

# Locomotor and Discriminative Stimulus Effects of Six Synthetic Cathinones

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## Introduction

Synthetic cathinones, also known as "Bath Salts" are man-made stimulants which are chemically related to cathinones. They have similar effects to amphetamines, which are psychomotor stimulants that disrupt the normal reuptake of dopamine, norepinephrine, and 5-HT (Baumann et al.). Thus, producing a rewarding experience for the user. There has been an increase in the number of synthetic cathinones flooding the streets as "legal highs". This has caused the legal system to struggle in an attempt to classify these drugs and define their abuse potential. Knowing the abuse potential is important to make users aware of the compounds' psychological and physical consequences. The purpose of this study is to determine if BDMP, MMMP, 3-MMC, 4F-3Me- $\alpha$ -PVP, 4-CDMC, and 3,4-MD-PV8 cause similar behavioral effects in the locomotor activity and discriminative stimulus assays as methamphetamine.

## Materials & Methods

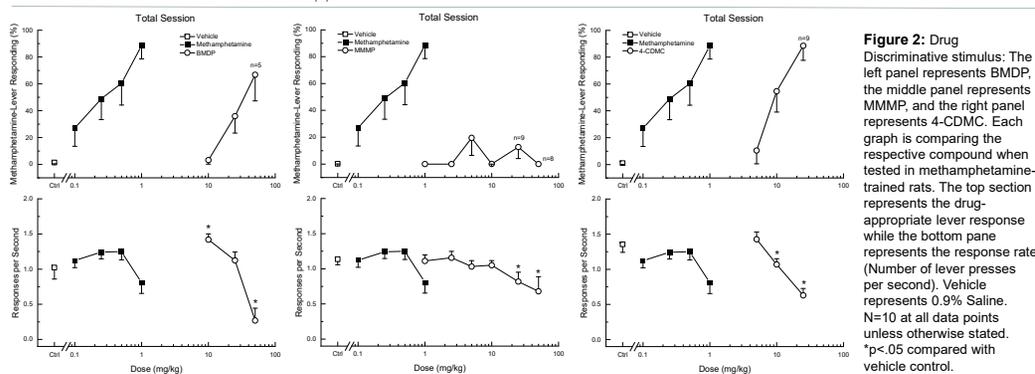
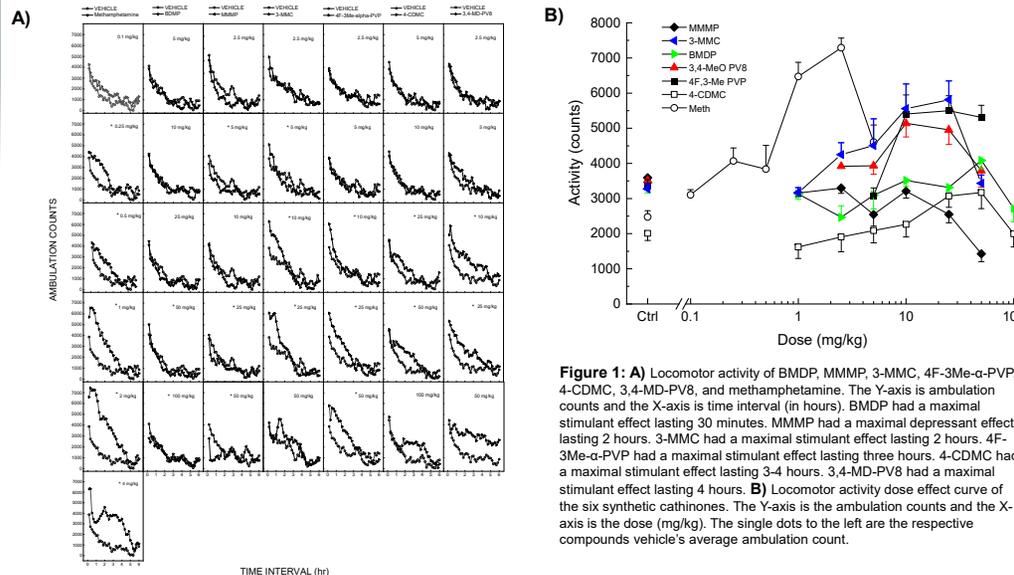
### Locomotor Activity

Separate groups of 8 non-habituated male Swiss-Webster mice were tested in a time course/dose-response study of the effects of the test compounds on locomotor activity. Tests were conducted in clear acrylic locomotor activity testing chambers within sound-attenuating chambers. Activity was monitored by panels of photobeams and photodetectors located horizontally along the sides of the chamber. Separate groups of eight mice were injected (IP) with either vehicle (0.9% saline) or test compound immediately before testing. Horizontal activity was measured for 6h within 10-min periods.

### Drug Discrimination

32 single-housed, adult male Sprague-Dawley rats were trained to discriminate between IP injections of methamphetamine (1 mg/kg) and 0.9% saline. The rats were trained to identify these treatment conditions in a double-alternating pattern (i.e.: day 1-2: drug; day 3-4: saline), then tested under an FR10 schedule when they achieved 80% treatment-appropriate lever responding in 8 out of 10 sessions (in first reinforcer and total session). Following successful treatment identification, substitution tests for BMDP, MMMP, and 4-CDMC were conducted.

## Results



## Summary

- In the locomotor activity test, all of the compounds were less potent and less efficacious than methamphetamine ( $ED_{50}$ =0.59 mg/kg).
- Potencies of the test compound ranged from 4.36 to 40.2 mg/kg with rank order of potencies: 3-MMC>3,4-MD-PV8= 4F-3Me- $\alpha$ -PVP > 4-CDMC>BMDP>MMMP
- In the drug discrimination test, only 4-CDMC fully substituted for the discriminative stimulus effects of methamphetamine.
- BMDP produced only 67% methamphetamine-appropriate responding at 50 mg/kg. Higher dose were not tested due to rate suppressant effects.
- Methamphetamine ( $ED_{50}$  = 0.31 mg/kg) was more potent than BMDP or 4-CDMC ( $ED_{50}$ = 4.9 mg/kg).
- All of the compounds tested significantly decreased response rate at the top doses tested.

## Conclusions

- Most of the test compounds have abuse liability similar to (+)-methamphetamine, although the locomotor stimulant effects of BMDP and 4-CDMC were modest.
- MMMP was a depressant and had no meth-like discriminative stimulus effects, so likely has low abuse liability.

## References

Baumann, M. H., Walters, H. M., Niello, M., & Sitte, H. H. (2018). Neuropharmacology of Synthetic Cathinones. Handbook of experimental pharmacology, 252, 113–142. [https://doi.org/10.1007/164\\_2018\\_178](https://doi.org/10.1007/164_2018_178)

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