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How we decide what to eat: Toward an interdisciplinary model of gut–brain interactions

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Abstract

Everyday dietary decisions have important short-term and long-term consequences for health and well-being. How do we decide what to eat, and what physiological and neurobiological systems are involved in those decisions? Here, we integrate findings from thus-far separate literatures: (a) the cognitive neuroscience of dietary decision-making, and (b) growing evidence of gut–brain interactions and especially influences of the gut microbiome on diet and health outcomes. We review findings that suggest that dietary decisions and food consumption influence nutrient sensing, homeostatic signaling in the gut, and the composition of the gut microbiome. In turn, the microbiome can influence host health and behavior. Through reward signaling pathways, the microbiome could potentially affect food and drink decisions. Such bidirectional links between gut microbiome and the brain systems underlying dietary decision-making may lead to self-reinforcing feedback loops that determine long-term dietary patterns, body mass, and health outcomes.

This article is categorized under:

Economics > Individual Decision-Making
Psychology > Brain Function and Dysfunction
Psychology > Reasoning and Decision Making

KEYWORDS

dietary decision-making, homeostatic control, microbiota–gut–brain axis, neural correlates, self-control

1 | INTRODUCTION

Eating decisions are among the most frequent types of decisions, made every day. Any single food decision by itself—whether one has a salad or a burger for lunch—might seem less important for overall weight management, but over time these decisions can cumulate into substantial weight gain, metabolic disorders such as diabetes, and even premature death.

Unhealthy diets, overeating, and obesity significantly increase the risk of chronic diseases such as cardiovascular disease, type 2 diabetes, hypertension, coronary heart disease, and several types of cancer (Chu et al., 2018; Y. C. Wang et al., 2011). Since 1975 obesity rates in the world have nearly tripled, and the substantial direct and indirect costs of the health consequences put a considerable strain on healthcare and other economic resources. Estimates for these costs in industrialized countries run as high as nearly US$425 billion annually (OECD, 2019). Against this background, it is crucial to better understand the factors that drive individual differences in dietary decision-making and ultimately cause weight gain and other negative health outcomes.

How do we decide what to eat? Eating decisions are shaped by the context of the choice situation as well as the internal state of the decision maker. For instance, decisions will be different when we are in a large food court with a great variety of options to choose from than when we get lost on a hiking trip with little or no food on hand. They will also be affected by internal factors such as hunger, stress, and negative mood. Importantly, like many other types of decisions, food decisions involve making trade-offs among various attributes of the food options, which can act on various goals of the decision maker. For example, if the decision maker gets lost on a hiking trip and is extremely hungry, the short-term goal might be to find any kind of food that is high in energy, no matter whether it is very tasty or not (thus maximizing calorie intake to restore energy homeostasis and not taste pleasure). Food decisions often also require weighting different attribute trade-offs over time—for example, the decision maker might be looking for an immediate reward and choose the chocolate cake over the fruit salad. But if chosen consistently over time, the fruit salad option would help to maximize long-term rewards in the form of better health and well-being. The psychology and cognitive neuroscience of decision-making, also known as decision neuroscience or neuroeconomics, has advanced our understanding of the brain signatures of reward-based or value-based decision-making and how they determine behavior (Rangel et al., 2008; Weber & Johnson, 2009).

Yet this research has so far often ignored physiological factors, including homeostatic processes such as signals from the gut and nutrients, as well as the potential role of the gut microbiota composition, which has been studied in nutrition science and microbiology. Recent evidence points to an important role of the gut microbiome—the combination of bacteria and other microorganisms living in our gut—for the host's health and homeostatic as well as reward processes (García-Cabrerizo et al., 2021; Long-Smith et al., 2020; Torres-Fuentes et al., 2017). The gut, together with the microbiome that inhabits it, is therefore often considered our "second brain." Methodological advances in sequencing and bioinformatic tools (Gevers et al., 2012) have enabled a growing awareness of the communication among our intestinal bacteria, the brain, and behavior (Gupta et al., 2020; Mayer, 2011; Williams & Elmquist, 2012).

For the study of dietary decision-making and its control, this implies an interesting yet understudied bi-directional communication between the nutrients we eat and how we choose them. In addition, what we eat also shapes the bacteria in the host gut, and a growing area of research has investigated how the bacteria in the gut affect the health, well-being, and behavior of the host through communication with the host's brain (Bravo et al., 2011; Desbonnet et al., 2010; Johnson & Foster, 2018; Mayer et al., 2014). However, these bi-directional interactions between the gut microbiome and the brain have not yet been integrated systematically in the study of how we choose what and how much to eat (García-Cabrerizo et al., 2021; E. Mayer et al., 2014; Torres-Fuentes et al., 2017; Van de Wouw et al., 2017).

Taken together, although several disciplines study dietary decision-making from their own perspectives, it still remains poorly understood why we choose what and how much we eat. One hurdle is the insufficient dialogue among these areas of research (Berthoud, 2011; Rangel, 2013). Here, we propose an interdisciplinary perspective that integrates findings from (a) the psychology and cognitive neuroscience of decision-making with (b) research in nutrition science and microbiology. The goal of this article is to give a brief overview of the current state of the art in these complementary perspectives on dietary decision-making and how they could be integrated in order to advance our understanding of dietary decision-making and its control. We then point to open questions that could guide future research on dietary decision making.

2 | PHYSIOLOGY AND BRAIN SYSTEMS UNDERLYING FOOD CHOICES

Since energy intake is crucial for survival and keeping the organism in good health, multiple physiological systems have evolved to regulate food intake and metabolism. Here, we organize our discussion of the regulation of eating and

dietary decisions into two broad systems: (a) homeostatic drivers that regulate eating based on energy needs and the availability of macronutrients and micronutrients (reviewed in Section 2.1) and (b) cognitive and affective factors that arise from interactions between the environment and the central nervous system (CNS), and that determine how we assign value to food at time of choice and how we regulate these signals (reviewed in Section 2.2). Importantly, these two types of drivers of dietary decision-making do not act in isolation but interact strongly with each other—to the point that a separation into different systems may be artificial. These interactions are discussed in Section 2.3.

2.1 | Homeostatic regulation of eating

The human body is metabolically dependent not only on oxygen, water, and micronutrients, but also on energy-supplying nutrients in the form of carbohydrates, fat, and proteins (Plata-Salamán, 1991; Tortora & Derrickson, 2018). These macronutrients must be stored, since food intake is irregular but energy consumption, which maintains basic cellular processes, is a continuous process. Body weight and the amount of fat tissue have to be kept relatively stable over longer periods in the adult human organism. If not matched by energy expenditure, an increased energy supply will lead to weight gain and adiposity, with multiple negative health consequences (Plata-Salamán, 1991). Thus, to ensure energy balance, the human organism has established several mechanisms to regulate food intake in the short term and long term.

Physiologically, the feeling of hunger should trigger food intake, while the feeling of satiety should end food intake. Ideally, this control mechanism should guarantee that an adult's body weight is kept relatively constant. However, the increasing prevalence of obesity, especially in Western societies, suggests that the control mechanisms of hunger and satiety are failing (H. Zheng & Berthoud, 2007). The regulation of hunger and satiety and their control of eating behavior has therefore become one of the central topics of nutritional physiology in recent years (Heisler & Lam, 2017; Plata-Salamán, 1991; Stengel & Taché, 2012; Tremblay & Bellisle, 2015).

Sensations of hunger and satiety are communicated from the body to the brain by several neural, hormonal, and metabolic signals (Figure 1), which are modulated by a large number of factors (Plata-Salamán, 1991; Stengel & Taché, 2012; Zanchi et al., 2017). Of particular interest for this review are two types of signals: (a) various gastrointestinal peptide hormones and (b) various neurotransmitters and neuromodulators of the central nervous system and of peripheral systems that are involved in this complex regulation of hunger and satiety. They are described in the following two sections.

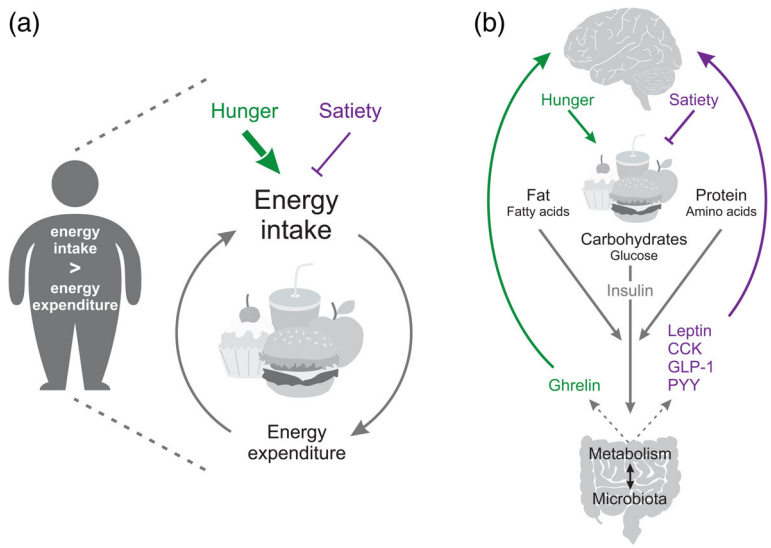

FIGURE 1 The homeostatic regulation of eating behavior. (a) Energy intake and expenditure need to be balanced in order to maintain a healthy body weight. Energy (food) intake is regulated by hunger and satiety signals. Becoming overweight is the consequence of a dysregulation of these systems and a resulting excessive energy intake. (b) The energy-rich macronutrients and their metabolism in the gastrointestinal tract control energy intake by causing feelings of hunger and satiety in the CNS either directly or via metabolic and hormonal signals. Orexigenic signals (e.g., ghrelin) promote eating and feelings of hunger, while anorexigenic (e.g., insulin, leptin, CCK, GLP-1, and PYY) signals decrease eating and promote feelings of satiety. Additionally, the gut microbiota interacts with the gut metabolism and thereby also influences the regulation of hunger and satiety. CCK, cholecystokinin; GLP-1, glucagon-like peptide 1; PYY, peptide YY

2.1.1 | The role of gastrointestinal peptide hormones for the regulation of food intake decisions

The primary goal of the homeostatic system of food intake is to ensure sufficient energy supply. Such regulation is based on two-way communication: Macronutrients and their metabolites serve as sources of energy (see Box 1). But macronutrients themselves also have regulatory effects: The transfer of nutrients into the blood (i.e., their resorption) is accompanied by the secretion of numerous hormones. These hormones in turn influence the blood level of various nutrients, thus regulating further hormone release via a negative feedback mechanism.

The gastrointestinal peptide hormones, which are released after food intake, contribute significantly to the peripheral regulation of food intake. The paraventricular and ventromedial nuclei of the hypothalamus and structures

BOX 1 How energy supply and storage affect hunger and satiety

Numerous studies have experimentally investigated the effects of insulin and glucose on the regulation of hunger and satiety (Bornet et al., 2007; Woods, 2013). As the main component of dietary carbohydrates, glucose is an immediately usable, energy-supplying substrate. Not all cells are necessarily dependent on glucose as an energy source, but under physiological conditions the brain "prefers" glucose as an energy source. According to the glucostatic theory of food intake (Bernstein & Grossman, 1956; Bornet et al., 2007; J. Mayer, 1952), the CNS availability of glucose therefore acts as a primary signal to regulate food intake. However, since in animal experiments low blood glucose (hypoglycemia) does not necessarily trigger the beginning of food intake and high blood glucose does not necessarily lead to its termination, it is not clear whether the blood glucose level acts as a direct or indirect signal to the central nervous system. What is known is that insulin plays a role in this regulation, which lowers not only the level of blood glucose but also the concentration of free fatty acids, ketone bodies, and amino acids in the blood plasma. This leads to the assumption that the regulation of food intake is driven not by blood glucose levels but by the intensity of the glucose metabolism in the brain. According to this idea, an increased glucose metabolism in the brain after a meal triggers the feeling of satiety. In addition to the central metabolism of glucose, the availability of glucose and glucose catabolites in the liver may also play a role and could be signaled to the brain via the vagus nerve. While glucose concentration and glucose utilization have an impact on food intake, they are not the only regulatory control system of hunger and satiety (J. Mayer, 1966, 1996).

The main energy storage of the organism, the adipose tissue, is also involved in the regulation of hunger and satiety. Depending on its size, the adipose tissue produces various signals that regulate energy supply, according to the lipostatic theory (Cammisotto et al., 2010; Kiess et al., 2000; Speakman et al., 2002). These include metabolites from the adipose tissue, such as free fatty acids and glycerine, which are produced when fat depots are mobilized and which have an effect on hunger and satiety. Since both fat and glucose metabolism are under the control of insulin, glucostatic and lipostatic regulatory systems also interact with each other.

Amino acids are also involved in the energy homeostasis, since they are directly used to supply energy in certain metabolic situations. Amino acids also have a number of metabolites, such as amines, purines, and pyrimidines, including several neurotransmitter precursors that fundamentally control the feeling of hunger and satiety (e.g., tryptophan, a serotonin precursor). Further, it has been shown that the concentration of amino acids in the blood plasma is inversely correlated to food intake (Hajishafiee et al., 2020; Peters & Harper, 1981), suggesting that the central nervous system can detect the level of circulating amino acids. While the energetic aspect of the amino acids is probably of minor relevance for the regulation of hunger and satiety, the types and *relative abundance* of amino acids in plasma seem to have a regulatory effect. In particular, the level of branched chain amino acids (BCAA) might have an effect on hunger and satiety. In participants of higher weight, the administration of relatively small amounts of a mixture of amino acids resulted in a reduction in food intake (Peters & Harper, 1985; Solon-Biet et al., 2019). Administration of tryptophan alone reduced the amount of food consumed in lean participants (Birdsall, 1998; Reilly et al., 1997; Wurtman & Wurtman, 1995). The regions of the brain that respond to changes in plasma amino acid levels appear to be outside the hypothalamus in brain regions such as the amygdala and the prepiriform cortex (Reilly et al., 1997; Torii et al., 1998).

GLOSSARY

Value	Amount of pleasure/happiness or displeasure/punishment derived from a choice option. Value can be expected before the choice is made, experienced when choice is implemented, or remembered after consumption. It can be stable or constructed on the spot because of a certain context. Positively signed value is linked to concepts in psychology and neuroscience such as reward, wanting (i.e., the motivational aspect of an expected value), and liking (i.e., the experienced value). It is also related to the concept of utility in economics, which in addition to value also considers the *probability* of receiving the value of the options for choice.
Valuation system	Brain systems that correlate with the magnitude of value. Their role is thought to be the integration of various attributes of the choice options. Current meta-analyses suggest that the two most prominent brain regions of the valuation system are the ventromedial prefrontal cortex (vmPFC) and ventral striatum (vStr). Note that there are other brain regions, such as the amygdala and insula, that are also involved in the coding of taste-related and emotional information during dietary decisions but not in their direct integration during decision-making.
Control system	Brain systems that are involved in the detection of conflict/temptation and the exercise of cognitive regulation and control. These brain systems are most prominently the anterior cingulate cortex (ACC) and the dorsolateral prefrontal cortex (dlPFC).
Homeostatic system	The body mechanism that aims to maintain a stable, relatively constant internal environment (e.g., with respect to energy and body temperature levels) since people's ability to adjust to conditions that are optimal for survival is crucial from a biological perspective.
Hormones	Signaling and messenger molecules that regulate body functions. They can be released by hormone-producing cells into the surrounding tissue (paracrine secretion) or into the blood vessels (endocrine secretion).
Neurotransmitters	Chemical messengers that allow communication between nerve cells.
Glucostatic theory	The idea that the brain monitors blood glucose levels and induces food intake when blood glucose levels are low.
Lipostatic theory	The theory that adipose tissue, the main energy storage of an organism, produces various signals depending on its relative mass, including metabolites and hormones, that interact with the brain and control eating behavior.
Metabolites	Substances that arise as intermediate or end products of metabolic processes in an organism.
Microbiota versus microbiome	The term "intestinal microbiota" refers to the entirety of all bacteria and other microorganisms (viruses, fungi, yeasts, and archaea) in the intestine. The term "intestinal microbiome" refers to the entirety of all microbial genes (DNA) in the human intestine. The two terms are often used synonymously.
Microbiome diversity	The degree to which the microbiome is composed of many different (versus very few) bacterial species. Higher diversity can be reflected in a higher number of species, more balanced prevalence of different species, or higher phylogenetic diversity among those species.
Gut–brain axis	Bi-directional communication between the central and enteric nervous systems, linking emotional and cognitive centres of the brain with peripheral intestinal functions.
Microbiota–gut–brain axis	Network of connections involving multiple biological systems that allows communication among gut bacteria, the gastrointestinal tract, and the brain. It is crucial in maintaining homeostasis of the gastrointestinal, central nervous, and microbial systems and—as first evidence suggests—also for reward processing in these systems.

associated with the fourth ventricle are likely to be involved in this control mechanism via the functioning of a number of neurotransmitters and neuromodulators, including noradrenaline, endorphins, and neuropeptide Y. Thus, the gastrointestinal hormones may control food intake in the short and long term (Abdalla, 2017; Cummings & Overduin, 2007).

The peptide hormone ghrelin has a special and complex role in food intake initiation (Dostálová & Haluzík, 2009; Klok et al., 2007; Konturek et al., 2004; Pradhan et al., 2013). Most of the ghrelin in the blood is synthesized by endocrine cells in the stomach and the proximal small intestine. Ghrelin is involved in the secretion of gastric acid (i.e., gastrointestinal motility), as well as in various cardiovascular, immunological, and reproductive processes. Ghrelin also regulates glucose homeostasis, since an infusion of ghrelin results in an increased blood glucose level, decreased glucose tolerance, and insulin secretion. Furthermore, ghrelin is involved in the regulation of body weight. Nakazato et al. (2001) found that ghrelin increased food uptake in rats and led to a positive energy balance with an increase in body weight, especially of body fat

mass. However, after numerous and often conflicting studies in humans, it is still under debate to what extent ghrelin might be useful for treating obesity in humans (Boguszewski et al., 2010; Kojima & Kangawa, 2005).

Cholecystokinin (CCK) is a well-investigated peripheral satiety hormone. The secretion of CCK is stimulated by eating a mixed diet, and the CCK concentration in the blood increases within a few minutes after food intake (Plata-Salamán, 1991). CCK has multiple effects, both at the level of the gastrointestinal tract and in the brain. The effects of CCK have been shown to be mediated by the vagus nerve, since severing the vagus nerve results in a suppression of CCK effects on satiation, at least for low doses (García-Cabrerizo et al., 2021). Several studies found that intravenously administered CCK causes a reduction in food intake of up to 16% in lean and higher weight participants (Cummings & Overduin, 2007; Gibbs et al., 1973; Murphy et al., 2006). In contrast, people with bulimia have low CCK plasma levels and respond poorly to administration of CCK (Geracioti et al., 1989; Hadley & Walsh, 2003; Hannon-Engel, 2012).

The hypothalamus produces other regulatory peptides, including neuropeptide Y (NPY), galanin, corticotropin-releasing hormone (CRH), melanocyte-stimulating hormone (MSH), and glucagon-like peptides-1 (GLP-1), that are crucial for the control of food intake (Williams et al., 2001; Williams & Elmquist, 2012). GLP-1 is one of the neuropeptides that reduces food intake by acting directly on the brain. Both the place of synthesis of GLP-1 and its receptors have been found in hypothalamic areas that are related to the regulation of food intake. It is assumed that the satiating effect of GLP-1 results from an interaction with NPY, the most potent stimulator of food intake: Possible interactions between GLP-1 and leptin are the object of ongoing research in neurobiology (Cummings & Overduin, 2007; Murphy et al., 2006; Zac-Varghese et al., 2010).

2.1.2 | The role of neurotransmitters and neuromodulators for the regulation of food intake decisions

Via the central nervous system, energy consumption and the selection of macronutrients are also influenced by several neurotransmitters and neuromodulators, including serotonin (5-hydroxytryptamine), norepinephrine, and various endogenous opioids. The effects of serotonin are the best known to date and suggest a bi-directional relationship between diet and serotonin metabolism (Leibowitz & Shor-Posner, 1986; Meguid et al., 2000; Shor-Posner et al., 1986). Serotonin is synthesized from the amino acid L-tryptophan. Thus, all processes that influence the plasma level of tryptophan and its uptake through the blood–brain barrier also have an effect on the biosynthesis of serotonin.

The availability of tryptophan depends to a large extent on whether the food is high in protein or high in carbohydrates (Strang et al., 2017; Wurtman & Wurtman, 1995). When someone eats protein-rich food, the serotonin level in the brain is low because the flow of tryptophan—the starting point for serotonin synthesis—is blocked. In contrast, consumption of carbohydrates leads to an increase in tryptophan levels and thus to increased serotonin synthesis. To a certain extent, the same effect can also be achieved by administering isolated tryptophan. In turn, and as a negative feedback mechanism, serotonin concentration in the brain influences the preference for protein or carbohydrate. In animal experiments the physiological relevance of this idea has been confirmed (Bendotti & Samanin, 1987; Lawton & Blundell, 1993; Morrison et al., 2012): After a meal rich in carbohydrates, rats prefer proteins in their subsequent food intake and vice versa. After a diet rich in carbohydrates, an increased serotonin concentration can be measured in the brains of the test animals.

A vast literature in neurophysiology has described the pathways by which these hormones and metabolites communicate with the brain circuits in the brainstem and the hypothalamus, which together can be described as the "homeostatic system" (see Figure 2 and for reviews, see Dagher, 2012; Morton et al., 2014; Williams & Elmquist, 2012).

More specifically, this homeostatic system includes the hypothalamic arcuate nucleus and nucleus of the solitary tract, the paraventricular nucleus (PVN), and the lateral hypothalamic area (see Figure 2; for detailed reviews, see Roh et al., 2016; G. Williams et al., 2001).

2.2 | Brain systems underlying (dietary) decision-making

The idea of the homeostatic eating model described above is that we eat when our energy resources are depleted and abstain from eating or stop eating when our energy levels are replenished. Yet eating behavior is also influenced by many other factors, such as the availability of food (e.g., in an all-you-can-eat restaurant), social and cultural context (e.g., at typical mealtimes), and internal cognitive and affective factors (e.g., boredom, stress, or dietary goals). For

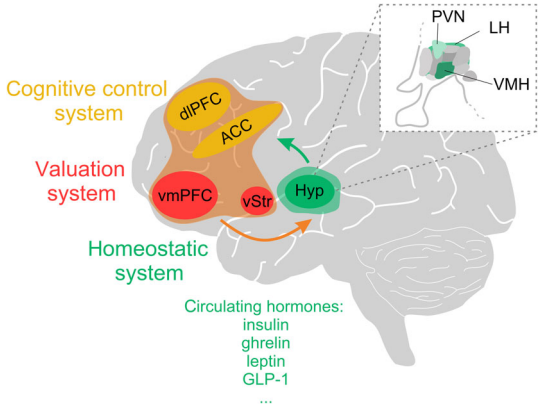

FIGURE 2 Schematic representation of the several brain circuits, including the homeostatic system (green), valuation system (red), and cognitive control system (yellow) that interactively regulate eating behavior. Metabolic signals are forwarded to the brain by circulating hormones and the vagus nerve and are processed in the hypothalamus. The metabolic signals that arrive in the hypothalamus are integrated with reward signals that are generated in the valuation system and are modulated by the cognitive control system. ACC, anterior cingulate cortex; dlPFC, dorsolateral prefrontal cortex; GLP-1, glucagon-like peptide 1; Hyp, hypothalamus; LH, lateral hypothalamus; PVN, paraventricular nucleus; VMH, ventromedial hypothalamus; vmPFC, ventromedial prefrontal cortex; vStr, ventral striatum

instance, we often continue to eat until our plate is empty, no matter how the portion size relates to our caloric needs (Wansink et al., 2005). We also often eat when we are not even hungry, such as when snacking on peanuts at a party (Berridge, 2004). We also tend to eat differently and typically less healthily when we are stressed (Adam & Epel, 2007; Tomiyama, 2018). Of note, the effects of acute and chronic stress on diet and weight gain are complex and bi-directional, with changes in glucose metabolism also affecting the hypothalamic–pituitary–adrenal (HPA) activity (Sinha, 2018). Together, these examples illustrate the role of motivational, affective, and social factors for dietary decision making and its control. In the next section we review which brain systems encode the value of rewards, including foods, at time of choice and their modulation by motivational, affective, and social factors to alter and regulate dietary decision-making.

2.2.1 | The brain's valuation system

How do we choose between sandwiches at lunchtime? How is this decision different from choosing which pair of jeans to buy, which stock to invest in, and so forth? Such choices play a prominent role in our everyday life, which explains why decision-making is studied in a variety of ways in different disciplines, including economics, psychology, behavioral ecology, and computer science. One idea common to many of these disciplines is that decision-making is guided by subjective representations of value (Rangel et al., 2008). Economic concepts such as "value," "utility," and "efficiency" provide a biologically sound framework for describing different kinds of choice behavior (Glimcher, 2004, 2010).

Within this framework of value-based decision-making, receiving rewards and avoiding punishments can be viewed as a proximate goal that, once reached, tends to enhance survival and reproductive success (Rangel et al., 2008). What do we know about valuation signals in choice situations? In disciplines ranging from value learning in computer science (Sutton & Barto, 1998) to expected utility theory in economics (von Neumann & Morgenstern, 2007), prospect theory in psychology (Kahneman & Tversky, 1979), and information-processing theories in consumer psychology (Bettman, 1979), most decision theories share the following idea: At the time of decision-making, the relevant attributes of the options for choice (such as tastiness and healthiness of food in our case) are integrated into a subjective value (SV) signal, one for each option, that can be formalized most simply as follows:

$$\mathrm{SV} = \sum\nolimits_i (w_i \cdot \mathrm{attribute}_i), \tag{1}$$

where, w_i denotes the weight assigned to each attribute i.

Value signals are subjective because people differ with respect to how much they think a ham sandwich is tasty (i.e., affecting the attribute level), and one person might put more emphasis on healthiness than another (i.e., affecting the weight put on the attribute). These valuation signals indicate how much value a decision maker expects to derive from the consumption of each food offered in a given choice situation. Much of the foundational research in neuroeconomics has focused on localizing brain systems that compute and represent these expected subjective valuation signals at the time of decision-making (for reviews see Bartra et al., 2010; Clithero & Rangel, 2014; Levy & Glimcher, 2012, but see also Hayden & Niv, 2020). There is a growing consensus suggesting that the ventromedial

prefrontal cortex (vmPFC)—together with other structures, especially the ventral striatum (vStr) and the posterior cingulate cortex (PCC)—plays a key role in encoding various aspects of subjective valuation (Bartra et al., 2010; Clithero & Rangel, 2014; Levy & Glimcher, 2012). Similar findings have been reported in studies that feature direct neural recordings in animals (Padoa-Schioppa & Assad, 2008; Stalnaker et al., 2015).

The evidence indicates that these neural signals have the characteristics of a "common currency" (Platt & Plassmann, 2014). In other words, they are both abstract and independent of the choice options' nature (i.e., whether choices concern food in a restaurant or shares on the stock market). The neural signals encoding value at time of choice overlap with brain regions that are involved in encoding value during consumption, often referred to as "experienced," "outcome" value, or "liking" (for a comparison, see Bartra et al., 2010). They likely act in concert with other brain areas, including the insula and amygdala, which respond to food cues and other (especially primary) rewards (Gupta et al., 2020; Tang et al., 2012). Activity in these areas is also strongly influenced by sensory cues, especially the taste and smell of highly palatable food. However, a detailed review of work investigating valuation during actual food consumption, such as taste pleasantness and "liking" encoding, is outside the scope of this review due to space constraints (for a recent review, see De Araujo et al., 2017).

On the neurotransmitter level, the dopaminergic system appears to play an important role in encoding value at time of choice: Dopaminergic neurons in the midbrain are well known for their role in hedonic, motivational, and reinforcement processes. For example, palatable food intake, when the food's taste is unexpected or better than expected, leads to dopamine signaling and can increase the learned value of the food item in the brain's memory system (Volkow et al., 2017). Increased dopaminergic signaling due to such palatable food intake can act as motivator or reinforcer and lead someone to repeatedly choose a piece of cake over a fruit salad each day at lunchtime (Nicola et al., 2005; Rangel, 2013; Volkow et al., 1996; Wise, 2004). That means that dopamine signaling is essential in a person's active seeking of a particular rewarding food and thus in the computation of its expected value, as opposed to being involved in encoding the taste pleasure of eating the rewarding food and thus in the computation of its outcome value (De Araujo et al., 2017; Pecina et al., 2003; Robinson & Berridge, 2004; Volkow et al., 2002).

2.2.2 | The brain's cognitive control system

A related question of important current debate in psychology and cognitive neuroscience (Berkman et al., 2017; Shenhav et al., 2013; Vosgerau et al., 2020) is how choices are made between options whose attributes reflect conflicting goals or temptations—such as choosing between an apple and a piece of chocolate cake when dieting—and how that decision context differs from deciding to spend money today instead of saving it and delaying consumption. Daily life is rife with various goal-oriented choices to be made between complex options that are associated with conflicting attributes. Conflict typically arises when some attributes are associated with concrete and immediately rewarding outcomes (e.g., the tastiness of chocolate cake) and others are associated with abstract and delayed ones (e.g., the healthiness of an apple). A normatively "good" decision requires computing predicted value signals that weigh both types of attributes properly, which involves discounting future outcomes at an appropriate rate (i.e., given the state of the decision maker). Current neuroeconomic theories (Hare et al., 2009; McClure, 2004; McClure et al., 2007) suggest the involvement of at least two brain systems in self-control, with major hubs in the prefrontal cortex: the brain's valuation system and the brain's cognitive control system—most prominently, the dorsolateral prefrontal cortex (dlPFC), which is presumed to implement control based on a conflict signal from the dorsal anterior cingulate (Botvinick et al., 2004; Buhle et al., 2013; Egner & Hirsch, 2005; Ochsner et al., 2012).

Related work on dietary self-regulation has established that participants can be trained to focus on one of the two conflicting goals—for example, a health goal that leads to better food choices (Giuliani et al., 2014; Kober et al., 2010; Siep et al., 2012; Sun & Kober, 2020; Yokum & Stice, 2013). Other research has shown that more general up-regulation and down-regulation of positive thoughts about healthy food and negative thoughts about unhealthy foods can result in healthier choices (Hare et al., 2009, 2011; Hutcherson et al., 2012). Dietary self-control behavior has been predicted based on correlations between such cognitive regulation processes and (a) the extent to which the dlPFC–vmPFC network is jointly activated (Hare et al., 2009, 2011; Hutcherson et al., 2012; Lopez et al., 2017) and (b) individual differences in gray matter density in the vmPFC and dlPFC (Schmidt et al., 2018).

Cognitive control of dietary decisions is susceptible to different states and context factors. For instance, acute stress reduces the influence of health goals compared with taste aspects on food choices, and this behavioral shift is paralleled by a decrease in dlPFC–vmPFC connectivity and an increase in vStr–vmPFC activity (Maier et al., 2015), in line with a

large body of evidence that links stress to altered eating patterns and to increased risk for weight gain and obesity (Adam & Epel, 2007; Pagoto et al., 2009; Sinha, 2018). Further, recent evidence points to a modulatory role of serotonin in dietary decision-making and in self-control and patience more broadly (Vlaev et al., 2017). Administration of a single dose of the serotonin reuptake inhibitor citalopram (compared with placebo) led to an increase in healthy compared with unhealthy food choices, suggesting that serotonin may amplify the consideration of long-term (e.g., health) goals (Vlaev et al., 2017). These findings are in line with previous results, which showed that optogenetic stimulation of serotonergic neurons increased patience for food rewards in mice (Miyazaki et al., 2014). In contrast, depletion of the serotonin precursor tryptophan increased sweet food consumption in higher-weight but not lean female individuals (Pagoto et al., 2009). Future research could further investigate the role of serotonin in food preferences and (dietary) self-control, and how those might be interrelated.

2.3 | Interactions between the homeostatic and value-based drivers of food choices

Homeostatic and value-based systems do not act independently but interact strongly with each other in determining food choice (Berthoud, 2011; Rangel, 2013). As described above, serotonin is influenced by nutrient levels and influences appetite for carbohydrates versus proteins, and at the same time may interact with cognitive control mechanisms and affect how health attributes influence food valuation.

Dopamine, another neurotransmitter, plays an even more central role for the brain's valuation system (Rangel, 2013; Rangel et al., 2008). At the same time, the dopamine system also interacts in several ways with the homeostatic system. Dopaminergic neurons in the ventral tegmental area (VTA) express receptors for homeostatic hormones, including leptin, ghrelin, GLP-1, and insulin (Figlewicz et al., 2003; Labouèbe et al., 2013; Skibicka et al., 2011). Thus, peripheral leptin, insulin, and GLP-1 can directly inhibit dopaminergic neurons from the VTA, while ghrelin can stimulate dopaminergic neurons (Ferrario et al., 2016; Labouèbe et al., 2013; X.-F. Wang et al., 2015). For example, eating a piece of cake causes leptin levels to rise and ghrelin levels to fall. Increased leptin levels lead to a stronger inhibition of dopaminergic neurons in the VTA. Similarly, decreased ghrelin levels lead to less stimulation of dopaminergic neurons in the VTA. In consequence, dopaminergic neurons are less active after consumption of a piece of cake. The reduced activity in the reward circuitry decreases the reinforcing value of the cake and reduces the likelihood of eating a second piece of cake (Narayanan et al., 2010; Palmiter, 2007; Volkow et al., 2011). These examples emphasize that gut hormones also control eating behavior beyond their effects on the hypothalamus. In addition, peripheral hormones also exert an indirect effect on the reward circuitry by stimulating areas of the hypothalamus (e.g., the lateral hypothalamus) that send projections to the VTA (Bonnavion et al., 2016).

Interactions between dopamine and homeostatic hormones can also work in the opposite direction. The anticipation of a non-food-related reward such as a drug reduces leptin levels in the plasma (You et al., 2016). Similarly, ghrelin levels before and after a meal are not purely dependent on nutritional status but are affected by the anticipation of a food reward (Drazen et al., 2006; V. Ott et al., 2012). Marketing labels highlighting the properties (indulgent vs. sensible) of a consumed food affect ghrelin levels (Crum et al., 2011).

In line with these observations, recent findings suggest that the rewarding and thus reinforcing properties of food stimuli do not arise solely from perceived taste pleasantness. Instead, internal homeostatic and nutritive signals (i.e., the presence of macronutrients, including glucose and fat, in the gut) also affect the central dopamine release and reward processing (De Araujo et al., 2017). For instance, a recent study by Thanarajah et al. (2019) used combined fMRI and PET to investigate the time course of regional changes in dopamine response during and after consumption of a milkshake. They showed both an immediate and a delayed (15–20 min after consumption) peak in dopaminergic brain responses. Areas including the vmPFC, orbitofrontal cortex, vStr, insula, and hypothalamus showed immediate dopamine response, whereas delayed peaks in dopamine response were found in putamen, vStr, amygdala, anterior insula, and subcortical areas (Thanarajah et al., 2019). The authors suggested that this delayed response in dopamine indicates that the nutritive value of food is able to reinforce its consumption independent of the experienced "liking" (e.g., taste and smell). An observed negative correlation of immediate and delayed dopaminergic response further points to an interaction of brain and gut for food valuation. However, other recent work points to a more complex picture and suggests that nutrient content, perceived taste (e.g., sweetness), and metabolic signals interact in unexpected and non-linear ways with brain reward signals (Veldhuizen et al., 2017).

3 | MICROBIOTA–GUT–BRAIN INTERACTIONS

We have outlined how homeostatic information about nutrients from the gastrointestinal tract can influence brain responses and dietary decision-making. In this section, we describe how the gut microbiota—the bacteria and other organisms that live in our intestinal tract—influence host health and well-being. We then discuss how the gut microbiota might interact with homeostatic and value-based drivers of dietary decision-making via the so-called "microbiota–gut–brain axis" (Foster & Neufeld, 2013; García-Cabrerizo et al., 2021; Mayer et al., 2015; Wang & Wang, 2016).

3.1 | The role of the gut microbiome for human health and well-being

With up to 10^{13} bacteria and more than a hundred different bacterial species, the human gastrointestinal tract houses the majority of physiologically relevant microbiota (Chatelier et al., 2013). Most of these bacteria live in symbiosis with their host. The totality of all microorganisms that colonize humans, including their genetic material, is called the microbiome. Our understanding of the complexity and diversity of the microbiome results mainly from recent advances in sequencing technology that enable a detailed analysis of all bacteria and viruses colonizing humans (Bella et al., 2013).

The development of the human microbiome is a complex process that is crucial for the physiology of the human body. It begins at birth, when the fetal intestine is colonized with microorganisms from the birth canal and from the mother's skin. In the course of life, the microbiome is influenced strongly by the host's diet, but also by genetics, age, gender, environment, stress, and health (Huttenhower et al., 2012; Rodríguez et al., 2015). Of these factors, diet has a particularly important influence on the composition of the gut microbiome (for reviews see Ezra-Nevo et al., 2020; Tengeler et al., 2018). Non-digestible but fermentable dietary fibers are a major energy source for gut bacteria. In a mouse model representing the human gut ecosystem, Turnbaugh et al. (2009) demonstrated an altered bacterial gene expression and metabolic potential after a change from a low-fat to a high-fat diet. Diets including high amounts of plant-based proteins have different effects on the gut microbiome and bacterial byproducts than diets with more animal-based proteins (Singh et al., 2017). Dietary supplements such as prebiotics (non-digestible fiber) and probiotics (live bacteria) as well as antibiotic treatment can also modulate the gut microbial composition (Preidis & Versalovic, 2009).

It is known that gut microorganisms play an important role in maintaining health and also in the pathogenesis of a wide variety of diseases (Cani, 2018; Chatelier et al., 2013; Gupta et al., 2020; Shreiner et al., 2015). Intestinal microorganisms contribute to the human metabolism in several ways. First, they ferment dietary fibers that are indigestible for humans into short-chain fatty acids (SCFA) and thus supply their host with energy. Second, they have important hormonal properties, modulate the immune system, and support the intestinal barrier function (Wasilewski et al., 2015).

There is preliminary evidence that the gut microbiome has an impact on cognitive and emotional processing via the gut–brain axis and can play an important role for brain functioning (Dinan & Cryan, 2017; Foster & Neufeld, 2013). For example, animal studies have shown that modulation of the microbiota affects signaling along the gut–brain axis and can affect anxiety and eating behavior (Foster et al., 2017). Studies in humans have found a distinct gut microbial pattern in patients with anxiety, depression, attention deficit hyperactivity disorder, autism spectrum disorder, and other mental illnesses (Dinan & Cryan, 2015; Fattorusso et al., 2019; Madan et al., 2020; Simpson et al., 2020). More specific to eating decisions, cardiometabolic diseases (CMDs) and obesity have been associated with changes in the composition of the gut microbiota (Aron-Wisnewsky & Clement, 2015; Shoaie et al., 2015). Several studies point at changes in microbiota composition after bariatric surgery in patients with obesity, suggesting links between gut microbiota alterations and metabolic improvement observed after surgery (Aron-Wisnewsky et al., 2012).

Taken together, it is likely not only that our food choices affect the composition of our gut microbiota, but also that the gut microbiota may in turn affect brain responses to food and how we choose what we eat. Yet little is known regarding the mechanisms at play.

3.2 | How could the microbiome affect dietary decision-making?

Growing evidence suggests a crucial role for the gut microbiota in the development of obesity (Chatelier et al., 2013; Torres-Fuentes et al., 2017; Turnbaugh et al., 2006, 2009). But what could be the mechanisms underlying this link

among gut microbiota, unhealthy food choices, and overeating? In what follows, we describe *how* the gut microbiome may influence brain function and dietary behavior. Generally, the gut microbiome and the brain communicate bi-directionally via the systemic and neural pathways that comprise the microbiota–gut–brain axis (for an overview, see Figure 3). Information that reaches the brain via circulation of the blood (i.e., the systemic pathways) includes the effects of microbial metabolites, interactions with gut peptides, neurotransmitter synthesis, and modulation of the immune system. The vagus nerve, one of the cranial nerves, is the principal neural pathway of gut-to-brain communication (Cryan & Dinan, 2012). How each of these communication pathways might affect dietary decision-making is discussed in the following sections.

3.2.1 | Microbial metabolites

The gut microbiome composition could influence (food) reward processing and decision-making via metabolites such as short-chain fatty acids (SCFA) (García-Cabrerizo et al., 2021), a major product of gut microbial fermentation (Den Besten et al., 2013). Evidence linking SCFA metabolism and reward processing comes from animal and human studies and various reward domains. For example, one study found that antibiotic treatment in mice led to a reduction of gut

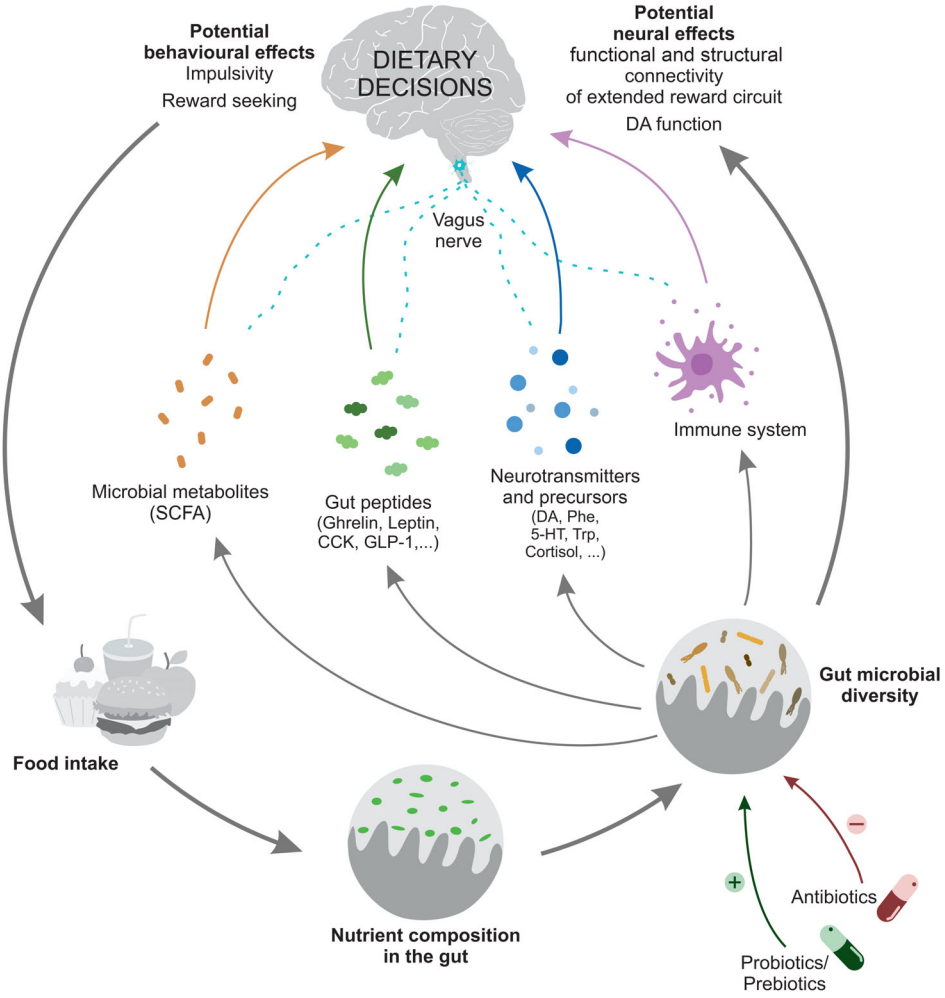

FIGURE 3 A reinforcing feedback loop of dieting behavior, gut microbiome, and food reward processing. Gut microbial diversity strongly depends on the nutrient composition in the gut. Thus, gut microbial composition varies with dietary patterns. In turn, gut microbial signaling via bacterial metabolites, gut peptides, neurotransmitters, and immune pathways affects dietary decision-making in the CNS. Several behaviors that are relevant for dietary decisions (e.g., impulsivity, reward seeking) are sensitive to gut microbial changes. 5-HT, serotonin; CCK, cholecystokinin; CNS, central nervous system; DA, dopamine; GLP-1, glucagon-like peptide 1; Phe, phenylalanine; SCFA, short-chain fatty acids; Trp, tryptophan

bacteria and increased sensitivity to cocaine reward, but administering bacterial fermentation products such as SCFA reversed these effects (Kiraly et al., 2016). In humans, an intervention that increased levels of the SCFA propionate reduced the valuation of high-energy foods in humans (Byrne et al., 2016). Propionate also reduced activity in the brain reward circuit (dorsal and ventral striatum) and decreased subjective appeal of high-energy food and energy intake (Byrne et al., 2016).

Providing further support for the hypothesis that gut metabolites can affect processing in brain areas related to reward and decision-making, a recent exploratory study (Osadchiy et al., 2018) found an association of gut microbiota-derived metabolites with the connectivity of the extended reward circuit in humans. More specifically, the authors found that microbial-derived fecal indole metabolites (enzymatically converted from the dietary amino acid tryptophan) were positively correlated with functional and anatomical connectivity between the central hub of the brain's reward and motivation system (i.e., the nucleus accumbens) and regions shown to be involved in taste processing (i.e., the amygdala and anterior insula; Berridge & Robinson, 2016; Ikemoto & Panksepp, 1999; Yiannakas & Rosenblum, 2017).

3.2.2 | Gut peptides

Peripheral ghrelin levels are sensitive to nutrition and to the composition of the gut microbiome and may thus constitute another pathway for gut–brain interactions in dietary decision-making. Both a 12-week dietary intervention with oligo-fructose (Parnell & Reimer, 2009) and changes in gut microbial composition resulting from antibiotic treatment (Yanagi et al., 2017) led to a reduction of plasma ghrelin. As outlined above, both neurophysiological and behavioral reward sensitivity is modulated by peripheral ghrelin levels; for example, higher ghrelin levels are associated with higher reward sensitivity and impulsivity (Ralevski et al., 2017).

3.2.3 | Neurotransmitters

Gut microbiota produce a variety of neurotransmitters and neurotransmitter precursors (Wasilewski et al., 2015) that could influence brain functioning and behavior. These include dopamine and serotonin, which are involved in reward-related decision-making (Fischer & Ullsperger, 2017; González-Arancibia et al., 2019; Strandwitz, 2018) and in interactions of valuation signals with homeostatic processes, as described above. For example, a recent study (Aarts et al., 2017) found an increased abundance of Bifidobacterium in stool probes of ADHD patients compared with controls; this was associated with an increased availability of a gut microbial enzyme that is involved in the synthesis of the dopamine precursor phenylalanine. Using fMRI, Aarts et al. (2017) further showed that the increased abundance of this enzyme was related to decreased ventral striatum activity during reward anticipation.

As described in Section 2.2, serotonin has been associated with healthier food choices and reduced consumption of sweet food (Miyazaki et al., 2014; Pagoto et al., 2009; Vlaev et al., 2017). While the link between serotonin and sweet food consumption seems to be moderated by body weight (Pagoto et al., 2009), it is interesting to note that gut microbial composition differs between lean participants and those with obesity (Ley et al., 2006). This association of serotonin levels and food choice suggests that bacterial modulation of tryptophan and serotonin levels (Clarke et al., 2013; O'Mahony et al., 2015; Yano et al., 2015) could mediate the effects of the gut microbiome on eating behavior. Tryptophan and serotonin levels might be especially sensitive to nutritional and microbial changes, as around 90% of the body's serotonin is synthesized in the gastrointestinal tract (Yano et al., 2015).

3.2.4 | Immune modulators

The modulation of the immune system is another important pathway of the gut–brain axis (Fung, 2020). Gut bacteria can activate the innate immune system and induce the release of pro-inflammatory and anti-inflammatory cytokines (for a review, see Zheng et al., 2020). These inflammatory markers can reach the brain, trigger neuroinflammatory reactions, and modulate serotonin and dopamine levels (Felger & Treadway, 2017; Miller et al., 2013), and as a consequence might have broad impact on reward processing and (dietary) decision-making (Bradley et al., 2019; Treadway et al., 2019). For instance, patients treated with the inflammatory cytokine tumor necrosis factor alpha (TNF-alpha)

have decreased activity in the ventral striatum during a gambling task, as well as changes in dopamine functioning in the same region (Capuron et al., 2012). In mice, treatment with lipopolysaccharide—a bacterial endotoxin that promotes inflammation—decreased the willingness to invest effort for food while reward sensitivity remained unchanged (Vichaya et al., 2014), and similar alterations in incentive motivation have been observed in humans (Lasselin et al., 2017). Thus, systemic inflammation is a further candidate mediator of bacterial effects on reward-seeking and eating behavior, but few studies have investigated the entire causal chain from gut microbiome composition via inflammation to value-based decision-making.

3.2.5 | Vagus nerve

Another route by which gut-derived nutritive signals might reach the brain is through neural signaling via the vagus nerve. As part of the autonomic nervous system, sensory fibers of the vagal nerve connect the gut and brain. Nerve endings in the gastrointestinal tract are able to sense nutrient-related chemicals (including ghrelin, GLP-1, and CCK; Browning et al., 2017). These gut-derived nutrient signals are forwarded to the central nervous system and elicit neural, endocrine, and behavioral reactions for the regulation of eating behavior (Howland, 2014; Le Roux et al., 2005; Waise et al., 2018). Extensive research in rodents has demonstrated that signaling of the vagus nerve affects the brain's reward-learning circuitry (De Araujo et al., 2012; Han et al., 2018; Suarez et al., 2018). For example, vagal afferent signaling increased reward sensation and motivation in mice and induced dopamine release from the substantia nigra onto the dorsal striatum (Han et al., 2018).

In humans, a recent study demonstrated the involvement of interoceptive gut-to-brain signals in reward processing via transcutaneous auricular vagus nerve stimulation (taVNS). In this study, taVNS decreased reward-learning in a go/no-go task (Kühnel et al., 2020). Another study found that when human participants worked for food and money rewards, taVNS did not increase subjective wanting per se or effort maintenance but boosted the desire to work for rewards, particularly those rewards that were wanted less (Neuser et al., 2020).

4 | TOWARD AN INTERDISCIPLINARY MODEL OF DIETARY DECISION-MAKING

The goal of this review was to provide a brief and interdisciplinary overview of dietary decision-making—what makes us eat what we eat. Advances have been made in multiple fields, and we specifically focused here on (a) the physiology of the homeostatic system, (b) the neuroeconomics of dietary decision-making, and (c) emerging evidence for a role of the gut microbiome in reward-based dietary decision-making. While these research areas have been largely separate from each other, there is a growing recognition of the need for more interdisciplinary research to understand dietary decisions and obesity from a more integrative perspective (Gupta et al., 2020; Rangel, 2013).

We highlighted emerging findings that suggest important interactions among dietary decision-making, neurophysiology, and gut microbiome composition. More specifically, it is becoming increasingly clear that homeostatic and peripheral physiological factors have important effects on dopaminergic and serotonergic function and the brain's processing of food rewards. So far, few studies to our knowledge have directly tested the effects of gut microbiome composition and its metabolites on brain responses to food cues and the brain circuits underlying dietary decision-making. Yet the microbiome is well positioned to influence these responses, potentially via its effects on metabolites, amino acids, and/or direct vagal communication with the brain.

What are the potential brain networks that could mediate such microbiome effects on dietary decision-making? Hypothetically, these interactions may take place via various brain systems and circuits. First, as discussed above, the gut microbiome may influence dietary decision-making via its effects on homeostatic signals and regulators. In this case, the composition of the gut microbiome may covary with processing in hypothalamic and other subcortical circuits. Second, via its effects on dopaminergic processing and on reward processing, the microbiome may directly or indirectly shape wanting and responses in the brain valuation system, including ventral striatum and vmPFC. In this case, we would expect that changes in microbiome composition are reflected in changes in how these brain areas respond to food cues. Third, given the importance of dopamine not only for value-based decision-making but also for cognitive control (Cools & D'Esposito, 2011; Ott & Nieder, 2019), the microbiome, especially via its effects on systemic inflammation, may also affect self-control and the cognitive regulation of food choices based on long-term (e.g., health) goals. In

this case, microbiome composition may covary with the processing in frontoparietal circuits associated with cognitive control and self-regulation, especially dlPFC. Finally, a fourth possibility is that the microbiome may influence sensory and interoceptive processing—for instance, how attuned we are to homeostatic but also gustatory and interoceptive signals. We note that these four potential levels of microbiome–brain interactions in dietary decision-making are not necessarily exhaustive and certainly not mutually exclusive, but could provide a framework for future studies.

While we highlight potential mechanisms by which the composition of the microbiome may affect dietary decision-making, the reverse pathway—the effects of dietary decision-making on the composition of the gut microbiome—is supported by a large body of evidence and thus is at least equally important (Cotillard et al., 2013; David et al., 2015). Given this bi-directional relationship, it is conceivable that obesity and other eating-related disorders reflect maladaptive "vicious circles" between unhealthy eating patterns that are reinforcing and are reinforced by a maladaptive composition of the gut microbiome, increased levels of inflammation, and a perturbation of basic homeostatic regulation mechanisms. From an evolutionary perspective it is plausible that intestinal microbes can manipulate the reinforcing properties of food and consequently eating behavior to favor the fulfillment of their own nutritional needs and survival (Alcock et al., 2014; Johnson & Foster, 2018; Leitão-Gonçalves et al., 2017). Thus, there is a need for future research to investigate potential links between gut microbiome and reward processing specifically in response to food stimuli. Future research in this area and future review pieces like this one need to integrate in more depth the microbiota–gut–brain axis communication during food consumption, particularly the impact of this communication for experienced value and "flavor liking" signals.

In sum, many questions remain unanswered thus far and need to be addressed to further advance our understanding of the complexity of eating behavior and obesity. Future studies could further experimentally manipulate the composition of the gut microbiome to test causal effects on the gut–brain axis and behavioral measures of dietary decision-making—food consumption and its control—in both human and animal models. An especially important point will be to characterize the *mechanisms* that might mediate gut microbial effects on brain responses and behavioral outcomes, and how they may be targeted to improve individual decision-making, long-term dietary patterns, and health.

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CONFLICT OF INTEREST

The authors have declared no conflicts of interest for this article.

AUTHOR CONTRIBUTIONS

Hilke Plassmann: Conceptualization; writing-original draft; writing-review & editing. **Daniela Schelski:** Conceptualization; visualization; writing-original draft; writing-review & editing. **Marie-Christine Simon:** Conceptualization; writing-original draft; writing-review & editing. **Leonie Koban:** Conceptualization; writing-original draft; writing-review & editing.

DATA AVAILABILITY STATEMENT

Data sharing is not applicable to this article as no new data were created or analyzed in this study.

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