COMMENTS

We welcome comments by our readers reflecting agreement or disagreement with the material published in Experimental Biology and Medicine *and, at the discretion of the Editor-in-Chief, will publish such comments.*

Comments to the Editor Concerning the Paper Entitled "Histidine Suppresses Food Intake through Its Conversion into Neuronal Histamine" by Yoshimatsu et al.

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While the authors of the manuscript "Histidine Suppresses Food Intake through Its Conversion into Neuronal Histamine" may have identified one aspect of histidine effects on suppressing food intake they have neglected to recognize several prior studies which demonstrated histidine-induced suppression of food intake by a direct effect on zinc metabolism (1–3). Histidine is an extremely bioactive amino acid which has multiple physiological functions. It plays a major role in zinc metabolism acting as the major zinc binding moiety in serum (1–3). Normally, zinc is bound to one or two of the available 16 histidine moieties on albumin (1, 2). Administration of histidine to animals (3) or humans (4) strips zinc from its albumin binding sites initiating a Zn-His complex which produces significant tissue zinc depletion and (15) manifested by subsequent increased urinary zinc excretion. Through this mechanism, it causes severe pathological changes in multiple organ systems by a type of "chelation" of zinc (1–3). In animals, it causes zinc deficiency (3). In humans, it also causes zinc deficiency leading to functional losses of taste, smell, appetite and food intake and other neurological abnormalities (4).

These effects are reversed completely by zinc administration while maintaining histidine intake at any given level, indicating that histidine-induced suppression of appetite relates specifically to this mechanism of zinc depletion (4) since taste and smell function, appetite and food intake all returned to normal through this effect. Indeed, loss of appetite with histidine administration through this induced zinc deficiency was used as a novel technique to induce reduced food intake in humans and to induce human weight loss (5, 6). In this sense it was and has been used as an anorexergeric agent albeit there can be significant side effects with this use due to the effects of zinc depletion on these multiple organ systems (4).

While there are multiple layers of activity related to administration of a chemical moiety as active as histidine it is important and relevant for authors to review the past, not just the relatively recent, literature so that a more complete understanding of the effects they perceive can be placed in the complex of mechanistic and physiological understanding.

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