Research Highlight

Hormone level and dopamine tells the value of food

Zuo-ren WANG*

Acta Pharmacologica Sinica (2012) 33: 208–209; doi: 10.1038/aps.2011.211; published online 16 Jan 2012

Ideal food should be delicious and nutritious. But sometimes, the food you eat is delicious but not nutritious, or nutritious but not delicious. To let animals know which to be delicious or nutritious is an important or valuable question. In a recent article published in *Nature Neuroscience*^[1], Friedman JM *et al* addressed this question and showed that the level of hormone leptin and dopamine system co-regulated the reward value of food in mice.

Leptin, a 16 kDa protein encoded by the Ob (Obese) gene, is a hormone that has a central role in regulation of fat metabolism, appetite and the balance between energy intake and consumption^[2]. Leptin was identified and its role in fat metabolism was firstly revealed by Friedman JM *et al* in 1994. In mouse genetic screen study, they found that mutation in the genes encoding either leptin itself or leptin's receptor caused massively obese in mice, and this could be rescued by injections of leptin. These findings in mice coincided with the observations that humans carrying homozygous mutations in leptin gene suffered severe obesity. These results indicated that leptin signals are important in regulating fat metabolism. Later studies revealed that instead of a signal to consume the surfeit of fat, leptin is

a signal informing the brain of enough nutrients in the body. Thus, when an animal is full up, its leptin level goes high that in turn sends a satiety signal to the brain and stop the animal from eating more. On the contrary, when an animal is in hunger, its leptin level drops, thus sends less satiety signal to the brain; and this drive the animal to looking for nutritious food.

Dopamine is a neurotransmitter involved in modulating many important brain functions. Dopamine is released by the dopaminergic neurons in hypothalamus, substantia nigra and especially ventral tegmental area (VTA) — a brain region tightly linked with rewarding process. Many studies showed that rewarding process is highly related to the activation of the dopaminergic neurons in the VTA of the middle brain^[3]. A trick that the authors used in their research is to mimic the rewarding process by specifically activating of the dopaminergic neurons in VTA.

The technique that Friedman JM *et al* used in this article is optogenetics, a recently developed tool, in which light-activatable cation channel (*eg*, Channelrhodopsin II, ChR2) or light-activatable chloride pump (*eg*, Halorhodopsin from *Natromonas*, NPHR) are used to activate or silent the function of the interested neurons^[4]. They generated a kind of genetically engineered mice, in which ChR2 protein was specifically expressed in the dopaminergic neuron in VTA. An optic fiber was then introduced to the VTA of the mice. When laser pulses

were delivered to VTA through the optic fiber, the dopaminergic neurons were activated, mimicking a rewarding process. Next, they measured the preference index of the mice to two kinds of “sugar”, sucrose and sucralose. Sucrose is a kind of natural sugar with nutrient, which sucralose is a synthetic sweetener with very low calories. They found that the mice naturally prefer the nutritious sucrose to the low-calorie sucralose, suggesting that nutrient of sucrose confer it a higher rewarding value, and sucralose has a lower rewarding value. Interestingly, this could be reversed when sucralose was paired with activation of the dopaminergic neurons. When the sucralose solution was applied to the mice, laser pulses were simultaneously delivered to activate the dopaminergic neurons in VTA. In this scenario, the mice switched to prefer sucralose. These results suggest that preference to a food not only depends on the sensation on the tongue, but also the brain judgment of its reward value of the food. Furthermore, the authors investigated whether the leptin level affects the judgment of food reward value. When the mice were deprived for food for 24 h, the dropping of leptin level coincided with that the value of sucrose increased. Upregulation of leptin by injection can reverse this effect. These results indicated that leptin could regulate the reward value of nutrient.

The findings made by the authors are not only important to our fundamental understanding of the regulatory mecha-

Institute of Neuroscience, State Key Laboratory of Neuroscience, Shanghai Institutes for Biological Sciences, Chinese Academy of Sciences, Shanghai 200031, China

Correspondence: Prof Zuo-ren WANG
(zuorenwang@ion.ac.cn)

nisms of appetite and fat metabolism, but also provide important clues for weight control and therapeutics for metabolism-related disorders, such as obesity and nervosa. If the leptin level in people with obesity or nervosa can be modulated, their appetite or desire for

food, and their body weight can be controlled.

1 Domingos AI, Vaynshteyn J, Voss HU, Ren X, Gradinaru V, Zang F, *et al.* Leptin regulates the reward value of nutrient. *Nat Neurosci* 2011; 14:

1562–8.

- 2 Friedman JM. Leptin at 14 y of age: an ongoing story. *Am J Clin Nutr* 2009; 89: 973S–979S.
- 3 Schultz W. Getting formal with dopamine and reward. *Neuron* 2002; 36: 241–63.
- 4 Fenno L, Yizhar O, Deisseroth K. The development and application of optogenetics. *Annu Rev Neurosci* 2011; 34: 389–412.