PKC γ actions related to mGluR5 within NAc shell on environment elicited cocaine conditioning

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Drug Addiction

- Principal Components:
  - Seeking and taking the drug compulsively
  - Losing the control of intake the drug
  - Developing a negative emotional response when the drug is not present.

Changes in neurotransmission systems within specific brain structures may induce drug reward effects associated with drug dependence.

Cocaine

Psychostimulant

Drug Abuse Potential
Mesolimbic Dopamine System

Figure 2 (above): Neurochemical neurocircuits in drug reward.
Figure 3 (right): Neurochemical neurocircuits in drug reward within Nucleus accumbens and Ventral tegmental area

Metabotropic glutamate receptor 5

All mGluRs are located within NAc subregions (core or shell).

Group I of mGluRs are critical in cocaine addiction.

If the mGluR5 stimulation is reduced, the drug-seeking behavior will be inhibited.

mGluR5 stimulation activates PKC.


Protein Kinase C (PKC)

Figure 4: mGluR5 molecular pathway.
Objective

Examine the effect of blockade of PKC \( \gamma \) in the expression of cocaine conditioning.
Methods

Animal Model
Male Sprague Dawley Rats (250g – 275g) from PSM. A total of 22 rats were used.

Surgery
Cannulae within the NAc shell were implanted in rats. Recovery period: 4 days
Cocaine Conditioning in Locomotor Activity Chambers

- Daily infusion directly to NAc shell
- 10 µM Ro 31-8220 mesylate (PKC inhibitor)
- Saline 0.9%

- Exposed to a specific environment
  - Visual (black) and olfactory (orange) cues
  - Systemic intraperitoneal cocaine injections (15mg/kg)

- Animals were placed in the chambers with the environment cues, but without any pre-treatment.

Microinfusion (0.5 µL/min) (D1 to D5)

Locomotive chambers (D1 to D5)

Test day (D7)
Data analysis

After D7, rats were sacrificed and their brains were removed and frozen for further histological analysis (cannulae verification).

Data from the TruScan Photobeam Activity System was obtained and presented as mean ± standard error of the mean (SEM).

Figure 9: Frozen rats brain of the experiment.
Figure 10: TruScan Photobeam Activity System Data spreadsheet with statistical analysis.
Results – Training Session

Figure 11: The effects of vehicle and PKC inhibitor infusions directly to the NAc shell during five consecutive days in the total move time of rats in the locomotor activity chamber.
Results – Training Session

Figure 12: The effects of vehicle and PKC inhibitor infusions directly to the NAc shell during five consecutive days in the ambulatory distance of rats in the locomotor activity chamber.
Results – Training Session

Figure 13: The effects of vehicle and PKC inhibitor infusions directly to the NAc shell during five consecutive days in the total movement of rats in the locomotor activity chamber.
Results – Testing Session

Figure 14 (left): The total move time of rats in the locomotor activity chamber with the previous environment cues, but without any pre-treatment; neither vehicle or PKC inhibitor.

Figure 15 (right): The ambulatory distance of rats in the locomotor activity chamber with the previous environment cues, but without any pre-treatment; neither vehicle or PKC inhibitor.
This preliminary data suggests a possible role of PKC \( \gamma \) on acquiring the association between an environment and cocaine use.

Further experiments are needed to fully characterize these findings.
Conclusion

There was no effect on cocaine sensitization.

Small effect on the cocaine conditioning expression was observed.


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