Diffusion Tensor Imaging for White Matter Alterations in Chronic Cocaine Dependents

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Introduction: The critical role of mesolimbic reward system in cocaine dependence has been well understood, however, the microscopic structural basis for the dopamine circuitry responses remains unclear [1]. Cocaine addiction associated neuronal dysfunctions have been wildly reported inside and outside the dopamine system, although, previous studies on the associated white matter (WM) abnormalities were limited for group sizes and subject characterizations [2]. Previous diffusion tensor imaging (DTI) studies [3~4], for example, examined small subject groups, while no comprehensive characterizations were provided on subject's brain functions, addiction-related behaviors, or other demographic factors. In addition, the lack of voxel-based DTI data analysis has become a barrier from illustrating the whole brain results without regional bias. The absence of quantitative cocaine addiction assessments also led to the difficulty of interpreting some DTI findings. Here we present a DTI study using relatively large and better characterized subject pools. Our goal was to investigate the patterns of WM alterations both inside and outside the dopamine reward system. We hypothesized that the alterations of the WM integrity and its correlation with the cocaine dependence assessment may vary across regions for both directions and magnitudes.

Methods: Active cocaine users (CU) (N=39, age=39±5 yrs, 70% male, education=13±1.3 yrs, WAIS_V=58±7, cocaine use history=4.3±2 yrs, cigarette smokers=20) without major illness or history of neurological or psychiatric disorders, volunteered to participate this study. A quantitative cocaine dependence (CD) was assessed in a scale of 0~7 using computerized SCID interview. Healthy controls (HC) (N=38, age=38±6 yrs, 60% male, education=13±1.7 yrs, WAIS_V=57±8, cigarette smokers=11), who have no current or past DSM-IV dependence (except nicotine) as screened by interview and urine drug tests, served as the group for matched comparisons. A Siemens 3T Allegra MR scanner was used to perform T1-weighted anatomical imaging (1x1x1 mm), and DTI (2x2x3 mm, b=1000 s/mm^2) scans. DTI data were pre-processed off-line to estimate the FA index in each imaging voxel, and the Track-Based Spatial Statistics (TBSS) toolbox [5] was used to spatially normalize the DTI images across the subjects, and up-sampled the images to 1x1x1 mm resolution. A general linear model in AFNI [6] was used for voxel-based statistics to regress out unintended factors.

Results: Voxel-based analysis (see Fig.1) indicated significant FA alterations ($p<0.05$, corrected) in both directions in multiple WM regions, including decreased FA in CU group at ventral tegmental area (VTA) cortical spinal tract, bilateral ventral thalamus (THA), and right inferior longitudinal fasciculus (ILF), as well as increased FA at internal capsule (IC), genu corpus callosum (g.CC), medial prefrontal (PFC). Within CU group, across subject correlations ($p<0.05$, corrected) between FA and a dependence assessment index CD*UY (i.e. CD score multiplies the cocaine use years UY) were also identified in these regions. ROI-based analysis (see Fig.2) shows more detailed data distributions in those regions. In general, FA and CD*UY correlations tend to distribute in the regions with increased FA in CU. We also noticed that smoking related FA changes occurs more significantly in CU than HC.
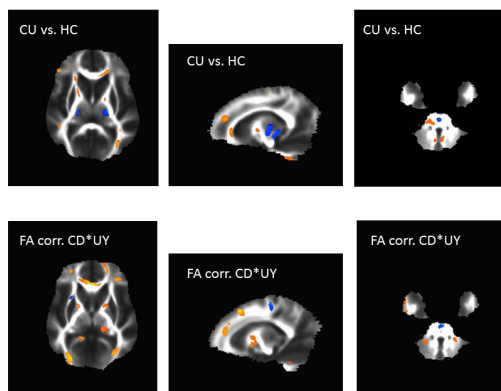

Fig.1: Voxel-based FA analysis: CU vs. HC alterations (upper row), and FA correlates CD*UY within CU group (lower row) at the identical slices.
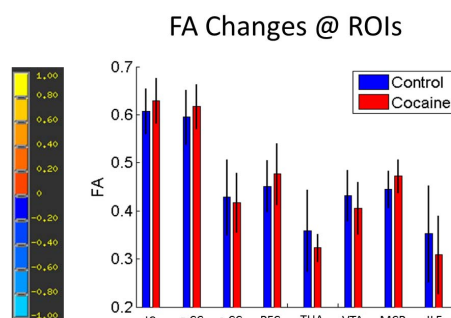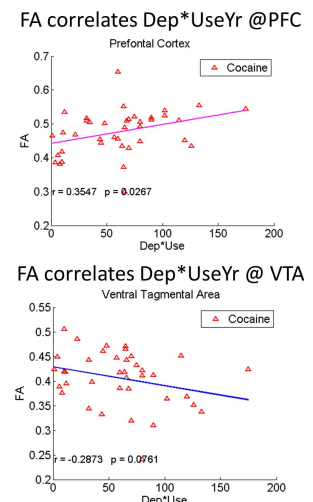

Fig.2: ROI-based FA analysis: CU vs. HC alterations occur in both directions. The corrections (in CU) between FA and the CD*UY are on the right for PFC and VTA.

Discussions and Conclusion: By using larger group sizes and more comprehensively characterized subjects, we hope the present study would provide more specific and reliable observations on how the cerebral WM structures would response to the chronic cocaine addictions. Our data suggest that the CU-related WM integrity alterations do occur in both directions in a regionally selective pattern, and that the across-subject correlations in CU between FA and the index CD*UY are generally consistent with the group-comparison results, especially for regions with increased FA in CU. Thus we further hypothesize that the increased FA in those regions might reflect a neuronal plasticity mechanism toward compensating the impaired functions in the circuitry. The next step of the study will be performed to test this hypothesis by incorporating DTI, fMRI and resting-state fMRI network analysis [7].

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