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The mechanism of interaction of GLP-1 and leptin on feeding in rats

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Glucagon-like peptide-1 (GLP-1) and leptin are anorectic hormones produced in the small intestine and white adipose tissue, respectively. Investigating how these hormones act together as an integrated anorectic signal is important to elucidate a mechanism to regulate feeding. We here demonstrate that coadministration of subthreshold GLP-1 and leptin dramatically reduces food intake in rats. Although coadministration of GLP-1 with leptin did not enhance leptin signal transduction in the hypothalamus, it significantly decreased phosphorylation of AMP-activated protein kinase (AMPK). In addition, co-administration of GLP-1 with leptin significantly increased proopiomelanocortin (POMC) mRNA levels. Considering that α-melanocortin stimulating hormone (α-MSH) is derived from POMC and functions through the melanocortin-4-receptor (MC4-R) as a key molecule involved in feeding reduction, the interaction of GLP-1 and leptin on feeding reduction may be mediated through the α-MSH/MC4-R system. As expected, the interaction of GLP-1 and leptin was abolished by intracerebroventricular preadministration of the MC4-R antagonists such as agouti-related peptide and SHU9119. Taken together, GLP-1 and leptin cooperatively reduce feeding at least in part via inhibition of AMPK following binding of α-MSH to MC4-R. Furthermore, we present that this interaction of GLP-1 and leptin was canceled in rats with midbrain transaction. This finding indicates that the hindbrain would be important to integrate the information of interaction of GLP-1 and leptin.

Biography

Yukari Date has completed her MD at the age of 25 years from Oita Medical College and PhD at age of 34 from University of Miyazaki. After graduation of doctor course, she continued her studies regarding to feeding and energy metabolism as a postdoctoral fellow at National Cardio-Vascular Research Canter and University of Miyazaki. She is the Professor of Frontier Science Research Center, University of Miyazaki. She has published more than 80 papers in reputed journals.

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