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. Previous PET and SPECT 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, 18-34 years of age, were studied. Ten subjects were chronic cannabis users; eight were demographically matched controls. Subjects underwent a [¹¹C]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 (BPND) was used as an index of D₂/D₃ receptor availability; this parameter was estimated at each image voxel for every subject. SPM5 software was used to test for differences in BPND between groups and, in cannabis subjects, for associations between BPND and markers of cannabis use.

Results: There were no differences in D₂/D₃ receptor availability between cannabis users and controls. Smokers of either cannabis and/or tobacco had 10.2% lower BPND values than nonsmokers in the bilateral putamen (“any-smokers”: 2.66 ± 0.2; nonsmokers: 2.97 ± 0.2). In cannabis users, RAC BPND 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 BPND. 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 BPND in heavier users). Additional studies are needed to identify the neurochemical consequences of chronic cannabis use on the dopamine system.

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