Decreased Nigral Stress-induced Dopamine Response in Cannabis Users with and without Psychosis

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Background: Early cannabis use is an important environmental risk factor for developing psychosis, and have been linked with decreased striatal dopamine (DA) release. Striatal DA results from the activity of midbrain DA neurons projecting mainly from the substantia nigra. The influence of cannabis use on midbrain DA function remains unclear.

Objective: The current study aims to examine the effect of chronic cannabis use to nigral DA response in individuals with and without psychosis.

Methods: 24 subjects at clinical high risk for psychosis (CHR), 9 antipsychotic-naïve subjects with schizophrenia (SCZ) and 25 healthy volunteers (HV) underwent two positron emission tomography (PET) scans using the DA D₂/D₃ agonist radiotracer, [¹¹C]-(+)-PHNO. Psychosocial stress-induced SN DA release was estimated as the percentage differences in BPND (%[¹¹C]-(+)-PHNO displacement) between stress and sensory-motor control sessions.

Results: We observed a significant cannabis use by sessions interaction on [¹¹C]-(+)-PHNO BPND in the substantia nigra (F=8.79, p=0.004), with greater [¹¹C]-(+)-PHNO % displacement in non-cannabis users (10.90%) relative to users (-13.22%) across diagnostic groups. The effect of cannabis use on [¹¹C]-(+)-PHNO displacement did not differ between diagnostic groups (F=0.53, p=.59). A significant negative correlation between nigral [¹¹C]-(+)-PHNO displacement and negative symptoms was observed in CHR non-cannabis users (r=-0.89, p<0.001) but not in CHR cannabis users (r=-0.03, p=0.94).
Conclusions: Decreased nigral DA stress response is observed in chronic cannabis users with and without psychosis. Chronic cannabis use has similar effect on nigral DA stress responsiveness in individuals with psychotic spectrum disorder and otherwise-healthy individuals but may alter the underlying mechanisms of negative psychotic symptoms.