

COMMENTS

Response to the Comments by D.M. Aronoff

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We appreciate the constructive comments of Dr. Aronoff. Our present article, indeed, did not touch the direct and/or indirect effects of endogenous pyrogens possibly activated by orexins on thermogenesis. We are very much in agreement with Dr. Aronoff's proposal, because a series of our studies on central thermoregulation reported that endogenous pyrogens mediated activation of hypothalamic histamine neurons. Additionally, hypothalamic histamine and orexins neurons are known to make tight neuronal networks and functional coordination. In our present paper, however, the results concerning pyrogens are too voluminous to be included. The effects of orexins on endogenous pyrogens together with the effects of potency in cyclooxygenase blockade on the orexins-induced thermogenesis were already investigated. Since hy-

pophagia, hypothermia, and arousal level regulated by hypothalamic histamine neurons seem to have a tightly functional relation with orexin neurons, a series of advanced studies on the neuronal projection(s) between those two-neuron systems has been carried out using H₁ receptor deleted mice and is now almost finalized. The corresponding behavioral and physical evaluations are in progress now. We plan to report these findings in another publication not only for reinforcement of the present results but also for demonstration of further advanced concept that histamine-induced circadian thermoregulation is controlled, at least in part, by orexins neurons. This is the main reason why we did not include the findings recommended by Dr. Aronoff. We hope readers would generously understand the reasons.