URINE THC METABOLITE LEVELS CORRELATE WITH STRIATAL D_2/D_3 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. Previous PET and SPECT studies have demonstrated deficits in striatal D_2/D_3 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 D_2/D_3 receptor availability between currently-using chronic cannabis users and healthy controls.

Methods: Eighteen right-handed males, 18-34 years of age, were studied. Ten subjects were chronic cannabis users; eight were demographically matched controls. Subjects underwent a [^{11}C]raclopride (RAC) PET scan. On the scan day, urine samples were obtained from cannabis users for quantification of urine Δ-9-tetrahydrocannabinol (THC; the active compound in cannabis smoke) and THC metabolites (11-nor-Δ-9-THC-9-carboxylic acid and 11-hydroxy-THC). Striatal RAC binding potential (BP_{ND}) was used as an index of D_2/D_3 receptor availability; this parameter was estimated at each image voxel for every subject. SPM5 software was used to test for differences in BP_{ND} between groups and, in cannabis subjects, for associations between BP_{ND} and markers of cannabis use.

Results: There were no differences in D_2/D_3 receptor availability between cannabis users and controls. Smokers of either cannabis and/or tobacco had 10.2% lower BP_{ND} values than nonsmokers in the bilateral putamen ("any-smokers": 2.66 ± 0.2; nonsmokers: 2.97 ± 0.2). In cannabis users, RAC BP_{ND} values were negatively associated with both urine levels of cannabis metabolites and self-report of recent cannabis consumption.

Conclusions: There is an inverse relationship between chronic cannabis use and striatal RAC BP_{ND}. This may be caused by inhibition of monoamine oxidase (MAO) by the pyrolyzation of cannabis, which could lead to increased endogenous dopamine levels (and hence, lower BP_{ND} in heavier users). Additional studies are needed to identify the neurochemical consequences of chronic cannabis use on the dopamine system.

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