Abnormal White Matter Integrity in Adolescent Students with Internet Addiction Disorder Revealed by Tract-Based Spatial Statistics

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Introduction Internet addiction disorder (IAD), also called problematic or pathological internet use, is characterized by poorly controlling his or her use of the internet, and has been becoming a serious mental health issue around the globe [1-3]. Current studies on IAD were focused on the associated psychological examinations, such as impulsivity, insomnia, self-consciousness, anxiety, depression, aggression, and interpersonal relations. In this study, we used diffusion tensor imaging (DTI) to investigate white matter integrity in adolescent students with IAD.

Materials and Methods *Subjects:* Eighteen adolescent students with IAD (two females; mean age: 17.2±2.6; age range: 14-24) were recruited from the department of child and adolescent psychiatry, Shanghai mental health center. They met the internet addiction criteria by Beard and Wolf [4]. Seventeen age, gender, and years of education matched normal students (two females, mean age: 17.6±2.5; age range: 15-24) without personal or family history of psychiatric disorders were selected as healthy controls. Six questionnaires were used to assess the participants' behavioral features, namely adolescence time management disposition scale (ATMD), Young's diagnostic questionnaire for internet addiction scale (YDQ), adolescent behavior rating scale (ABRS), Barrett impulsiveness scale (BIS), behavior evaluation scale (BES) and family assessment device (FAD). *Image acquisition:* DTI scans were performed with a 3.0-T Achieva MR scanner with the following parameters: TR/TE: 8,044/68 ms; NEX: 3; matrix: 128×128 zero-filled to 256×256; FOV: 256 mm×256 mm; slice thickness: 4 mm without gap, spatial resolution of 1 mm×1 mm×4 mm/voxel, 15 non-collinear gradient encoding directions with b=800 s/mm^2. *Data analysis:* DTI data were processed using FDT within FSL (http://www.fmrib.ox.ac.uk/fsl). First, the diffusion-weighted images were aligned to the non-diffusion-weighted (b_0) image. Then, the diffusion tensor was estimated by the multivariate linear fitting algorithm, and the tensor matrix was diagonalized to obtain its three pairs of eigenvalues and eigenvectors. Voxel-wise diffusion indices including fractional anisotropy (FA) were calculated. Whole-brain voxel-wise statistical analysis of FA images was performed by tract-based spatial statistics [5]. To identify FA differences between groups, the skeletonized FA data were fed into the voxel-wise statistics analysis. Threshold-free cluster enhancement (TFCE) was used to obtain the significant differences between groups at $p<0.01$ after accounting for multiple comparisons. The results were located and labeled by JHU-ICBM-DTI-81 white matter (WM) labels atlas.

Results There were significant inter-group differences on YDQ ($p<0.001$), ABRS ($p<0.001$) and BES ($p<0.001$), a trend difference on FAD ($p=0.09$), and no differences on ATMD ($p=0.95$) and BIS ($p=0.48$). The spatial distribution of significantly reduced FA in the IAD group is presented in Figure 1. Compared to control subjects, the IAD subjects showed reduced FA ($p<0.01$; TFCE-corrected) in the following regions: WM in the orbital frontal and temporal lobes, cerebral peduncle, commissural fiber of corpus callosum, association fibers including sagittal stratum, superior front-occipital fasciculus, superior longitudinal fasciculus and cingulum gyrus, and projection fibers such as corona radiation, internal capsule and external capsule. There were no WM regions with increased FA in the IAD group. In addition, we found FA in the left genu of corpus callosum negatively correlated with the BES (r=-0.623, $p=0.006$; Figure 2A), and FA in the left anterior corona radiation negatively correlated with the YIAS (r=-0.483, $p=0.042$; Figure 2B).

Discussion To the best of our knowledge, this is the first DTI study reported for IAD adolescent students. Our study suggests that the IAD subjects show extensive white matter abnormalities. Some of our findings in IAD, such as the corpus callosum and orbital frontal WM abnormalities, have also been demonstrated in substance overuse disorders, suggesting that IAD may have some common neurobiological mechanisms with substance addictions. In addition, FAs in the left genu of corpus callosum and the left anterior corona radiation were negatively correlated with behavioral features, which indicates that DTI might be valuable in providing data on neurological prognosis for IAD. Future longitudinal follow-up should examine whether DTI measures of WM integrity can effectively predict the effectiveness of specific early interventions in IAD.

Acknowledgements This work is supported by grants from Natural Science Foundation of China (Nos. 30800252 and 20921004), Knowledge Innovation Program of Chinese Academy of Sciences, and Foundation of President of Chinese Academy of Sciences.

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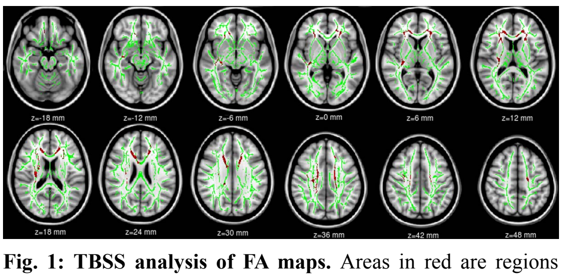

Fig. 1: TBSS analysis of FA maps. Areas in red are regions where FA was significantly lower ($p<0.01$, corrected by TFCE) in IAD relative to controls. green: the mean FA skeleton. The left side of the image corresponds to the right hemisphere of the brain.

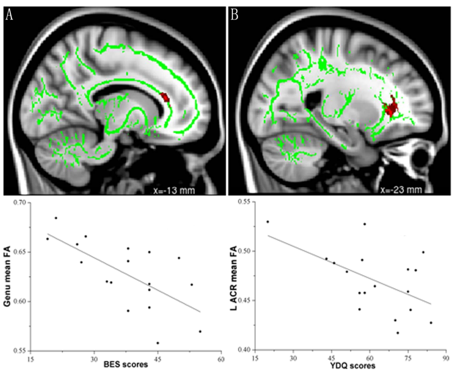

Fig.2: Correlation analysis in IAD. Significant correlations between behavioral features and FA in IAD. To aid visualization, regions showing significant correlations (red) are thickened using the tbss_fill script implemented in FSL. Figure 2A shows FA in the left genu of the corpus callosum correlates negatively with YDQ (r=-0.623, $p=0.006$). Figure 2B shows FA in the left anterior corona radiation correlates negatively with the BES (r=-0.483, $p=0.042$).