Altered corticostriatal functional networks in adolescents with Internet addiction disorder revealed by resting-state fMRI

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Introduction Internet addiction disorder (IAD), a prevalent mental health concern around the world, has attracted considerable attention from the public community [1-3]. Convergent evidences through the neuroimaging literature demonstrated that the striatum and prefrontal cortex are related to IAD. In this study, we used resting-state functional connectivity (rsFC) to investigate the integrity of corticostriatal functional networks in IAD.

Materials and Methods *Subjects:* Twenty-nine right-handed participants, comprising 14 IAD adolescents (2 women; mean age: 17.1±2.7) and 15 age-, sex- and education-matched healthy controls (2 women; mean age: 17.9±2.5), participated in this study. IAD subjects met the criteria by Beard and Wolf [4]. Six questionnaires were used to evaluate behavioral features. *Image acquisition:* Rs-fMRI scans were carried out by a 3.0 Tesla Phillips scanner with the following parameters: TR/TE: 2,000/30ms; flip angle: 90°; matrix: 64×64; FOV: 23 cm×23 cm; slice thickness: 4 mm without gap. Each run contained 220 volumes. *Data preprocessing:* For each subject, the first 10 volumes were discarded and the remaining 210 volumes were corrected for acquisition time delay, realigned for head motion, normalized to the MNI space, re-sampled to a 3mm isotropic voxel, smoothed with a 6-mm FWHM Gaussian kernel. After removing the WM and CSF signals, the time series were band-pass filtered temporally (0.01-0.08 Hz). *Subregions of striatum*: Six previously validated bilateral striatal regions of interest were used, which are inferior ventral striatum (±9, 9, -8; VSi), superior ventral striatum (±10, 15, 0; VSs), dorsal caudate (±13, 15, 9; DC), ventral rostral putamen (±20, 12, -3; VRP), dorsal rostral putamen (±25, 8, 6; DRP) and dorsal caudal putamen (±28, 1, 3; DCP) [4]. *Functional connectivity analysis:* For each subject, a cross-correlation coefficient map for each subregion was calculated and converted to a z-value map. Then the z-value maps were entered into the two-sample t test with age and sex as covariates to evaluate rsFC differences between groups. A corrected threshold of $p_{alpha}<0.05$ was considered significantly. Step-wise multiple regression analyses were performed to check whether the rsFC are correlated with the behavioral scores.

Results Consistent with previous studies [4], we found that each striatal subregion showed a region-specific rsFC map. The spatial pattern of the rsFC map for each striatal subregion appeared to be similar in IAD subjects and healthy controls. However, IAD had significant changes in connectivity strength for every striatal subregion (Fig. 1). The VSi show decreased FC in the caudate head, bilateral subcallosal anterior cingulate cortex (ACC) and posterior cingulate cortex. The VSs show reduced FC in the bilateral dorsal/rostral ACC and ventral anterior thalamus, and the left subcortical areas including the putamen, pallidum, insula and inferior frontal gyrus (IFG). The DC show decreased FC in the bilateral dorsal/rostral ACC. The left DC also showed reduced FC with the left ventral lateral thalamus, as well as the right DC displayed lower positive relationships with the left IFG. The left DCP show increased FC in the bilateral caudal cingulate motor area. The left VRP show decreased FC in the right IFG. Moreover, we found that rsFC between the right VSs and bilateral dorsal caudate was negatively correlated with the Young's Internet Addiction Scale (YIAS) (r=-0.560; p=0.038; Fig. 2A), rsFC between the right VSs and bilateral rostral ACC (r=-0.540; p=0.046; Fig. 2B), between the left DC and bilateral dorsal/rostral ACC (r=-0.566; p=0.035; Fig. 2C), and between the left VRP and right IFG (r=-0.609; p=0.021; Fig. 2D) were negatively correlated with the Screen for Child Anxiety Related Emotional Disorders (SCARED).

Discussion In this study, we identified six resting-state functional networks associated with striatal subregions (VSi, VSs, DC, VRP, DRP and DCP) based on rsFC. These functional networks are known to engage in affective and motivation processing, and cognitive control. We found that IAD shows altered connectivity strength for every striatal subregion. Moreover, altered corticostriatal functional circuits were associated with behavioral scores. Our findings suggest that IAD is associated with alterations of corticostriatal functional circuits and rsFC may be used as a qualified biomarker to understand the underlying neural mechanisms or to evaluate the effectiveness of specific early interventions in IAD.

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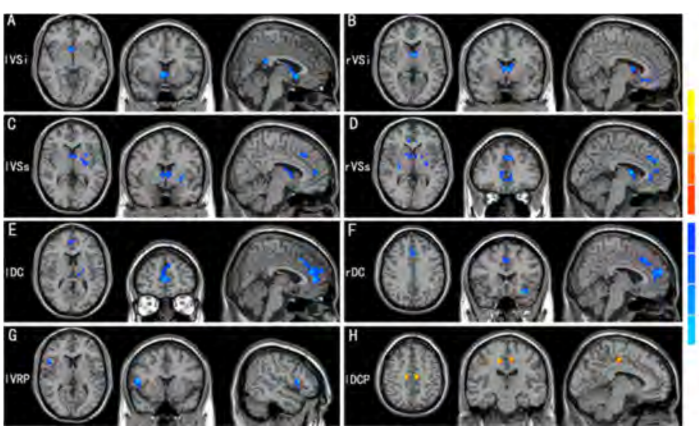

Fig. 1: Significant rsFC differences between IAD and healthy controls (p<0.05, AlphaSim corrected). (A) lVSi, (B) rVSi, (C) lVSs, (D) rVSs, (E) lDC, (F) rDC, (G) lVRP and (H) lDCP. Hot and cold colors indicate rsFC increases and decreases in IAD when compared with controls. l: left, r: right.

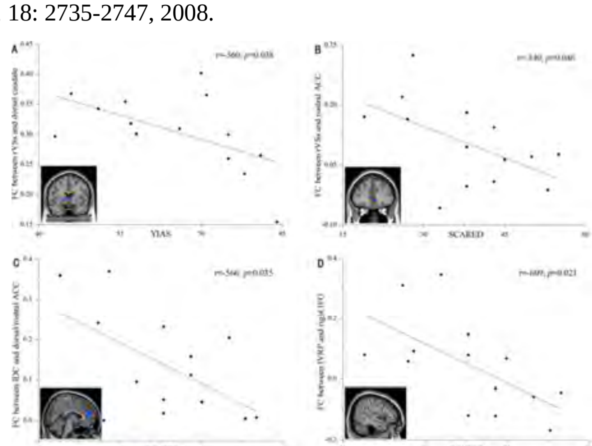

Fig. 2: Correlation analysis between rsFC and behavioral measures within IAD. rsFC between rVSs and dorsal caudate was negatively correlated with YIAS (A), rsFC between rVSs and rostral ACC (B), between lDC and rostral/dorsal ACC (C), between lVRP and right IFG (D) were negatively correlated with SCARED.