The MT₁ Melatonin Receptor As A Principal Mediator Of Methamphetamine-Induced Sensitization in C57BL/6

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Introduction

- Melatonin is a hormone which mediates circadian time keeping meaning it signals the duration of nighttime to the brain and peripheral tissues of the body.
- Methamphetamine (METH) is a psychostimulant that increases locomotor activity and euphoric sensations in the user.
- Genetic deletion of both MT₁ & MT₂ melatonin receptors abrogates locomotor sensitization in C3H/HeN mice that received 6 repeated METH pretreatments.¹
- Locomotor sensitization is a way to investigate long-lasting neuroadaptations through observing increases in the locomotor activity in magnitude as a result of repeated exposure to a drug of abuse.²
- However 6 repeated METH pretreatments did not induce locomotor sensitization in C57BL/6 mice.
- Previous work reported locomotor sensitization in C57BL/6 mice by a single high dose (5 mg/kg) METH pretreatment³ and by a single cocaine pretreatment.⁴

Goal
To investigate the role of MT₁ melatonin receptor in locomotor sensitization expressed by C57BL/6 mice after a single METH pretreatment.

Methods

Two Injection Protocol

- C57BL/6 mice: 6-8 week old males
- C57WT: Expresses MT₁ & MT₂ receptors
- C57MTKO: Genetic deletion of MT₁ receptor
- Tests at Zeitgeber time (ZT) 5-7 for day experiments and ZT 19-21 at night (ZT 0 = lights on, 12h:12h light-dark cycle)
- Drugs:
  - METH (1.2 mg/kg, i.p.)
  - Vehicle (VEH): Saline

Results

Day Experiments (ZT 5-7)

- Locomotor activity data (distance traveled) was collected and analyzed using the LocoScan Behavior Analysis System (CleverSys Inc., Reston VA)

Night Experiments (ZT 19-21)

- Locomotor activity data (distance traveled) was collected and analyzed using the LocoScan Behavior Analysis System (CleverSys Inc., Reston VA)

Conclusions

- Locomotor sensitization is expressed by C57BL/6 having both MT₁ and MT₂ receptors after a single pretreatment of METH.
- Genetic deletion of MT₁, melatonin receptors abrogates locomotor sensitization during day and night in METH-pretreated C57BL/6 mice.
- The MT₁ melatonin receptor regulates the sensitized response to METH and may be a good pharmacological target for drug discovery.

References

1. Hutchinson et al. (2010) Program 669.12, Neuroscience Meeting Planner

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