

ADULT COCAINE-INDUCED BRAIN METABOLIC ACTIVATION IS ALTERED IN A SEX-DEPENDENT MANNER BY CHRONIC PERIADOLESCENT CANNABINOID EXPOSURE IN RATS

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Introduction: Cannabinoid exposure during the periadolescent period has been shown to augment the rates of cocaine self-administration in female but not male Wistar rats[1]. However, how this cannabinoid history alters cocaine-induced brain activation remains unknown.

Methods: Male and female Wistar rats were administered with the cannabinoid agonist CP 55,940 (0.4 mg/2ml/kg i.p.) or its vehicle (ethanol:cremophor: saline; 1:1:18) once daily from postnatal day 28 to 38 (a period which encompasses the periadolescent developmental stage). At adulthood (postnatal day 100 approximately) brain metabolism was studied by PET imaging with 8F-Deoxyglucose (2 mCi) after saline injection and two days later after cocaine injection. All images were spatially registered[2], smoothed with a 1 mm isotropic Gaussian kernel and masked to remove extracerebral tissues. Voxel values were normalized to the overall brain average, analyzed with Statistical Parametric Mapping software (SPM5) at uncorrected $p < 0.001$ and extent threshold =10 voxels.

Results: Vehicle male Wistar rats showed a hypoactivation in the caudate-putamen after cocaine injection. Metabolic levels of CP-treated male rats remained the same after cocaine. CP-exposed females showed higher metabolism in the septal nuclei after saline, as compared to vehicle rats. However, cocaine injections induced a hypoactivation of the septal nuclei only in CP-females bringing the activation level of this structure to values similar to those of vehicle injected female rats (Figure 1).

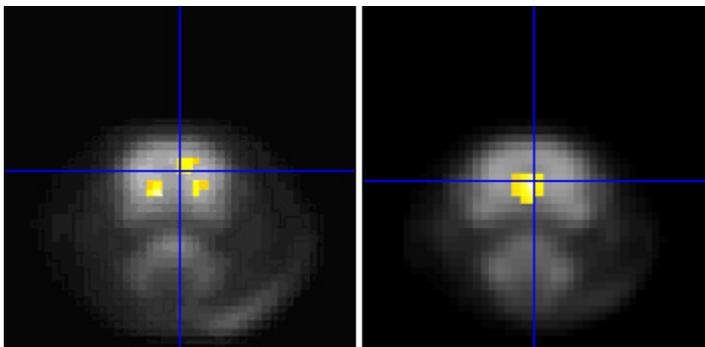


Figure 1: Representative coronal images, hypoactivation in the caudate-putamen after cocaine injection (males, left) and hypoactivation of the septal nuclei after cocaine injection (females, right).

Conclusions: A metabolic response was obtained after cocaine injection which depended upon sex and cannabinoid treatment. Given the involvement of the caudate-putamen and the septal nuclei in cocaine actions, these results may be relevant in explaining the altered susceptibility to cocaine effects in adult individuals exposed to cannabinoids during periadolescence.

References:

- [1] Higuera-Matas A et al; Neuropsychopharmacology. 33(4): 806-813 (2008)
- [2] Pascau J et al; Mol Imaging Biol. 11(2):107-113 (2009)