

# Cannabis Use and Dopamine

## An [<sup>18</sup>F]-DOPA Positron Emission Tomography (PET) Study in cannabis users

Dr Michael AP Bloomfield<sup>1</sup>, Dr Celia JA Morgan<sup>3</sup>, Dr Alice Egerton<sup>1,2</sup>, Prof Shitij Kapur<sup>2</sup>, Prof H Val Curran<sup>3</sup>, Dr Oliver D Howes<sup>1,2</sup>

<sup>1</sup> Medical Research Council Clinical Sciences Centre, Hammersmith Hospital, Imperial College London;

<sup>2</sup> Institute of Psychiatry, King's College London;

<sup>3</sup> Clinical Psychopharmacology Unit, University College London

### 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 [<sup>18</sup>F]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 [<sup>18</sup>F]-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.

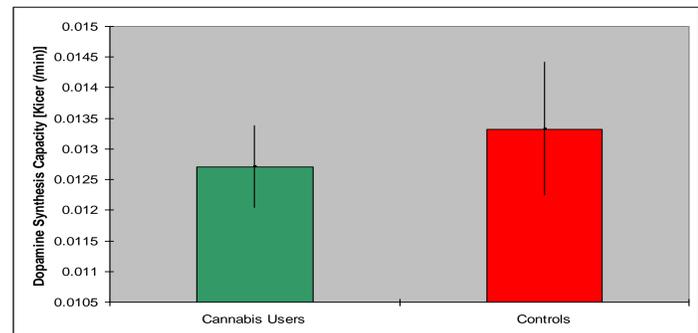
- Users reported experiencing a transient increase in psychotic-like experiences when they consumed their own cannabis, but did not meet the diagnostic threshold for a psychotic disorder and were not acutely intoxicated with cannabis at the time of scanning.

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

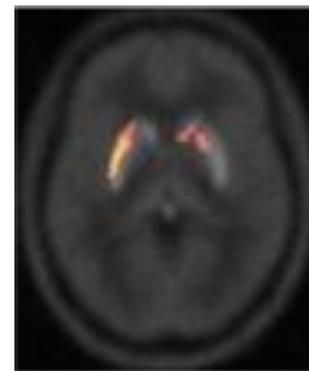
- Regions of Interest (ROI) defined in the striatum and functional subdivisions. [<sup>18</sup>F]-DOPA uptake relative to cerebellar reference region ( $K_i^{cer}$ ) calculated in each ROI.

- Voxel-based analysis of parametric  $K_i^{cer}$  images using SPM5.

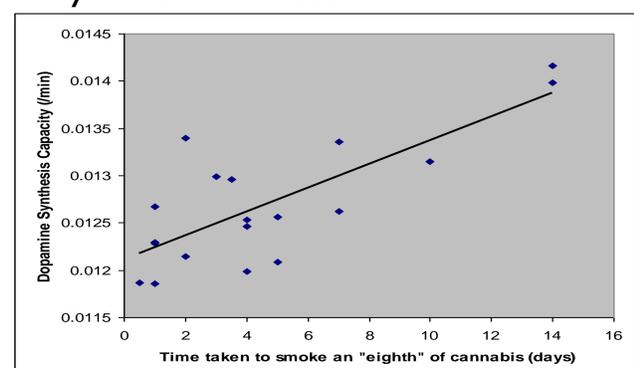
### RESULTS



- 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  $K_i^{cer}$  in the user group remained significant after co-varying for other drug use ( $F(1,37)=4.65$ ,  $p<0.05$ ).



- Voxel-based analysis confirmed reduced  $K_i^{cer}$  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.