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Laura Enax[1] · Bernd Weber[1,2]

[1] Center for Economics and Neuroscience, University of Bonn, Bonn, Germany
[2] Department of Epileptology, University Hospital of Bonn, Bonn, Germany

Neurobiology of food choices—between energy homeostasis, reward system, and neuroeconomics

Introduction

We make a vast amount of conscious and unconscious decisions every single day. Food decisions, in contrast to many other kinds of decisions, occur very frequently and regularly [1]. If, what, when, and how much we eat, depends on a variety of different physiological, psychological, and external factors. Some individuals may have different energy requirements due to overeating or malnutrition, whereas other individuals restrictively control what and how much they eat. Food decisions depend on the context and can consequently change, as for example in stressful situations or in company. Visual and olfactory cues influence whether we want to and how much we eat. In contrast to other domains of decision-making, such as financial decisions, food additionally fulfills a physiological requirement that is essential for survival [2]. Most probably because of this biological need, a variety of effective and interacting subsystems exist, which promote or inhibit energy intake [3]. Circulating hormones, such as leptin and insulin, inform the brain about available energy stores and regulate food intake [4, 5], whereas rewards and expectations affect its initiation. In addition, certain genetic variants and their interaction with environmental factors have been shown to increase the risk of developing obesity [6]. Cognitive control may furthermore determine the degree to which health attributes are integrated into the decision-making process, thereby influencing the susceptibility to high-energy intake. Public policy interventions that aim at changing the environment, for example, by improving customer information and changing food availability as well as pricing, can potentially affect individual preferences and promote healthy eating behaviors [7].

In the following paragraphs, we will first focus on physiological factors of food decisions by introducing molecular mechanisms of energy homeostasis. This will be followed by a report of results from research on the genetics of obesity and the impact of the reward system on food choice. We will then combine these insights with findings from neuroeconomics, i.e., decision-making research using neuroscientific methods. These different areas have been rarely combined but allow a deeper and more comprehensive insight into the interwoven subsystems that regulate food intake [2]. Additionally, some phenomena may not be fully explained by only one of the subsystems, such as homeostatic regulation. Improved knowledge of central, peripheral, and external factors that drive food intake is henceforth essential to create a better understanding of the underlying signaling pathways. This expertise can then be used to develop better therapeutic strategies for metabolic diseases, such as obesity or diabetes [5].

Mechanisms of energy homeostasis

Under normal conditions, there is a relatively stable balance ("homeostasis") between food intake and energy expenditure. Therefore, body fat and weight remain relatively stable over time. The ability to adapt energy intake depending on requirements is necessary for survival [8]. A very important brain region responsible for regulating energy homeostasis is the hypothalamus (see **Fig. 1**). Early studies have shown that a lesion in a hypothalamic subregion severely alters food intake and body weight [9]. Furthermore, it was shown that this induces, depending on the exact region of the lesion, malnutrition or obesity [9]. The reason for this lies in the fact that different metabolic hormonal signals take effect within the hypothalamus. It is known that the hypothalamus has bilateral connections to other brain regions such as the hippocampus (see **Fig. 1**) and the so-called reward system (see paragraph 4, [10]). The hypothalamus has additionally been shown to project to the spinal cord in order to regulate thermogenesis and peripheral metabolism [10].

Figure **2** shows an overview of different circulating metabolic signals that influence food intake. Circulating signals inform the brain about available energy stores and send a negative feedback signal to adjust energy intake and expenditure [3, 11, 12]. The adipocyte hormone leptin is secreted from fat cells and circulates proportional to energy stores. After external leptin administration, food intake is reduced [13]. If leptin cannot be produced (e.g., in the so-called ob/ob mouse), mice develop severe obesity with additional massive impairments in behavior and hormonal regulation. However, external administration of leptin can re-

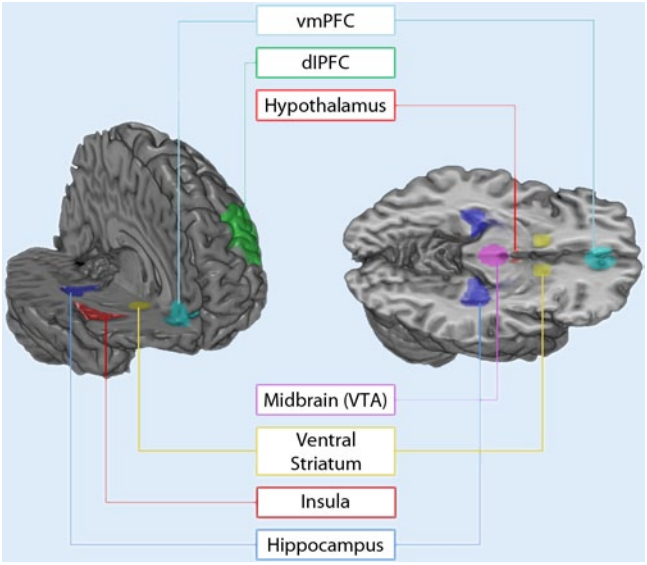

Fig. 1 ◀ Different brain areas are important for energy homeostasis, reward, and decision-making. Important regions mentioned in the text are colored. *VTA* ventral tegmental areal, *vmPFC* ventromedial prefrontal cortex, *dlPFC* dorsolateral prefrontal cortex

duce the severity of obesity in these mice [14]. This finding led to the idea that leptin may be used as pharmacotherapy to alleviate obesity. Despite this idea sounding promising, researchers found that overweight individuals are less sensitive to the "satiety signal" leptin (so-called "leptin resistance," similar to insulin resistance in type 2 diabetes; [15]). Leptin receptors can be found in the hypothalamus and parts of the reward system, among others [16]. More specifically, receptors can be found in the ventral tegmental area (VTA, see **Fig. 1**), which contains dopaminergic neurons. These dopaminergic neurons in the VTA are important for motivated behavior, reward, and addiction. External administration of leptin into the VTA decreases food intake, whereas the knockout of leptin receptor genes specifically in the VTA increases the motivation to ingest high-calorie food [17]. Additionally, different satiety signals, such as gastrointestinal hormones, interact [18, 19]. This interaction between different signals allows a complex fine-tuning of energy intake and expenditure. The pancreatic hormone insulin likewise circulates in proportion to energy stores and reduces food intake. Insulin is an important regulator of the glucose metabolism and can even be found in primitive organisms. In contrast, the negative feedback signaling hormone leptin has not been detected in several primitive organisms [20]. It is therefore assumed that leptin pathways developed later in evolution [21]. Since both hormones send information about available energy stores, these hormones have been termed "long-term signals." Of these, leptin has larger effects on energy intake compared to insulin [12].

In addition to long-term signals, "short-term signals" send information to the brain about the current energy intake. Gastrointestinal signals, as well as nutrients themselves, can modify food intake [22]. More specifically, researchers have shown that gut hormones secreted during and after food intake induce satiety and regulate energy intake. These signals include glucagon-like peptides (GLP1), peptide YY (PYY), and cholecystokinin (CKK, [22–24]). Nutrients in the form of free fatty acids and glucose, as well as gastric expansion, can terminate food intake [25]. In many cases, these signals reach the central nervous system (CNS) via the vagal nerve, which projects from the gastrointestinal tract to the nucleus solitaries in the medulla oblongata [11].

In contrast to the above-mentioned satiety signals, the hormone ghrelin powerfully stimulates food intake across species [26]. Ghrelin levels rise before a meal and drop after energy intake [27]. Administration of ghrelin increases food intake in lean and overweight individuals [28]. Ghrelin binds to the growth hormone secretagogue receptor (GHSR1a), stimulates growth hormone release, and has an impact on glucose metabolism and gut motility [29]. Ghrelin receptors are expressed in the hypothalamus, VTA, and ventral striatum, among others [26, 30]. Ghrelin binding to the VTA can stimulate dopaminergic neurons and hereby influence the reward system [30]. Ghrelin was formerly coined as the "hunger hormone," which has been questioned in recent studies [29]. Diano and colleagues could show that ghrelin binds bind to receptors in the hippocampus and affects learning and memory [31]. In addition, mice that do not produce ghrelin show little alteration in feeding behavior [29].

How can the hypothalamus integrate such diverse signals and establish energy homeostasis? An important system that best explains neuronal energy homeostasis is the melanocortin system. Neurons in the hypothalamic arcuate nucleus express receptors for most metabolic hormones and quickly react to ingested nutrients [10]. Two distinct neuronal populations having antagonistic effects can be found in the arcuate nucleus. Neurons that express proopiomelanocortin, a precursor of melanocortins, reduce appetite and increase energy expenditure upon activation, whereas neurons that express neuropeptide Y (NPY) and agouti-related peptides (agRP) can increase appetite and decrease energy expenditure. These neuronal populations within the arcuate nucleus can be directly controlled by ghrelin, insulin, and leptin [32, 33]. This in turn alters food intake, locomotion, and glucose metabolism [34]. The melanocortin system is indispensable for the regulation of food intake [35]. However, when this system is deactivated in a very early developmental stage after birth, compensatory mechanisms replace most of its functions [36]. Next to the arcuate nucleus, other parts of the hypothalamus are also responsible for regulating energy homeostasis. Neurons in the ventromedial portion of the hypothalamus, for instance, react to leptin and reduce food intake, whereas neurons in the lateral hypothalamus induce food intake. Bidirectional connections exist between these hypothalamic nuclei and different other brain regions [10]. For example, learning, motivation, and motoric responses can be altered, depending on nutritional status [10].

Abstract

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L. Enax · B. Weber

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Abstract

The rate of patients with obesity has been rapidly increasing, and this imposes a heavy economic burden on health-care systems. Food decisions, under the influence of different internal and external factors, lie at the core of this increasing health problem. Due to the biological necessity to consume sufficient amounts of food and to correctly regulate energy expenditure, there are different systems that control food intake. This article first focuses on neurobiological and hormonal foundations and explains various metabolic short- and long-term signals, such as leptin, insulin, and ghrelin. We then also present genetic factors, which directly or indirectly (via other genes or environmental influences) may affect nutritional status. Since the consumption of high-caloric foods is accompanied by dopamine release and the activation of the brain's reward system, we will then present the interdependence of metabolic and reward systems. Last, we will present a neuroeconomic perspective that complements research on metabolic and hedonic feeding regulation.

Keywords

Food decisions · Neuroeconomics · Decision-making · Neurobiology

Obesity genetics

The development of obesity results from an excessive accumulation of fat due to a long-lasting positive energy balance, that is, more energy is consumed than used. Obesity is one of the leading health problems in most industrialized nations, as it increases the risk of many chronic diseases, such as cardiovascular malfunctions and type 2 diabetes [37]. In parallel to the weight increase, high-caloric foods as well as a sedative lifestyle have become omnipresent [38]. However, a changing environment cannot be the only explanation for all phenotypes; albeit lifestyle has changed in many industrialized nations, not everybody becomes obese [39]. Additionally, the body mass index (BMI) is highly heritable [40].

Considering the complex homeostatic system and its interaction with reward and decision-making circuitries, it has proven difficult to attribute the cause of obesity to a few genetic variations. Monogenetic forms of obesity are caused by a single gene mutation. Similar to many other monogenetic diseases, monogenetic obesity is very rare and usually causes a severe, early-onset phenotype [39, 41]. More than 200 genetic mutations have been described, which lead to human (non-syndromic) obesity. Most mutations were found in a small number of specific genes [42, 43] that code for proteins playing a role in the melanocortin signaling pathway of the hypothalamus [44]. For example, a mutation in the proopiomelanocortin gene leads to early loss of function and severe obesity as proopiomelanocortin neurons normally synthesize a peptide that reduces hunger [45].

The more common, polygenetic form of obesity (i.e., the mutation/variation of several genes) proves to be even more difficult to uncover, partly because of the above-mentioned complexity as well as individual variability. The main strategy is to examine genetic variations (such as single-nucleotide polymorphisms (SNPs)) that lie close to, or within candidate genes. In contrast to monogenetic obesity, these SNPs do not directly lead to obesity but require additionally other genetic variations and/or environmental factors [39]. For example, genome-wide association studies have found that the fat mass and obesity associated (FTO) gene has an impact on BMI, whereby most likely hypothalamic control of food intake is altered [46]. Similarly, SNPs within the melanocortin signaling pathway (such as the MC4R gene) influence body weight, fat mass, and the risk of developing obesity [47]. More subtle variations in food choice, such as sugar intake and eating behavior subtypes, as well as eating disorders, seem to have a genetic component [48, 49]. Albeit many genes have been found to be associated with obesity, they mostly only explain little variance in BMI and fat mass [39]. This is highly surprising, as the heritability of obesity seems to be much higher [50]. Most researchers now assume that environmental factors interact with the genetic makeup resulting in some individuals possibly being more prone to becoming overweight. Additionally, "genetic redundancy," that is, the presence of several similar and overlapping signaling pathways, may explain less severe phenotypes [8]. Several SNPs may not be common enough to reach statistical significance in large-scale studies. Furthermore, the change of gene expression due to environmental factors (epigenetic alterations) may partly explain several phenotypes [51]. High-end genetic methods, such as "next generation sequencing" may further help to uncover the riddle of the genetic component of obesity.

Research on genetic causes and risk factors is essential to reveal signaling pathways, develop new therapeutic strategies, but additionally to promote individual intervention strategies. This is necessary because current, nonsurgical measures are often ineffective in the long term. For instance, physical activity and intake of obesity medications lead to, on average, a maximum of 10 % weight loss [52]. Remarkably, not only food intake was found to be associated with genetic variations but also energy expenditure, such as the amount of physical exercise performed per week [53, 54]. An FTO genetic variant was shown to alter dopaminergic activity in the midbrain, thereby influencing the reward system [55, 56].

The role of the reward system in food choice

In addition to brain regions controlling hunger and satiety, other neurotransmitters and brain regions have an impact on food intake and the development of obesity [57]. There is a constant interaction between the systems of energy homeostasis, as well as cortical and subcortical brain regions. As mentioned above, metabolic signals can influence activity of dopaminergic neurons and the reward system

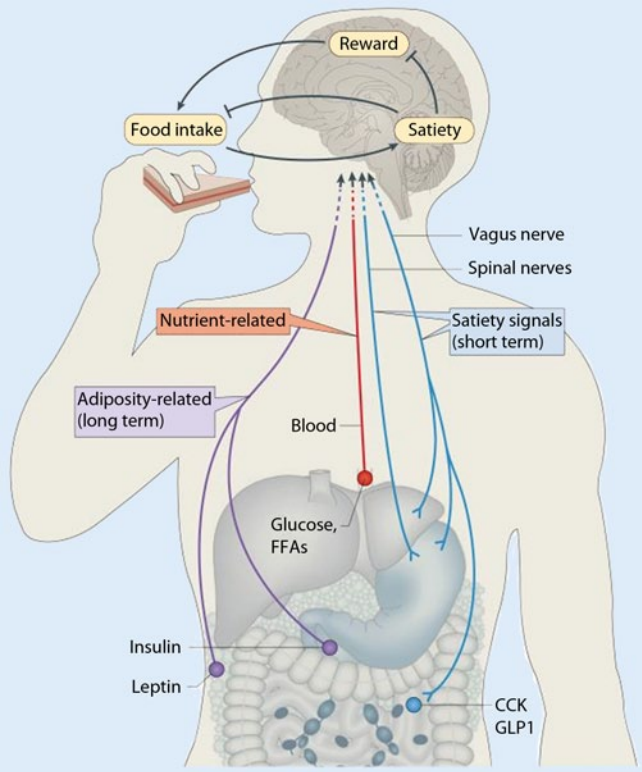

Fig. 2 ▲ In the central nervous system, different short- and long-term signals are integrated to ensure a balance between energy intake and expenditure. Leptin and insulin are long-term signals, whereas nutrients (such as glucose and free fatty acids) and gut hormones (such as cholecystokinin and glucagon-like peptides) belong to the short-term signals. These signals are used to regulate food intake and energy expenditure. When satiated, food is perceived as less rewarding, and satiety signals have a more pronounced effect, thus reducing intake. The opposite mechanism occurs in case of energy depletion in order to replenish energy stores (*CCK* cholecystokinin, *FFA* free fatty acids, *GLP1* glucagon-like peptides 1). Reprinted by permission from Macmillan Publishers Ltd.: Nature Reviews Neuroscience (Morton et al.), Copyright 2014

[58]. Across species, the reward system is very important in influencing food intake, possibly to promote survival [59]. Besides, high-caloric foods can alter reward learning [58]. Dopamine is an important neurotransmitter from the group of catecholamines and promotes (among other roles) motivation and approach-related behavior. It is the best examined neurotransmitter in the context of food decisions. Dopaminergic neurons project from the VTA to the dorsal striatum, hippocampus, and hypothalamus [58]. Food intake is accompanied by dopamine release, and the amount of release correlates with the subjective food palatability [60, 61]. However, dopamine does not code a simple reward value. Upon first contact with a reward and when a reward is unexpected, dopaminergic neurons in the VTA fire, leading to a higher release of dopamine within the ventral striatum [62]. Frequent presentation of the same stimulus, however, reduces the dopamine response, and the dopaminergic firing is conferred to the stimuli that predict a reward, such as the smell of a food item. The dopaminergic signal thereafter conveys a reward-prediction error, in other words, it codes if the stimulus correctly predicts the reward [63, 64].

Obese individuals show a higher activation of the reward system upon exposure to high-calorie foods, underlining the importance of the dopaminergic system in food choice [65]. However, actual consumption of high-caloric foods in obese individuals, compared to their lean counterparts, leads to a lower reward system activation [66]. Related to this finding, the availability of dopaminergic D2 receptors is reduced in proportion to BMI [67]. It is henceforth often assumed that overweight individuals compensate the lower release of dopamine or the lower availability of dopamine receptors with increased food intake [66]. In contrast, severe dopamine deficiency in mice greatly reduces food intake [68]. These mice also stop reacting to metabolic signals such as glucose or leptin deficiency [69, 70]. Although mice with a dopamine deficiency prefer sucrose, they do not consume much of it [71]. Dopamine therefore seems to increase the motivation to consume food and to show the necessary effort to receive the food items [58]; it influences the so-called "wanting". These observations led to the conclusion that the dopaminergic signaling pathway is necessary for food intake and acts downstream of the melanocortin system [72]. The bilateral connection between the reward system and hypothalamus is possibly important to integrate homeostatic and hedonic information [12]. For instance, leptin and gut hormones influence the rewarding value of food items. Administration of leptin into the VTA blocks dopamine transmission and reduces food intake [17].

The palatability of food is an important factor that drives food intake; highly palatable and therefore rewarding foods can induce food intake without physiological need. The endogenous cannabinoid system is important for the so-called liking, i.e., the appraisal of the palatability of a food item [73]. The palatability of foods is also processed in reward regions, as well as in the insula, the primary taste cortex (see ◘ **Fig. 1**). Satiated rats prefer punishments, such as the administration of an electric shock, if they can in return eat highly palatable foods. This happens even at the free availability of normal chow. Similar behavior has also been observed in drug addiction [74]. A positive correlation between BMI and reward discounting has been found as well [75]. The frequent and excessive consumption of high-caloric foods can induce neuroadaptive changes, which resemble those that can be observed in drug addiction. Similar genetic variations of the reward system were shown to increase the risk of drug addiction and obesity alike [4]. For instance, a genetic polymorphism in the dopamine D2 receptor genes, which is accompanied by reduced dopamine release in the striatum, alters reward processing and increases the risk of obesity [59].

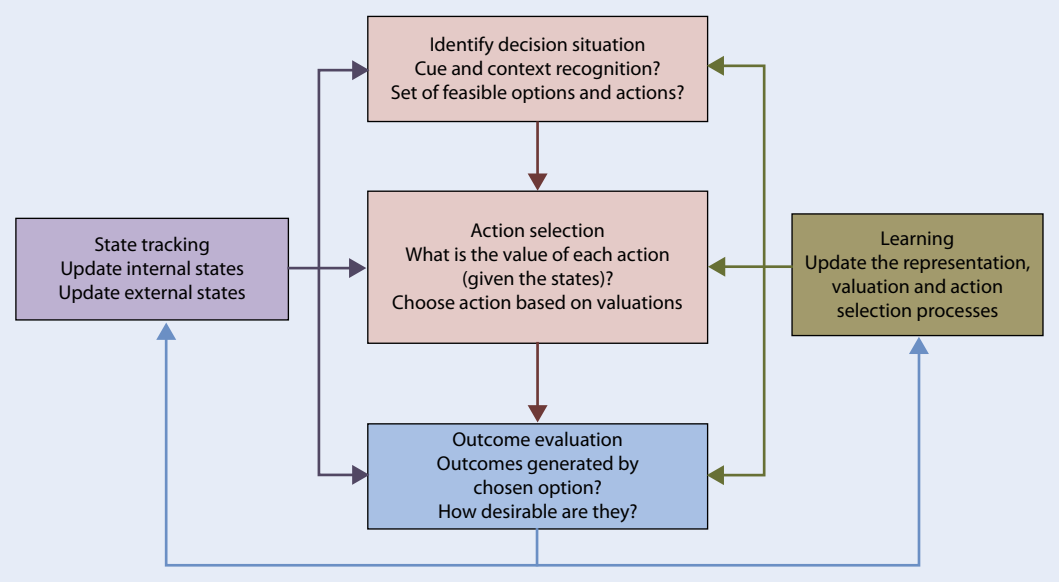

Fig. 3 ◀ Value computations before, during, and after a decision. Reprinted by permission from Macmillan Publishers Ltd.: Nature Neuroscience (Rangel), Copyright 2013

While developing obesity, striatal dopamine D2 receptors are down-regulated in rats and a knockout of the striatal D2 receptor gene accelerates the process of obesity development [76]. However, the hypothesis that obesity is a form of addiction is highly debated. For example, obese subjects often do not show the same characteristic behaviors that many addicts display, such as withdrawal symptoms, tolerance (higher amounts need to be consumed for satiety), and limiting other activities. Further, the obesity phenotype is highly heterogeneous [77]. Therefore, future research is necessary to better identify overlaps as well as differences between obesity and drug addiction.

Insights from neuroeconomics

The fields of energy homeostasis and neuroeconomics have seldom interacted. On the one hand, research on homeostatic regulation has focused on pathways that are specifically involved in energy regulation and has rarely considered other forms of decision-making. On the other hand, neuroeconomics aims to understand neurobiological substrates and internal computations in value-based decisions across contexts and domains [2]. Neuroeconomics aims to offer a biologically plausible model of human decision-making [78]. Strong evidence points to common mechanisms across decision-making contexts, including food choices [78, 79]. In contrast to many other daily decisions, survival requires sufficient amounts of food intake, and homeostatic regulation seems to strongly shape decision processes [2]. Functional magnetic resonance imaging (fMRI) has provided a window to study neural processes noninvasively. Current technology allows to investigate metabolic changes on a scale of millimeters and in a time window of seconds [80]. Functional MRI is one of several methods that neuroeconomics researchers have used to better understand decision-making processes.

A value-based decision occurs when an individual (this includes nonhumans) decides between alternatives based on the subjective value of each alternative [78]. This very general definition implies that very simple decisions (such as decisions between two food items) as well as complex decisions (such as financial investments) fall into this category. A very influential and widespread model divides the decision-making process into five distinct phases (**Fig. 3**). First, a decision situation has to be recognized, which may be influenced by internal and external states. Also, possible actions have to be identified. Considering food decisions, an internal state may be the feeling of hunger, whereas an external state may be the presence of food, thus resulting in the feasible action of preparing a meal. Second, the actions to obtain each alternative have to be evaluated, based on internal and external states [78]. In the valuation domain, researchers often assume three different valuation systems, which differ in flexibility and learning of new actions: (1) relatively automatic behaviors (Pavlovian controllers) and (2) habitual and (3) goal-directed valuation systems. These three systems seem to engage distinct but sometimes overlapping neural systems. An example of an automatic controller (1) would be the physical proximity to food or the sight of a restaurant sign; both may influence the time of food intake and the nature of the food we eat [2]. Learning positive food associations depends on the orbitofrontal cortex, amygdala, and ventral striatum. An example of the habitual system (2) would be the desire to drink a cup of coffee at a certain time of the day. Across species, the dorsolateral striatum seems to be crucial for controlling habits. The dorsolateral striatum is closely linked to the motor cortex in order for motoric actions to be quickly initiated [81]. The goal-directed system (3) is more flexible and based on the dynamic computation of a subjective value directly related to the values of action outcomes. Only the goal-directed system would include feelings of satiety in the valuation process and thereby incorporate internal states into the value computation [78]. Evidence suggests that a goal-directed valuation system exists in both humans and animals (e.g., rats, [82]).

A single choice alternative can consist of several attributes. These attributes can

be divided into two classes—basic, immediate attributes (e.g., taste of a food product), as well as more abstract, and possibly delayed attributes (e.g., health consequences). For a goal-directed choice, the value of each attribute has to be taken into account to calculate an overall value signal. Only the goal-directed system can include abstract attributes, such as long-term consequences, into the decision-making process [2]. Research using functional imaging and lesion studies has identified several brain areas important for the value computation process. The ventromedial prefrontal cortex (vmPFC), see **Fig. 1**, has been shown to strongly and reliably correlate with the subjective value of an option across domains and contexts [2, 78, 83–85]. The vmPFC is interconnected with the pre-supplementary motor cortex, possibly to directly prepare or implement motor actions based on the valuation process. Further, it receives input from all senses to create a stimuli representation. For example, information from the primary taste cortex, the insula (**Fig. 1**), alters valuation processes [86].

Interestingly, the stimulus representation in the vmPFC is not solely based on the chemical properties of a food product and the physiological state of an individual. Additionally, cognitive factors and experiences can alter the vmPFC activity. Just changing the price of an otherwise identical wine can, for example, influence taste ratings and the vmPFC valuation signal [87]. Thus, the vmPFC uses different sources and levels of information to calculate an overall value [2]. It is of great importance that the goal-directed valuation system works dynamically. For instance, the value of abstract health attributes may be higher after a physical health examination, and may be lower in state of hunger or stress. Moreover, external signals can change the valuation process [85]. Studies have shown that the dorsolateral prefrontal cortex (dlPFC; see **Fig. 1**) plays an important role in cognitive control and integrating health attributes into food choices and influencing vmPFC computations [85, 88]). In contrast to health-conscious eaters, unhealthy eaters engage the dlPFC to a lesser degree and only integrate taste attributes into the vmPFC value signal [88]. Evidence strongly suggests that cognitive control is impaired in obese individuals [89]. The ability to suppress the desire to consume palatable food items may therefore constitute a risk factor for the development of obesity [90]. Furthermore, compared to lean controls, obese individuals show reduced gray matter volume in the prefrontal cortex, which is important for cognitive control [91]. Based on the evaluation of each alternative, one of many possible actions has to be selected. The different valuation systems may "prefer" different alternatives—for example, the automatic system would directly initiate food consumption at the sight of high-calorie foods, whereas the goal-directed system may additionally use information on long-term health consequences in the decision-making process. Third, after action selection, outcomes are evaluated, i.e., an organism determines if the expected outcome was generated and evaluates the desirability of the outcome. Outcome recognition and evaluation are used to update the representations and foster learning processes in order to improve future decisions. The consumption of food products alters internal and external states, such as energy stores, which emphasizes the complex interaction with the homeostatic system [2, 78].

As mentioned above, reward learning and expectations influence food choice and intake [92]. Information on brands, quality beliefs, and nutrition claims can induce expectations and even override physiological needs [93, 94]. An interesting phenomenon, which cannot be solely explained by homeostatic regulation, is the observation that expectations can alter product experiences when the physical product properties are held constant. In addition to prices, attributes such as brand logos or word-level descriptions, can change taste perception on a reported and neural level [95, 96]. Price differences of an identical energy drink were shown to influence performance on a cognitive test [97]. Interestingly, hormonal responses can be altered by product information. In one experiment, participants received an identical milkshake, but the experimenters induced different expectations. When subjects expected a high-caloric shake, ghrelin levels steeply declined, and this is usually associated with appetite reduction and a feeling of satiety. Conversely, when subjects expected a low-calorie milkshake, ghrelin levels did not change very much. This study nicely demonstrates how closely cognitive, reward, and metabolic regulatory circuitries are intertwined (Crum et al. 2011).

How would a neuroeconomist explain obesity? From a neuroeconomics perspective, a "good" decision requires that all attributes and their associated reward value, including long-term consequences, have to be weighted in the decision-making process. In this sense, an unsuccessful attempt to lose weight cannot solely be attributed to tight homeostatic regulation. A failed dieting attempt is also seen as a consequence of decisions that do not correctly include long-term attributes in the decision-making process [2]. As obesity rates have dramatically increased only recently, it is unlikely that only biological mechanisms and certain genetic makeups are responsible for the high rates of overweight individuals. Environmental factors, such as a typical "cafeteria diet" can lead to high increases in body weight in rats [98]. External factors strongly affect our preferences, food knowledge, and can thereby induce behavior change [7]. Environmental factors, therefore, play an important role in the obesity epidemic and interact with the other decisional systems [2]. Due to the omnipresence and abundance of high-calorie foods in many industrialized nations, goal-directed and controlled decisions are harder to make. This is based on two assumptions: First, automatic behaviors are more easily activated when food is ubiquitously available, and a goal-directed behavior would imply that an individual has to overcome automatic behavior tendencies. Besides, the probability that the goal-directed system fails increases in the presence of distractors and stress [2]. Recent studies have shown that acute stress impairs self-control in goal-directed food decisions [99] and that cognitive load leads to a loss of cognitive control and higher influence of automatic systems [100]. The excessive consumption of high-caloric foods may impact different levels of regulation. On the one hand, high amounts of fats and sugar can disturb the homeostatic system [15, 101]. Additionally, high-caloric foods may nega-

tively influence cognitive processing and increase the reactivity to rewards [102], whereas impairments of cognitive control can further impede goal-directed choices [2]. These findings underline the necessity to additionally change environmental factors [103], for instance, by using target-group specific and evidence-based intervention strategies [7].

Conclusions

Food intake is indispensable for survival, which is why different regulatory systems exist and monitor food intake and energy expenditure. Several signals promote or terminate food intake and regulate the amount and nature of nourishment. Mutations in certain genes in this homeostatic system may disconcert the tightly controlled homeostatic system. Monogenetic forms of obesity are very rare and usually lead to a severe phenotype [42]. Food intake is inherently rewarding, possibly to promote survival, with high-calorie food products activating the reward system to an even higher degree [66, 74]. Today's environment offers a vast amount of high-caloric, and therefore highly rewarding, stimuli, which can lead to a positive energy balance. Although most people are aware of the fact that high-calorie food products may be detrimental in the long term, most individuals struggle with constant dieting. Cognitive trainings have yielded limited success, which reinforces the assumption that many behaviors are automatic, triggered by environmental cues. Therefore, interventions targeting automatic processing may aid to alleviate the obesity epidemic [8, 103]. Due to the complex interaction between metabolic regulation and decision-making systems, it is certain that a joint perspective is very important. Prior pharmacological trials targeting single neuronal receptors of the homeostatic system in obesity have not led to the expected breakthrough, but this may be due to the fact that an interacting homeostatic system also has the capacity to compensate other signaling pathways [8]. Additionally targeting the reward or decision-making circuitry may aid in reducing a further growth in the obesity crisis. The integrative research may promote new research findings and the development of individually targeted intervention strategies [2]. Further work is absolutely necessary to fully understand the rising number of overweight individuals and to promote multimodal intervention strategies that unite findings of different research areas.

Corresponding address

B. Weber
Department of Epileptology,
University Hospital of Bonn
Sigmund-Freud-Str. 25, 53127 Bonn
bernd.weber@ukb.uni-bonn.de

Laura Enax studied psychology and neuroscience at the University of Osnabrück, Germany, Nelson Mandela Metropolitan University, South Africa and University of Bonn, Germany, supported by the German National Academic foundation. She received her master's degree in neuroscience in 2014. Since then, she has been working on her PhD project at the University of Bonn under the supervision of Prof. Dr. Weber and Prof. Dr. Ettinger in the field of neuroeconomics of food decisions within the nutrition research competence cluster DietBB funded by the BMBF.

Bernd Weber studied medicine in Bonn and worked on pathological causes of central nervous system diseases in his doctorate thesis. Since 2005, he has been leading the department for structural and functional brain imaging at the Life & Brain Center Bonn and has been working on neurobiological foundations of human decision-making. He is co-founder and board member of the Center for Economics and Neuroscience at the University of Bonn. Since July 2010, he has been holding a Heisenberg professorship for neuroeconomics at the Medical Faculty of the University of Bonn.

Conflict of interest. The authors declare no conflict of interest.

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