Effect of MDMA abuse on axonal transportation of serotonergic nervous system in the rat brain

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Introduction

Why do people take MDMA (Ecstasy)?

People take MDMA to energize their activities while feeling more open with and closer to fellow party-goers.

What are the risks of MDMA use?

The acute risk while on the drug is serotonin syndrome. Serotonin syndrome is caused by the increase of serotonin in the brain and is manifested as confusion, hypertension, tachycardia, hyperthermia, headache, dehydration, and seizures.

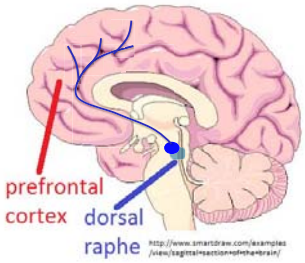
There are also short-term (days) and long-term (months to years) effects of MDMA use. The short-term effects include a serotonin deficit in the brain. This is because MDMA could inhibit the enzymes that synthesize serotonin. As a result, people feel depressed for days after uses.

The long-term effects are most likely due to changes in neural pathway. This includes (but is not limited to) serotonergic axonal transports between the raphe and prefrontal cortex. It is no doubt that an integral state of axonal transports would have a direct effect on the efficacy of serotonin neurotransmission.

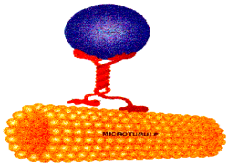
Hypothesis

Axonal transports have two opposite directions: retrograde and anterograde. We tested the hypothesis that MDMA abuse would impair both retrograde and anterograde transportation of the serotonergic neurons, resulting in long-term injury of serotonin transmission.

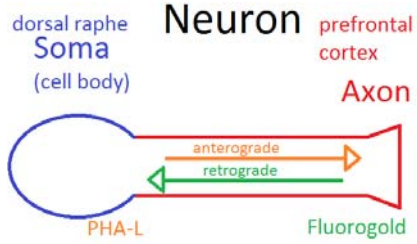
Background



The nervous system is made up of many cells called neurons. The nervous system uses serotonin as a neurotransmitter to stimulate postsynaptic neurons that control the feelings of well-being and closeness. The somas, or bodies, of these serotonergic neurons are mainly located in the midbrain dorsal raphe nucleus. The axons, which are the part of the cell going away from the somas, are distributed throughout the brain, including the prefrontal cortex. The soma and the axon terminals are always dynamically communicating by anterograde and retrograde transports. Their pathways are made up of microtubules that run down the length of the axon, which are used by carriers to carry substances between the cell body and the axon terminal.



In the laboratory, the integrity of these pathways can be estimated using fluorescent tracers. In this study, PHA-L was used for an anterograde tracer and fluorogold as a retrograde tracer.



Procedure

Day 1: MDMA administered to rats

Day 7: PHA-L to the dorsal raphe or fluorogold to the prefrontal cortex.

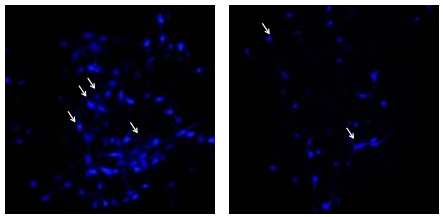
Day 14: Immunohistochemistry using fluorescent microscope

Results

Test 1: Retrograde Investigation

The integrity of axonal transports from the axon terminals to somas was examined with fluorogold that was previously injected in the prefrontal cortex.

Saline-treated MDMA-treated



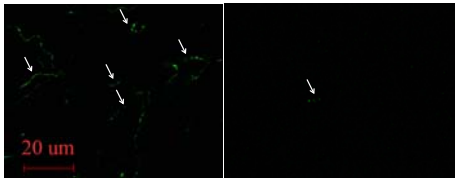
Left panel (control): There were numerous raphe cells that received the fluorogold previously injected in the prefrontal cortex

Right panel: In contrast, fewer cells had received fluorogold after MDMA abuse.

Test 2: Anterograde Investigation

The integrity from the raphe somas to cortical axon terminals was examined with the anterograde tracer PHA-L.

Saline-treated MDMA-treated



Left panel (control): The green fluorescents (indicated by arrows) are the axons using an antibody against PHA-L previously injected in the raphe region.

Right panel: Fewer cortical axons received PHA-L injected into the raphe in the animals treated with MDMA.

Discussion

There are many molecules involving in axonal transports such as microtubules, dynein and kinesin. At this point, however, we do not know what molecules can be impaired by MDMA abuse. Thus, it would be important in the future study to extend the current research and identify specific molecules.

Conclusion

MDMA abuse likely impairs both retrograde and anterograde axonal transports, resulting in the long-term injury of serotonin transmission in the brain.

Acknowledgement

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