# Core Body Temperature Regulation and Locomotor Activity

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Methamphetamine (Meth) enhances locomotor activity, and is known to cause life-threatening hyperthermia. There has been much debate about whether the locomotion plays a major role in hyperthermia caused by Meth or other stimulants. The existing model of the neural circuitry putatively involved in this phenomenon [1] accurately reproduces the temperature response to the different doses of Meth. We compared locomotor activity observed in the same experiments with activation patterns of neuronal populations as predicted by the model. We found that time-courses of locomotor activity closely resembles the activity of one particular node in the model putatively representing the medullary level. However, the data on locomotion did not match the model in the initial phase of the response within 1 hour after the injection. Therefore, we hypothesized that there were some changes in thermogenesis and heat exchange mechanisms that largely control temperature response during the first hour and make the influence of locomotion relatively small.

The objective of the study was to measure the temperature dynamics in rats running on a treadmill at different speeds and to construct a mathematical model explaining the mechanism of their core body temperature response to such an intervention that takes into account potential changes in heat exchange, sensory input and feedback control mechanisms. In the experiments for every speed of 0, 6, 12, and 18 m/min we had 4 rats running for 15 min. For each speed we averaged the temperature over 4 rats to get the average temperature response curve. First, we found that the temperature response curves for different treadmill speeds were not different statistically. Second, every response curve starts with a short but profound (~0.25 deg C in the first 5 min) drop in the body temperature followed by virtually linear rise of the temperature which significantly (by ~1 deg C) overshoots the baseline temperature.

To explain these findings we set up a model in a form of a system of two differential equations that described the change in the body temperature and the change in the body heat production under the hypothesis that there are contributions of varying heat exchange, sensory input and feedback mechanisms in thermogenesis. All parameters in the system were subject to fitting experimental time series of temperature response of rats to 4 consistent speeds of 0, 6, 12, and 18 m/min on treadmills. We found, that a sudden drop of the body temperature below the baseline in the first five minutes after rats were removed from their cages and placed on a treadmill was a result of the increased heat dissipation caused by changes in the body position and movement of rats. The following fast recovery of the body temperatures to the normal level was provided by the feedback mechanisms activated by the temperature drop and changed sensory input. Meth continues to stimulate thermogenesis even after the baseline temperature is achieved from feedback mechanisms. Estimated contribution of the locomotion was negligible as compared to the latter and hence played a relatively small role in the temperature change. We predict that varying locomotion might manifest itself in temperature dynamics after much longer (~1 hour) exposure to running.

The suggested system, which considers major factors defining body temperature response, can help to uncover the mechanisms of hyperthermia elicited by Meth, but also can be used to understand the thermoregulatory mechanisms which underlie the responses to simultaneous changes in environmental and physical conditions.

## References

[1] Y. I. Molkov, M.V. Zaretskaia, D.V.Zaretsky. Meth Math:Modeling Temperature Responses to Methaphetamine. Am J Physiol Regul Integ Comp Physiol. (Feb. 5, 2014). (doi:10.1152/ajpregu.00365.2013).