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Review

Nutritional Controls of Food Reward

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ABSTRACT

The propensity to select and consume palatable nutrients is strongly influenced by the rewarding effects of food. Neural processes integrating reward, emotional states and decision-making can supersede satiety signals to promote excessive caloric intake and weight gain. While nutritional habits are influenced by reward-based neural mechanisms, nutrition and its impact on energy metabolism, in turn, plays an important role in the control of food reward. Feeding modulates the release of metabolic hormones that have an important influence on central controls of appetite. Nutrients themselves are also an essential source of energy fuel, while serving as key metabolites and acting as signalling molecules in the neural pathways that control feeding and food reward. Along these lines, this review discusses the impact of nutritionally regulated hormones and select macronutrients on the behavioural and neural processes underlying the rewarding effects of food.

RÉSUMÉ

La propension à choisir et à consommer les nutriments palatables est fortement influencée par les effets de récompense des aliments. Les processus neuronaux intégrant la récompense, les états émotionnels et la prise de décision peuvent supplanter les signaux de satiété pour favoriser l'apport calorique excessif et la prise de poids. Alors que les habitudes alimentaires sont influencées par les mécanismes neuronaux de récompense, la nutrition et ses conséquences sur le métabolisme énergétique jouent en retour un rôle important dans la maîtrise de la récompense alimentaire. L'alimentation module la libération d'hormones à activité métabolique qui ont une influence importante sur la régulation centrale de l'appétit. Les nutriments eux-mêmes sont également une source d'énergie essentielle, servant de métabolites principaux et agissant comme molécules de signalisation dans les voies neuronales qui maîtrisent l'alimentation et la récompense alimentaire. Dans cet ordre d'idées, cette revue discute des conséquences des hormones régulées par l'état nutritionnel et des macronutriments sur les processus comportementaux et neuronaux sous-jacents aux effets de récompense des aliments.

Introduction

The brain relies on nutrition not only for provisional building blocks and source of energy fuel but also for its primary capacity to modulate metabolic signals that play an essential role in central nervous system (CNS) function. Nutritional influence on central controls of appetite is largely driven by the action of ingested foods to modulate endocrine hormones, cytokines, gut chemosensors and lipid molecules that cross the blood brain barrier (BBB) or signal via nerve inputs to the CNS. However, beyond these roles, increasing evidence is drawing attention to the capacity of nutrients to directly modify neural signalling, excitability and connectivity. The BBB is permeable to a number of biologically relevant substances, such as endogenous and exogenous compounds and soluble lipids and amino acids. We are only beginning to comprehend the multiple ways by which nutrition affects the brain. Indeed, the field of nutritional neuroscience is currently experiencing intense growth and interest.

Study of the impact of nutrients on the neural pathways controlling energy metabolism is rapidly expanding. A burgeoning line of investigation examines the deleterious effects of nutrient overload and its pro-inflammatory consequences on the neural pathways and mechanisms influencing energy homeostasis (1). The

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neurobehavioural processes that bridge emotions and feeding are now well-recognized to play a significant role in overeating and the development of obesity. Thus the present review discusses selected findings of our current knowledge of the impact of nutritionally regulated hormones, macronutrients and diet-induced obesity on brain reward circuitry.

Reward and appetite

Hunger and satiety signals generated by hypothalamic and hindbrain structures play a central role in feeding; however, why, when and what we eat are also powerfully affected by emotional, motivational and decision-making processes generated by corticolimbic pathways (2). Palatable (i.e. tasty) high-fat and high-sugar foods are rewarding. Consuming palatable, energy-rich foods activate components of the neural circuitry underlying reward and motivation to strengthen action-outcome associations and reinforce future behaviour directed at obtaining these foods. Consequently, the decision to eat is swayed by the rewarding effects of food in both conditions of hunger and satiety. The heightened emotional and behavioural responses to high-fat and sugar foods that evolved can be understood in terms of what these foods offer in energy value. In conditions of food scarcity, reward signals promote adaptive behavioural responses by enhancing motivation to procure high-calorie foods. Conversely, when energy-rich foods are abundant and require relatively little effort or cost to obtain, reward-based mechanisms can lead to a maladaptive outcome by promoting excessive caloric intake and weight gain. The significance of reward processing in the etiology of obesity is increasingly recognized. Sensitivity to food rewards is positively correlated with overeating and weight gain (3). Additionally, obese individuals show greater activation in corticolimbic brain regions important for reward and emotion in response to visual food stimuli (4–6). Our understanding of the biological basis of body weight regulation and obesity requires teasing apart the neural circuitry underlying the rewarding properties of food.

The study of food reward addresses the influence of metabolic signals, nutrients and emotional states on behavioural responses to food stimuli or their impact on neurobiological pathways and mechanisms regulating food reward. Importantly, not all factors that alter feeding, influence food reward. To assess the rewarding effects of food, operant (effort based) (7,8) or associative conditioning (e.g., conditioned place preference [9]) procedures can be used that measure goal-oriented behaviour for food. In humans, the rewarding (or hedonic) properties of food can be determined with subjective ratings of pleasantness or liking in response to visual images of food or food taste. Hedonic responses to taste in mammals are also studied using the taste reactivity paradigm (10). It is important to note that while the orosensory properties of food (i.e. palatability) play a role in food reward, brain reward circuits are largely influenced by the postingestive impact of calorie-dense nutrients independent of taste transduction (12). Last, the rewarding properties of different macronutrients can be selectively altered; for example, certain physiological and pharmacological manipulations can affect the rewarding effects of fatty foods without changing motivation for carbohydrate-rich foods. Thus, while this review concerns the influence of nutrition on food reward, it is important to note that reward-based mechanisms can in turn impact nutrient selection and intake.

Neural pathways and signals

Critical for neuroendocrine, autonomic and homeostatic functions, the hypothalamus is a brain structure with distinct nuclei that integrate blood-borne signals, such as hormones and nutrients, with brainstem and corticolimbic inputs to coordinate feeding, energy expenditure and glucose homeostasis. Information about the emotional and motivational aspects of feeding is generated by corticolimbic processes that can exert a powerful influence over hypothalamic centres to affect the type and amount of food ingested. Dopamine (DA) neurons of the mesocorticolimbic and nigrostriatal systems are an essential component of the neural circuitry underlying food reward. As shown in Figure 1, these 2 DA pathways originate in the midbrain and project to limbic and cortical structures that give rise to emotions, motivation and cognition (11,12). The nucleus accumbens (NAc), part of the ventral striatum, is considered an interface for emotion, motivation and action based on its numerous inputs from amygdala, prefrontal cortex (PFC) and hippocampus. A key structure for the processing of emotions and interpreting emotionally relevant stimuli is the amygdale, which integrates food-related sensory and physiological signals from the hindbrain and cortex and generates behavioural responses to stress and anxiety. The hippocampus retrieves internal and external cues related to hunger and satiety to generate food-related memories. Added to these signals are higher-order cognitive processes related to attention, working memory, decision-making and planning generated by the PFC and anterior insular cortex (AIC) (Figure 1). The medial PFC receives inputs from the AIC, a region important for relaying gustatory information, attributing emotional salience to food-related stimuli and implicated in risky decision-making.

Consumption of palatable food increases DA release in the NAc and mPFC (13,14). Drug-induced increases in DA levels of the NAc increases food-motivated behaviour, whereas specific DA ablation in the NAc using 6-hydroxydopamine has the opposite effect (15). Similarly, pharmacological blockade of both D1 and D2 receptors decreases effort-based behaviour for food (15). While these results indicate that DA reinforces food seeking, long-term high-fat feeding and diet-induced obesity (DIO) and obesity stemming from genetic mutations is linked with diminished DA signalling in the NAc (16–21). Obese individuals have lower striatal availability of the D2 DA receptor (18), whereas viral-mediated knockdown of striatal D2 receptors generates compulsive food seeking (22). Although recent clinical data show that systemic administration of a D2 receptor agonist (cabergoline) for 16 weeks to obese individuals fails to elicit weight loss (23), it may be that the widespread action of such systemic treatments may inadequately modulate striatal D2 receptors.

Several neurotransmitters, neuropeptides and neuromodulators participate in the modulation of food reward. As shown in Table 1, in some instances, the receptors and nuclei mediating the effects of these neural signals on the motivational properties of appetite

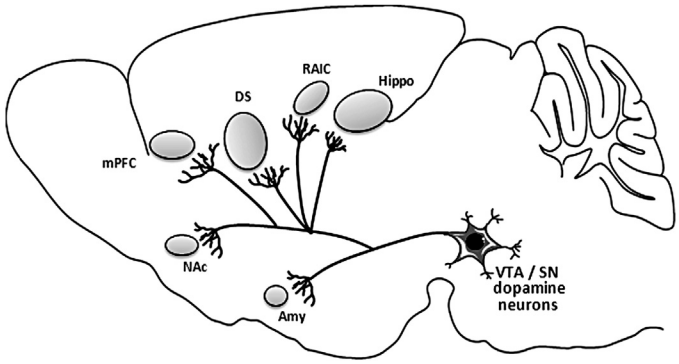

Figure 1. Mesocorticolimbic and nigrostriatal dopamine pathways. Sagittal view of the rodent brain depicting the axonal targets of mesocortioclimbic (originating in the ventral tegmental area: *VTA*) and nigrostriatal (originating in the substantia nigra: *SN*) dopamine pathways. VTA dopamine neurons innervates limbic brain regions including the nucleus accumbens (NAc) of the ventral striatum, the amygdala (Amy), hippocampus (hippo) and cortical brain areas including the medial prefrontal cortex (mPFC) and anterior insular cortex (AIC). The SN dopamine neurons send dense projections to the dorsal striatum (DS).