



NEUROSCIENCE 2012

 [Print this Page for Your Records](#)

[Close Window](#)

Control/Tracking Number: 2012-S-2945-SfN

Activity: Scientific Abstract

Current Date/Time: 5/3/2012 3:51:33 PM

Meth Math: Modeling temperature responses to methamphetamine

AUTHOR BLOCK: *Y. I. MOLKOV¹, D. V. ZARETSKY², M. V. ZARETSKAIA², P. J. DURANT², D. E. RUSYNIAK²;

¹Dept. of Mathematical Sci., Indiana Univ. - Purdue Univ. Indianapolis, Indianapolis, ; ²Emergency Med., Indiana Univ. Sch. of Med., Indianapolis, IN

Abstract:

Methamphetamine (Meth) can evoke extreme hyperthermia, which correlates with both neurotoxicity and death in laboratory animals and humans. The physiologic and pharmacologic mechanisms behind complex dose-dependency of temperature responses to Meth are not well understood in part due to Meth's complex pharmacology, which involves numerous neurotransmitters, receptors, and both central and peripheral sites of action. This complexity lends itself well to the use of mathematical modeling. The objective of this study was to model the neural circuitry involved in temperature responses to Meth.

Methods: Rats were implanted with telemetric transducers to record core body temperature. After recovery, we injected rats with one of three doses of Meth (1, 5, and 10 mg/kg) or a saline vehicle (n=6 for each dose). Based on the known thermoregulatory circuitry we created an artificial neural network involving three nodes (supramedullary, medullary and submedullary). These were connected sequentially, and were individually affected by Meth. Each neuronal population was described as a three layer perceptron. Both absorption from peritoneal cavity and elimination from blood stream were considered to follow first order pharmacokinetics.

Results: Temperature responses to Meth were complex and dose-dependent: Low doses (1 mg/kg) caused an immediate rise, rapid peak, and short duration of hyperthermia; Moderate doses (5 mg/kg) caused a delayed rise and peak, but prolonged duration of body temperature increases; High (10 mg/kg) doses caused an immediate rise, rapid peak, and prolonged increase in body temperature. All model parameters (weights of connections, sensitivity to the drug, pharmacokinetics and temperature response time constants) were subject to fitting these three time-series. Our model fits the experimental temperature curves within one standard deviation.

Our model suggests that temperature responses to a low dose of Meth involve neuronal excitation at a supramedullary level. The delay in peak response seen with a moderate dose of Meth involves neuronal inhibition at the medullary level. Finally, the rapid and robust increases in body temperature induced by a high dose of Meth involve excitation at the submedullary level.

Conclusion: Our mathematical model reveals that at least three potential neuronal thermoregulatory areas, with different sensitivities, are required to describe Meth's unique dose-dependent temperature responses. Further characterizing this model, and the putative neuronal sites of action, may lead to more effective strategies of prevention and treatment of amphetamine-like stimulant-induced hyperthermia.

:

Presentation Preference (Complete): Poster Only

Linking Group (Complete): None selected

Nanosymposium Information (Complete):

Theme and Topic (Complete): E.04.e. Thermoregulation ; C.17.m. Cocaine, amphetamine and related drugs:
Toxicity

Keyword (Complete): TEMPERATURE ; METHAMPHETAMINE ; MODELING

Support (Complete):

Support: Yes

Grant/Other Support : NIH Grant DA026867

Grant/Other Support : iM2CS-GEIRE

Special Requests (Complete):

Is the first (presenting) author of this abstract a high school or undergraduate student?: None

Religious Conflict?: No Religious Conflict

Additional Conflict?: No

Status: Finalized

[OASIS Helpdesk](#)

Powered by [OASIS](#), The Online Abstract Submission and Invitation System SM

© 1996 - 2012 [Coe-Truman Technologies, Inc.](#) All rights reserved.