

Reduced Resting CBF in the Mesolimbic-frontal Regions in Parkinson's Disease with Impulse Control Disorders

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Introduction Impulse control disorders (ICDs) constitute a group of psychiatric disorders, for which the essential feature is a failure to resist an impulse, drive, or temptation to perform an act that is harmful to the person or to others. A range of ICDs, such as compulsive gambling, buying, eating, and sexual behaviors, have been frequently reported to occur in Parkinson's disease (PD) patients (1-3). Accumulating evidences from case series and cross-sectional studies implicate dopamine agonist (DA) treatment with the development of most ICDs in PD (1-3). It was estimated that 10~15% of PD patients would develop ICDs at some point during the course of the disease (3). However, to date the neurobiological mechanisms underlying ICDs in PD are unknown. Using arterial spin labeling (ASL) perfusion MRI to non-invasively quantify cerebral blood flow (CBF) in PD patients with and without ICDs at a resting state, the present study aimed to examine neural correlates of ICDs in PD. We hypothesized that ICDs in PD may be associated with altered neural activity in the dopaminergic mesolimbic-frontal system.

Methods A total of 18 PD patients (age range from 40 to 76 years, 5 female) participated in the study, including 8 patients with at least one active ICD at the time of scan (ICD-A), 3 patients with a history of ICD but were remitted at the time of scan (ICD-R), and 7 patients with no lifetime history of any ICDs (non-ICD). These subjects were scanned on a Siemens 3 T Trio scanner using a pseudo-continuous ASL sequence (4) to acquire the resting perfusion data with the following parameters: TR = 4s, TE = 17s, Labeling time = 2s, Delay time = 1s, FOV = 22 x 22 cm, matrix = 64 x 64, 16 axial slices, 6mm thickness and 2 mm gap. Data were analyzed by SPM2. Perfusion weighted image series were generated by pair-wise subtraction of the label and control images, followed by conversion to absolute CBF image. One mean resting CBF image was generated for each individual subject. Both voxel-wise general linear modeling (GLM) and region of interest (ROI) analyses were conducted.

Results SPM voxel-wise analysis showed that patients with ICD have significantly lower regional resting CBF in the right striatum when comparing with patients without ICD (Fig.1a, uncorrected $p < 0.001$). Moreover, ROI analysis that separated the remitted and active ICD patients (Fig.1b) revealed significantly lower regional resting CBF in the striatum and left DLPFC for the active ICD patients than the non-ICD and remitted ICD patients (all $p < 0.05$), while no difference was found between the non-ICD and remitted ICD patients (all $p > 0.2$). In addition, a positive correlation (Fig.2a, $r = 0.86$, $p < 0.01$) was found between resting striatal CBF and the time-on-ICD in the active ICD patients, while a negative correlation was found between resting DLPFC CBF and the time-on-ICD (Fig.2b, $r = -0.74$, $p < 0.05$).

Conclusions The results of reduced resting CBF in striatal and prefrontal regions for active ICD patients indicate that deficient dopaminergic mesolimbic-frontal neural activity may underlie ICDs in PD. No difference between remitted ICD and non-ICD patients and positive correlation between resting striatal CBF in and time-on-ICD in the active ICD patients consistently suggest a spontaneous (although not fully successful) attempt to normalize neural abnormalities during the development of ICDs and support the hypothesis of homeostatic dopamine levels in striatum (5).

References

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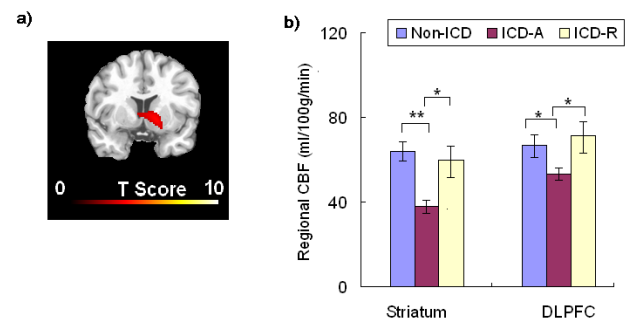


Fig.1 SPM maps (a) and regional CBF values (b) showing reduced resting CBF in the striatum and left DLPFC for active ICD (ICD-A) than non-ICD and remitted ICD patients (ICD-R).

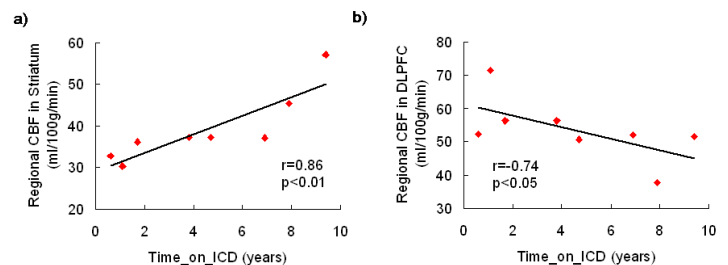


Fig2. Resting CBF in the striatum (a) and left DLPFC (b) showed significant correlation with time-on-ICDs in the active ICD patients.