Response to the Comments by R.L. Henkin

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The comment submitted by Dr. Robert I. Henkin that histamine-induced zinc deficiencies involved in the mechanism of feeding suppression is quite welcome. This query is essential and important for our better understanding of the effects of histamine and/or histidine on appetite. The definite answer to his question is still in need of further experimental verification. However, the possibility that his proposal will eventually be accepted appears to be quite low, for the following reasons: 1) There is a crucial methodological difference between Dr. Henkin's studies and ours. Our treatment with histidine was not sustained administration as he did, but a single one. 2) No specific behavioral change including motor dysfunction induced by zinc deficiency was detectable in our animals after histidine administration. 3) Suppression of food intake in our study was limited to the first day after the administration. The suppressive effect of histidine completely disappeared on the second day without any treatment such as supplementation of zinc. In contrast, anorexia in his study was detected 4 to 5 days after the first dose of histidine. 4) Pretreatment with α-fluoromethylhistidine (FMH), a suicide inhibitor of histamine synthesizing decarboxylase enzyme, attenuated histidine-induced feeding suppression in the present study. This result implies that histamine synthesized from histidine, but not histidine per se, affects food intake. Assuming that histidine-induced zinc deficiency is a major factor in the suppressive effect on food intake, it does not seem reasonable to explain the results from the FMH study together with other findings. At this point, however, our data do not permit us to exclude involvement of zinc deficiency in histamine-induced anorexia. Further studies will be needed to finalize the debate because we did not measure zinc concentration.