Cannabis Use and Dopamine
An [18F]-DOPA Positron Emission Tomography (PET) Study in cannabis users

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BACKGROUND

• Cannabis is the most widely used illicit drug in the world and users are at increased risk of schizophrenia.

• It remains unknown whether cannabis use is associated with the striatal dopaminergic dysfunction seen in other addictions or schizophrenic psychosis.

AIMS OF THIS PROJECT

• To image and compare dopamine synthesis capacity, using uptake of the radiotracer [18F]6-fluoro-L-DOPA, in regular cannabis users who experienced a transient increase in psychotic-like symptoms when they consumed their own cannabis with non-user controls

• To determine the relationships between cannabis use, dopamine synthesis capacity and induction of transient psychotic symptoms in vivo.

METHODS

• Striatal dopamine synthesis capacity was assessed using [18F]-DOPA PET in 19 regular cannabis users [mean (SD) age = 20.8(1.7)] compared to 19 healthy control subjects [mean (SD) age = 22.3(2.8)], matched for age and sex.

• Users reported experiencing a transient increase in psychotic-like experiences when they consumed their own cannabis, but did not meet the diagnostic threshold for a psychotic disorder and were not acutely intoxicated with cannabis at the time of scanning.

• Users abstained from cannabis for 12 hours prior to scanning. Urine drug screen confirmed no recent drug use (except cannabis in users).

• Regions of Interest (ROI) defined in the striatum and functional subdivisions. [18F]-DOPA uptake relative to cerebellar reference region (Kcer) calculated in each ROI.

• Voxel-based analysis of parametric Kcer images using SPM5.

RESULTS

• ROI analysis: Compared to controls, users had reduced dopamine synthesis capacity in the striatum (t(36)=2.54, p<0.05) and its associative (t(36)=2.54, p<0.05) and limbic subdivisions (t(36)=2.23, p<0.05) (effect sizes=0.8). Reduced striatal Kcer in the user group remained significant after covarying for other drug use (F(1,37)=4.65, p<0.05).

• Voxel-based analysis confirmed reduced Kcer in the user group relative to the non-user controls with a focus in the right putamen (p<0.05) corrected for multiple comparisons using the family-wise error rate.

• Within the user group, there were significant correlations between striatal dopamine synthesis capacity and severity of cannabis use (r=0.77, p<0.001) and age of onset of cannabis use (r=0.51, p<0.05), but not with induction of psychotic-like symptoms following consumption of the drug (r=0.32, p=0.19).

DISCUSSION

• Regular cannabis use is associated with presynaptic dopaminergic dysfunction in individuals who experience transient psychotic-like symptoms when acutely intoxicated with the drug, and that this is correlated with the degree of cannabis use.

• Regular cannabis use may cause down-regulation of the dopamine system, which might be exacerbated by early age of use.

• Further research is needed to investigate the neurobiological mechanisms underlying the associations between cannabis use, cannabis dependence and the development of an enduring psychotic illness.

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