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HOT TOPICS

"Neuroanatomical integration of homeostatic and hedonic brain regions to regulate consummatory behavior"

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Food consummatory behavior is a complex process that serves to maintain physiological homeostasis while simultaneously encoding the hedonic properties of food [1]. Hedonic foods (i.e., foods high in sugar and fat) are more reinforcing than low-calorie foods and robustly activate brain regions driving motivation, which promotes overconsumption regardless of homeostatic state. This hedonic "override" is thought to contribute to weight gain and obesity. As highly palatable foods continue to become more accessible and rates of the metabolic disease continue to increase, it is evident that there is a crucial need to enhance our understanding of the neural circuits that integrate homeostatic and hedonic pathways to identify novel therapeutic strategies to restore balanced consummatory behaviors.

The nucleus accumbens (NAc) is a brain region involved in motivation and food consumption [2]. In addition, a role for accumbal glutamate in consummatory behavior has been described where intra-NAc administration of AMPA receptor antagonists promotes the intake of food [3]. Although the NAc receives input from the midbrain, cortical, and thalamic structures, much remains to be learned about afferents from structures involved in maintaining homeostasis of consummatory behavior, such as the hypothalamus. Direct neuronal projections from the paraventricular nucleus of the hypothalamus (PVN) to the nucleus accumbens were identified in the context of social reinforcement [4]. In these studies, the PVN was shown to project directly to the NAc to regulate oxytocin and serotonin release and promote the reinforcement of social interactions in mice. However, a role for the PVN → NAc pathway in regulating food intake remained unstudied.

New work demonstrates that DREADD-based activation of the PVN → NAc circuit in rats stimulates the release of glutamate in the NAc and results in decreased intake of highly palatable food [5]. The neuronal origins of the PVN → NAc circuit were localized to parvocellular-rich regions of the anterior, medial, and posterior PVN. Additionally, glutamate was identified as the primary neurotransmitter utilized by this pathway thus providing a source of glutamate into the NAc in the regulation of food intake. Using viral-based tract-tracing and immunohistochemistry, the authors also demonstrate that neurons in the PVN → NAc pathway express VGLUT1, a marker of glutamatergic neurons. Furthermore, DREADD stimulation of the PVN → NAc pathway increased glutamate release in the NAc as measured by microdialysis.

It is becoming clear that the neural mechanisms underlying homeostatic and hedonic food intake are more integrated than previously recognized and suggests that as a field, we may need to rethink the overarching concepts of eating for pleasure vs eating to maintain energy balance. The direct neural interaction between homeostatic (PVN/hypothalamus) and hedonic (NAc) brain regions to regulate food intake provides evidence that these consummatory behaviors are biologically interlocked. Furthermore, compounds that facilitate glutamatergic output of the PVN → NAc circuit may represent a viable therapeutic strategy to normalize food consummatory behavior and decrease the burden of obesity and metabolic diseases.

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AES and JDH drafted, edited, and approved the final version.

ADDITIONAL INFORMATION

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