Urine THC Metabolite Levels Correlate with Striatal D2/D3 Receptor Availability

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Rationale: Although the incidence of cannabis abuse/dependence in Americans is rising, the neurobiology of cannabis addiction is not well understood. Recent imaging studies have demonstrated deficits in striatal D2/D3 receptor availability in several substance-dependent populations. However, this has not been studied in chronic cannabis users.

Objective: The purpose of this study was to compare striatal D2/D3 receptor availability between currently using chronic cannabis users and healthy controls.

Methods: Eighteen right-handed males, age 18-35 were studied. Ten subjects were chronic cannabis users; eight were demographically matched controls. Subject eligibility was determined during a screening interview, which included SCID-I and SCID-II assessments, self-report of past substance use, and drug toxicology screening. Subjects underwent a [11C]raclopride (RAC) PET scan; striatal RAC binding potential (BPND) was calculated on a voxel-wise basis with the multilinear reference tissue method. Prior to scanning, urine samples were obtained from cannabis users for quantification of urine Δ-9-tetrahydrocannabinol (THC) and THC metabolites (11-nor-Δ-9-THC-9-carboxylic acid; THC-COOH). Statistical analyses were conducted at voxel-wise level within the striatum. Two-sample t-tests were used to test for differences in BPND between groups. For cannabis subjects, multiple regression analyses were used to test for correlations between striatal BPND and urine THC/THC metabolite levels.

Results: There were no differences in BPND between cannabis smokers and healthy controls. Smokers – regardless of substance – had 10% lower D2/D3 availability than non-smokers. Voxel-wise analyses revealed that striatal RAC BPND values were associated with urine levels of cannabis metabolites.

Conclusions: Cannabis and cannabis metabolites in urine, markers of recent cannabis consumption, are negatively correlated with striatal RAC BPND. This provides the first evidence that degree of cannabis use is related to changes in the central DA system. Low BPND in both cannabis and cigarette users may indicate a deficiency in D2/D3 receptors as a function of chronic exposure to either or both substances. Alternatively, endogenous dopamine levels may be higher in smokers as a result of MAO inhibition from beta-carbolines in the inhaled smoke. Additional studies are needed to understand the complex relationships between chronic cannabis use and the dopamine system.