Methamphetamine Administration Affects CB1 Receptors and FAAH levels in the Striatum

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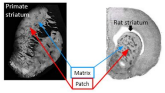
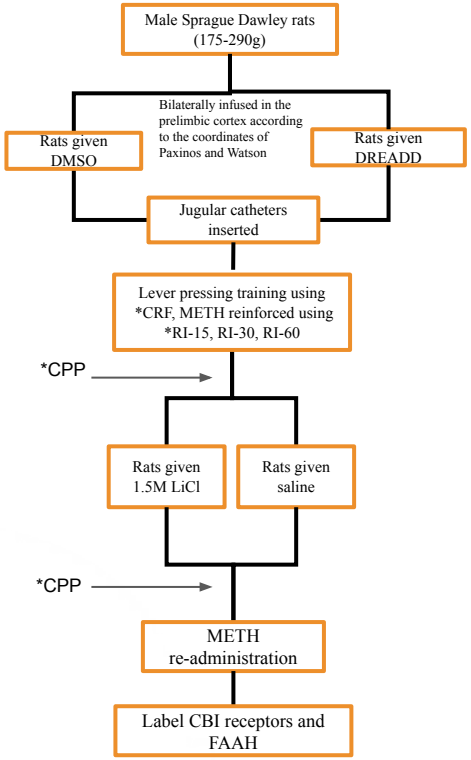
INTRODUCTION

- Habitual drug use is the continued use of drugs even if the reward is removed or replaced with aversion.
- Initial studies have shown that an imbalance between the patch and matrix compartments of the striatum might underlie habitual METH use. The high levels of mu opioid receptors in the patch are responsible for this imbalance (Jenrette et al., 2019).



- This project hypothesizes that habitual drug use will lead to a decrease in Cannabinoid receptor I (CBI) and an increase in Fatty Acid Amide Hydrolase (FAAH) levels.
- CBI is found in the axon terminal of neurons that originate in the sensorimotor cortex. Endocannabinoids bind to it and these neurons release glutamate. FAAH is an enzyme that hydrolyzes endocannabinoids (Horner, 2019).
- Methamphetamine (METH) use increases the endocannabinoid release (Nader et al., 2014), this might increase the levels of FAAH and decrease the number of cannabinoid receptors to maintain homeostasis. .

METHODS



*Conditioned Place Preference (CPP), *Continuous reinforcement (CRF), *Random interval (RI)

RESULTS

- Behavioral tests:

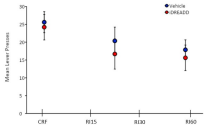


Fig 1: There was no significant difference between the DREADD and control rats in their ability to press levers for a METH reward for all the ratio and interval scales

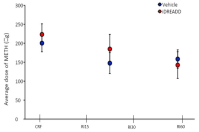


Fig 2: There was no significant difference between the DREADD and control rats in the amount of METH administered prior to pairing METH with LiCl

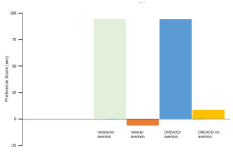


Fig 3: Non-Aversion group spent more time in the METH-paired side of the chamber. Aversion group spent less time in the METH-paired side

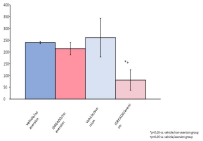
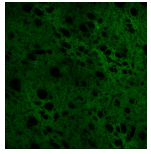


Fig 4: All groups that had Vehicle and/or Non-Aversion exhibited more lever presses than the DREADD rats which were given LiCl

- Immunohistochemistry:

Fig 5: Labelled CBI receptors in the matrix



DISCUSSION

It can be inferred that the impairment of the patch compartment can reduce habitual behavior as DREADD rats reduced METH use after it was paired with LiCl. Initial immunofluorescent staining of CBI was promising. However, co-localized staining of CBI and mu-opioid receptors need to be performed to draw conclusions about CBI levels between various groups and to determine if METH use is followed by CBI receptor changes. Since it is difficult to label enzymes such as FAAH, Oleoyl Trifluoromethyl Ketone, an FAAH inhibitor, will be used to determine if FAAH plays a role in long-term depression in the matrix following habitual METH self-administration.

REFERENCES

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