2016). Previous studies (Tu et al., 2012) have already revealed altered structure and connectivity of the striatum for both conditions. Given ample evidence that the striatum must be considered a mosaic of different subregions, we here investigated whether structural alterations in PD and SCZ are specifically attributable to individual striatal subregions and whether such pattern differs between PD and SCZ.

Methods:

The analysis is based on a new multi-modal map of the human striatum defined by connectivity-based parcellation (Fig. 1; Liu et al., 2018) To investigate any lateralization effects, we only considered 6 clusters per hemisphere that satisfied the Matched Cluster Criterion (MCC). In other words, these 6 clusters had clear homotopes on the respective other hemisphere, i.e., the dorsal, dorsolateral, rostral and ventral as well as caudal (dorsal and ventral part) striatum (Fig. 1, black boxes).
Structural alterations of these regions were investigated in 159 SCZ patients (f/m: 54/105, age range: 18-65) and 166 matched controls (f/m: 64/102, age range: 18-65), as well as 101 PD patients (f/m: 47/54, age range: 39-81) and 97 matched controls (f/m: 45/52, age range: 27-81) acquired in a multi-site setting. T1-images were processed using the CAT12 toolbox with standard settings.
We then extracted the (non-linearly modulated, i.e., adjusted for head size) and averaged GM volume within the whole striatum, as well as each striatal subregion for each subject. Statistical analysis was performed by five-ways analysis of variance (ANOVA), with the factors disease status, gender, age, subregion and hemisphere. The analysis for PD and SCZ was performed separately.

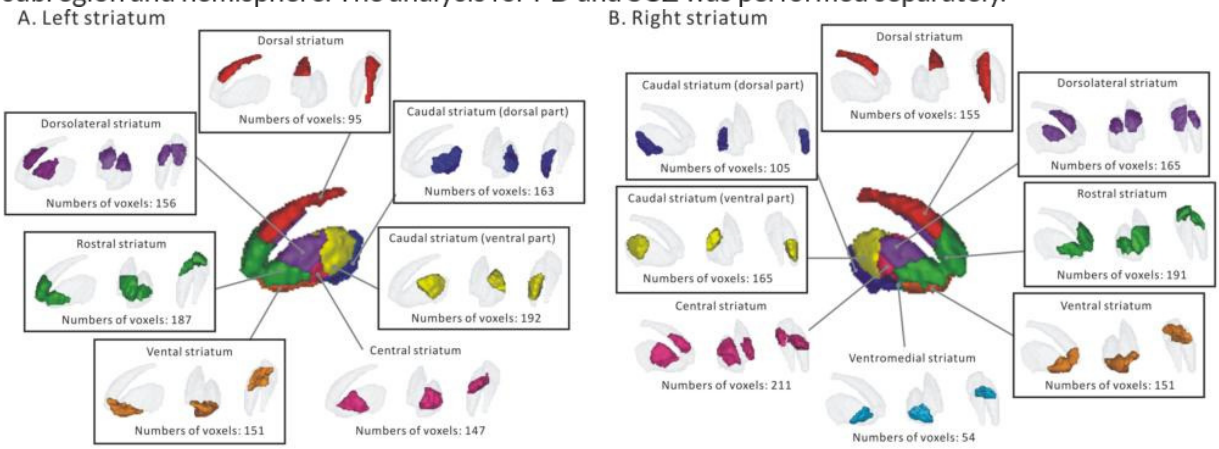

Fig. 1 The location and voxel count of each striatal subregion in multi-modal connectivity-based parcellation (CBP). Six striatal subregions (black boxes) satisfied the Matched Cluster Criterion (MCC) that are highly homotopes, including dorsolateral, rostral and ventral, caudal (dorsal and ventral part) striatum. These six striatal subregions are selected for VBM analysis.

Results:

We found significant main effects of all factors on averaged GM volume in both disorders (Fig. 2A). Specifically, both PD and SCZ patients showed significantly lower GM volume of striatum compared to HC. Females showed significantly higher GM volume than males. We also found the left hemispheric volume to be significantly larger than the right one. Younger subjects had higher GM volume than older subjects. Significant differences in GM volume among different striatal subregions were observed.
We then focused on interaction effects of the factor 'disease status' (PD and SCZ separately) (Fig. 2B-D). Significant interactions of disease status were found with the factors subregion, age, gender and hemisphere. Resolving these interaction effects showed PD patients to have significantly lower GM volume in left rostral, caudal (dorsal part), dorsolateral and ventral striatum than controls (Fig. 2B). Similar significant results were also found in the same striatal subregions on the right side. However, significantly lower GM volume was found in left and right rostral and ventral striatum for SCZ, compared to HC (Fig.

2B). The interaction effect of disease status and gender showed both male and female PD patients to have lower GM volume compared to HC (Fig 2C). This tendency was also observed in SCZ patients (Fig 2C). We also found significant interactions of disease status and age, which showed lower GM volume in older patients than HC (Fig 2D).

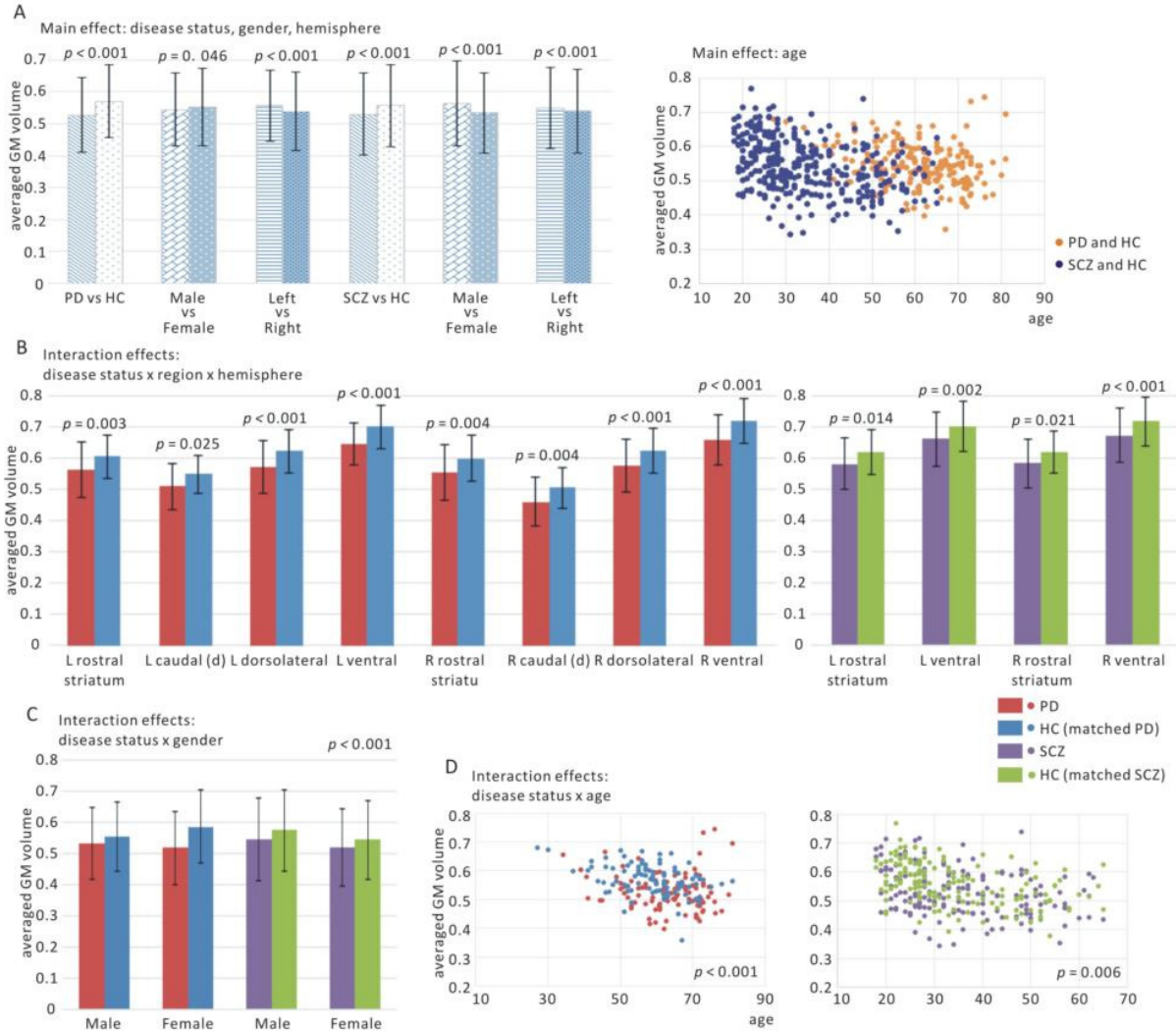

Fig. 2 Main (A) and interaction effect (B-E) in five-way ANOVA. The bars corresponds to the mean value and the error bars to the standard deviation.

Conclusions:

We found common structural alterations in rostral and ventral striatum for PD and SCZ, but differences in caudal (dorsal part), dorsolateral striatum were specifically attributable to PD. Meanwhile, the interaction of age and gender also contributes to altered GM volume in the striatum. These results suggested degeneration of dopaminergic nigrostriatal neurons resulting in differential striatal pathology for PD and SCZ, which in turn may relate to common and special morphological changes in striatal subregions.

Disorders of the Nervous System:

Parkinson's Disease and Movement Disorders [1]
Schizophrenia and Psychotic Disorders [2]

Imaging Methods:

Anatomical MRI
Multi-Modal Imaging

Modeling and Analysis Methods:

Segmentation and Parcellation

Keywords:

Basal Ganglia
Movement Disorder
Psychiatric Disorders
Segmentation
Structures
Sub-Cortical

1|2Indicates the priority used for review

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No

Please indicate below if your study was a "resting state" or "task-activation" study.

Resting state

Healthy subjects only or patients (note that patient studies may also involve healthy subjects):

Patients

Was any human subjects research approved by the relevant Institutional Review Board or ethics panel? NOTE: Any human subjects studies without IRB approval will be automatically rejected.

Yes

Was any animal research approved by the relevant IACUC or other animal research panel? NOTE: Any animal studies without IACUC approval will be automatically rejected.

Not applicable

Please indicate which methods were used in your research:

Structural MRI

For human MRI, what field strength scanner do you use?

3.0T

Which processing packages did you use for your study?

SPM

Provide references using author date format

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