Abnormal diffusion and fractional anisotropy in the brains of adolescent methamphetamine users

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Introduction: Methamphetamine (METH) is a highly addictive psychostimulant commonly used by adolescents and young adults. Diffusion tensor imaging (DTI) studies of adult METH users¹,² report white matter abnormalities associated with poor cognitive performance. We aimed to use DTI to investigate whether adolescent brain development was vulnerable to the effects of METH.

Methods: DTI scans were performed in 40 young (ages 13-23 years) METH users (16 males & 24 females, age 18.4±0.4 years) and 33 control subjects (15 males & 18 females, age 18.0±0.5 years). MRI was performed on a Siemens 3T scanner, and included T1 and T2 weighted structural scans, and axial spin-echo EPI DTI scans with full-brain coverage (12-directions, 28 slices, 4.6mm slice, 0.46mm gap, TR/TE=3700/88ms, 128x128x28, b factor=([0,1000]s/mm²). All images were reviewed for structural abnormalities, movement, and other artifacts. Fractional anisotropy (FA) and diffusion (trace) values for each voxel were calculated using DTIStudio version 2.03.³ Regions of interest (ROIs) were manually drawn, using fixed size ROIs, on FA and trace maps, cross-referenced with other available images for accurate placement. ROIs included the genu and splenium of the corpus callosum and bilateral caudate, putamen, globus pallidus, thalamus, frontal and parietal white matter.

Results: METH users started using the drug by age 14.7±0.3 years, and used 0.65±0.07 grams/day, 5.6±0.3 days/week for 30.4±4.6 months with a lifetime exposure of 605.5±143.6 grams, and they were abstinent 260.0±63.9 days at the time of the study. Compared to controls, adolescent METH users demonstrated lower diffusion in the left parietal white matter (-2.0%, p=0.02) and higher diffusion in the right caudate (+2.1%, p=0.05). METH users also had higher FA in the left parietal white matter (+10.4%, p=0.02) and right thalamus (+6.5%, p=0.01) but lower FA in the corpus callosum splenium (-3.6%, p=0.01). Correlations between METH usage parameters and significant DTI measures showed that caudate diffusion increased with duration of abstinence (days since last METH use r=0.35, p=0.04). No other METH usage parameters correlated with DTI results.

Discussion: Lower diffusion and higher FA was found in the parietal white matter of METH-exposed adolescents which suggests METH may affect the microstructure in this brain region. Specifically, lower diffusion in the parietal white matter may indicate more compact axons or greater dendritic or spine density from deceased pruning or increased branching during development, while higher FA indicates these changes lead to less directional coherence in this region. The higher FA in the thalamus may indicate greater cell density, fiber diameter, or directional consistency. However, higher diffusion in the caudate and in corpus callosum splenium indicate less organization, which may reflect cellular damage or compensatory neuroinflammation. In the caudate, this abnormality appears to continue to progress during early abstinence. While subjects in this study were not dependent on any other illicit drugs or alcohol, the influence from other drug use cannot be ruled out in this population since increased FA in cortical and subcortical white matter was also observed in adolescent nicotine smokers⁴, and since a higher percentage of our METH users smoked nicotine cigarettes (85%) compared to our control subjects (33%). We observed abnormal DTI measures in young METH users, longitudinal follow-up studies will further clarify whether these changes are transient or persistent with prolonged abstinence.


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