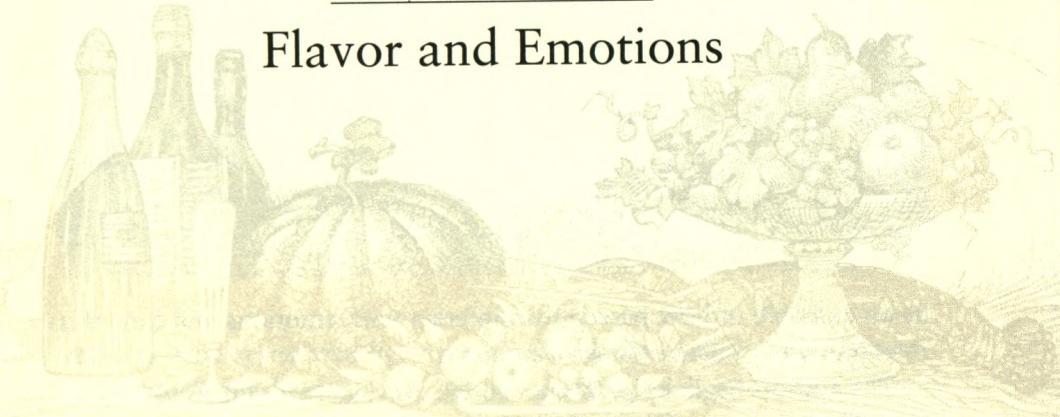


CHAPTER NINETEEN

Flavor and Emotions



In moving from the sensory input to the action output within the human brain flavor system, it is natural to begin with emotions. The word *emotions* is derived from “to move.” Just as movements of the mouth and tongue make flavor an active sense, so is it also an active sense in that we must be motivated to acquire the food and liquid we put in our mouths. As indicated in the previous chapter, these systems have a close relation to the part of the brain called the amygdala, and their activity can be seen as beginning with the motivation for *wanting* a food or liquid, which may be learned as a *liking* for it and then become a *craving* for it.

What kind of brain activity represents our motivation to desire a flavor, our emotion that makes us prefer it and want to obtain it? And if we become too highly motivated, too desiring, how does this brain activity pass over to craving it? These questions have stimulated much research that it is hoped will help us understand normal liking for food and abnormal craving for it.

Images of Desire

In the human, investigators have used functional brain imaging to answer these questions. Among the first to do so were Marcia Pelchat and her collaborators at the Monell Chemical Senses Institute in Philadelphia in 2004. It will be useful to describe this pioneering work in detail

BOX 19.1

Brain Regions Activated by Pleasant Food Smells

Orbitofrontal cortex	Cingulate	Parahippocampal gyrus
Insula	Amygdala	Anterior fusiform gyrus Striatum

as an example of how perceptions interact with emotions and how this interaction is studied in human subjects.

The authors begin by pointing out that craving a favorite food is experienced by most people, particularly young people, and may play a significant role in excessive snacking, eating disorders, and obesity. There is no strong evidence that cravings are for nutritional types of food, but there is evidence that a dull, boring diet stimulates strong cravings for more flavorful foods.

The authors noted that studies up to then had shown that food flavors activate certain brain areas. These areas were largely consistent with our discussion in the previous chapter and are summarized in box 19.1. These previous studies used hunger to stimulate the desire for the food. Hunger affects the whole body in a way that may obscure pure cravings for a desired food. The authors therefore decided instead to use a monotonous diet as a baseline for judging the activation of brain regions caused by craving.

At the time no one had done this kind of study. One hypothesis was that the areas activated by craved foods might be the same ones activated by pleasant foods. However, there are many foods we like without craving them. In addition, the authors were well aware that craving is also a characteristic of drug addiction. A great many people had been interested in the brain mechanisms underlying drug addiction and had worked out experimental procedures for bringing out drug cravings in patients, which could be studied using brain imaging. These activities had produced evidence that cravings for drugs, including alcohol, activated specific areas in the brain, which are summarized in box 19.2.

The overlap of the first four items in each table was intriguing. So the authors decided to focus on possible similarities in brain circuits when

BOX 19.2

Brain Regions Activated by Drugs of Abuse

Orbitofrontal cortex
 Insula
 Anterior cingulate
 Amygdala

Dorsolateral prefrontal cortex
 Hippocampus
 Caudate

subjects were stimulated by craved foods and by craved drugs: "We hypothesize that individuals receiving a monotonous diet will have greater food cravings and related activation in these candidate regions than individuals maintained on their normal diet." The hypothesis was bold in suggesting that a strong desire for particular foods we like—an exaggeration of otherwise normal feeding habits—might activate the same brain circuits as an abnormal addiction to substances of abuse, including social drugs such as tobacco and alcohol as well as illegal drugs such as cocaine. It was the kind of hypothesis that drives science, because it enabled the investigators to structure their study in an effective manner that not only was well focused on the subject at hand, but also allowed direct comparisons with the other studies.

The subjects were healthy college volunteers, some of whom were maintained for a couple of days on a normal diet and some on a monotonous diet. The monotonous diet consisted of a vanilla-flavored drink containing 240 kcalories plus protein and vitamins. The subjects consumed, on average, nine 8-ounce (226-gram) cans of the stuff a day, for a total of around 2,200 calories per day.

At the end of the second day, the subjects were tested in the brain scanner. They were first tested at rest. Then names of two foods they had selected that they really liked were presented to them visually, and they were asked to imagine the smell, taste, and texture of their favorite dish of the food while the brain scanner recorded their activity. Presenting the names instead of the pictures of the food avoided showing non-optimal versions of the food to different subjects; with the names, the subjects could themselves imagine their favorite version. The functional images of what is called the BOLD signal were obtained in a strong

BOX 19.3

Brain Regions Activated by Craving a Food

- Left hippocampus
- Left insula
- Right caudate nucleus

magnet (rated at 4 Tesla) that enabled activity in small brain regions to be seen.

The subjects all reported that they could easily imagine their favorite foods. The subjects on the monotonous diet in addition reported that they felt a craving for their liked food while imagining it, whereas craving was only reported by a portion of the subjects on a normal diet. No one reported a craving for the monotonous diet.

The brain scans were unequivocal. The subjects on the monotonous diet showed activation of specific brain regions while imagining their favorite foods, whereas those on a normal diet did not. The activated regions are shown in box 19.3. This result was significant, because all these regions fall within the group activated by drug cravings. Only the insula is shared with the pleasant food smells.

The authors thus consider that the results support their hypothesis of "a common circuitry for desire for natural and pathological rewards."

The hippocampus, the insula, and the caudate nucleus are three areas that also merit further discussion in the interest of neurogastronomy.

The *hippocampus* has been shown to be involved in cocaine addiction, possibly by reinvoking memory mechanisms that drive this behavior. It may similarly provide the memory traces that drive food craving. In psychological terms, the memory functions as the reinforcer for the learned craving. When the subject sees the drug, the incoming visual image is reinforced by the memory trace in the brain. The sites where they meet would be equivalent to the buffer of a mental image, as discussed in the previous chapter.

We have already met the insula as a site of convergence of taste and smell inputs; it has also been shown to be involved in taste memories

and in emotional behavior. Like the hippocampus, it may contain memories that act as reinforcers.

The *caudate* nucleus is a part of the system known as the *striatum* and plays multiple critical roles in sensorimotor coordination in the brain. It contains a high concentration of dopamine, the neurotransmitter released by fibers from the so-called substantia nigra (a region in the brain stem that appeared black to the early histologists who discovered it). This system is vulnerable to a range of disorders. Degeneration of the dopamine-containing cells in the substantia nigra and the terminals of their fibers in the striatum causes Parkinson's disease, which is associated with tremor of the hands, slowing of movement, and a range of other disorders, including (surprisingly) a decline in the sense of smell. Disorders of dopamine are also believed to be involved in schizophrenia.

Among the normal functions of the striatum are its involvement in the formation of motor habits, which is of interest; food cravings can be regarded as habits that are hard to break. Dopamine is also involved in the reward system of the orbitofrontal cortex, which we will discuss in chapters 21 and 22. With regard to drug cravings, it has been suggested by Ingmar Franken, Jan Booij, and Wim van den Brink in the Netherlands that "in conditioned subjects dopamine has a role [in] the earlier, motivational phase, i.e., before the use of the drug and before the experience of pleasure per se. This motivational phase can be labeled as the desire phase of drug use: [in other words] craving." This comment emphasizes the complex relations between the brain systems that produce the brain states we call motivation, leading to desire and craving, as well as to pleasure.

Finally, by subtracting the brain foci due to monotonous food cues from foci of liked food cues, the investigators were able to identify more regions that were activated when the subjects only thought about liking a food as well as craving it, as summarized in box 19.4.

Among these are the following that should be of interest for understanding the brain mechanisms for creating not only the perception of a food or flavor but the motivational and emotional states that make us like it.

The *left fusiform gyrus* on the bottom of the temporal lobe is interesting, because many studies have shown that activity in this area reflects

BOX 19.4

Brain Regions Activated by Liking a Food

Left fusiform gyrus

Bilateral cingulate gyrus

Left parahippocampal gyrus

Left caudate nucleus

Right amygdala

Right putamen

our perception of an emotion we are expressing. It works together with the nearby amygdala and parahippocampal gyrus in the following way. When hungry subjects view pictures of food, functional brain scans show activity specifically in these areas, as reported by Marsel Mesulam and his colleagues at the Northwestern Medical School in Chicago in 2001. The authors interpret their results as follows: "These results support the hypothesis that the amygdala and associated inferotemporal regions [the lower parts of the temporal lobe] are involved in the integration of subjective interoceptive [inside the body] states with relevant sensory cues processed along the ventral visual stream [the parts of the visual system that are involved in identifying objects]."

In plain language, this means that when we are hungry and view a picture of a food that we like, the picture sets up activity in the visual pathway that reaches cells in these regions to produce our personal internal "food image" of that food. This "interoceptive" image produces an emotion of liking those foods, as well as a motivation to acquire and consume them. It is an example of a mental image that is distributed among different regions and different modalities, a "multiregional multimodal image" that represents emotional and motivational states rather than the perception of what is pictured. The implication for the neuro-gastronomist is that when you sit down to enjoy your meal, the hungrier you are the more active are your internal "emotional flavor images" of the food flavors you are perceiving. Pelchat and her colleagues call these *images of desire*. They are to the flavor action system what the flavor images are to the flavor sensory systems.

The *amygdala* is usually more involved than indicated here. As we have seen, it is sensitive to the intensity of taste stimuli, among other things. It

also has an essential role in a wide range of emotional behavior in all mammals.

The *cingulate gyrus* is also of special interest to neurogastronomy. It is a ring of cortex just above the fibers of the corpus callosum that interconnect the two hemispheres. Several brain-scanning studies have shown that this is the brain region most consistently activated by stimuli that have a strong emotional quality and that figure in both food liking and food and drug craving. We have seen that it is part of several of the frontal lobe systems involved in those states.

Finally, the authors note that activity in the *orbitofrontal cortex* does not show up in their results. This may be due to the difficulty of imaging the BOLD signal in this part of the cortex, which is so close to the underlying bony braincase. But they note it may also be due to the fact that orbitofrontal activity may be involved in thinking about food in general, whether it is liked or disliked. This only reminds us that a scientific study combines biology, experimental methods, and interpretation, leaving unexplained results that require further study.

The overlap between cravings for food and drugs of addiction has become a major theme in modern studies, as is discussed in detail in chapter 22.

Chocolate: From Craving to Disgust!

A second perspective on brain mechanisms in food craving comes from a study by Dana Small and her colleagues in 2001 on craving for chocolate. They recruited nine subjects who described themselves as “chocolate lovers” and were high on a scale of “chocoholics.” Four and a half hours after breakfast, they began to be tested in a brain scanner with a square of chocolate. The diabolic strategy behind the study was not only to examine the brain areas activated by the chocolate at the start, but to continue the experiment with successive squares of chocolate until the subjects had been fed to satiety—until they could not stand to eat another square of chocolate.

The subjects varied, some of them quitting when they reached 16 squares (about a half bar of chocolate), whereas others lasted up to 74 squares

BOX 19.5

Brain Regions Activated by Chocolate

Like	Dislike
Subcallosal region	Orbitofrontal cortex
Orbitofrontal cortex	Parahippocampal gyrus
Insula and operculum	Prefrontal regions
Striatum	
Midbrain	

(about two and a half bars). There was a five-minute rest period between each square. As the study progressed, from hunger to satiety, the subjects were asked with each square how it rated on a scale of “delicious, I really want another piece” to “awful, eating more would make me sick.”

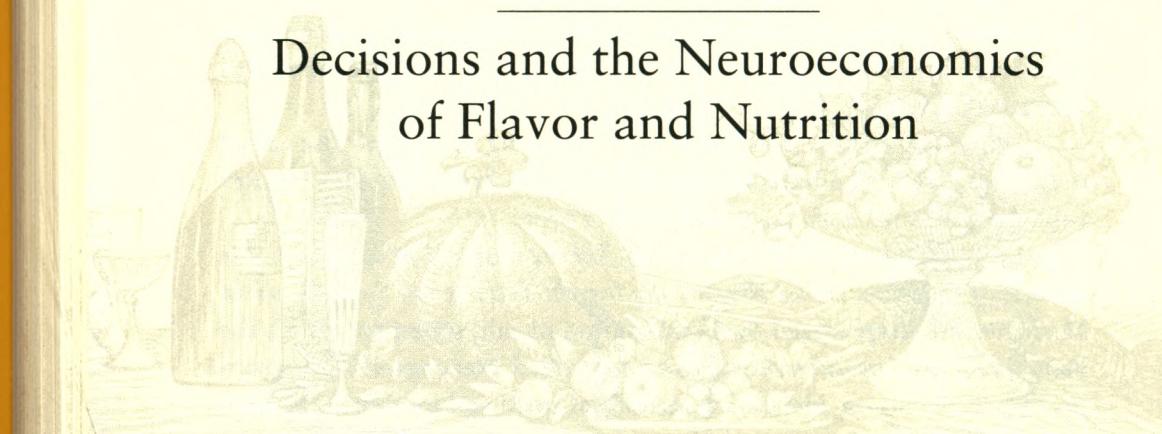
The brain scans thus provided evidence regarding the brain areas that were active when subjects were hungry and highly motivated to eat a craved-for food and those that were active when the subjects forced themselves to eat the same food when it tasted “awful.” The results are summarized in box 19.5. At the beginning, the active brain areas were the subcallosal region [under the corpus callosum connecting the two hemispheres], the orbitofrontal cortex, the insula and operculum, the striatum, and the midbrain. We can call this the *flavor image of chocolate when it is desired*. At the end, the active areas were the orbitofrontal cortex, the parahippocampal gyrus, and the prefrontal regions. This can be called the *flavor image of chocolate when it has been eaten to satiety*. Neurogastronomes may use this as an indication of how the activity within our brains shifts with the consumption of even our favorite foods.

A subtle aspect of this research strategy was that what changed was the *reward value* of the chocolate. There is much current interest in brain science in the reward value of a stimulus, because it signals what an animal holds important, is motivated to work for, and will make decisions about acquiring or not acquiring in relation to alternatives. Wolfram Schultz in Switzerland introduced this notion with his studies of how the dopamine system in the brain is activated when a monkey is making such

decisions about reward value. The chocolate study was an example of making decisions about reward value in relation to hunger or satiety. As discussed in chapter 12, reward value is one of the key functions of the orbitofrontal cortex, the neocortical end station of the olfactory pathway. This will be discussed further when we consider how the brain makes decisions about flavor (chapter 22).

CHAPTER TWENTY-TWO

Decisions and the Neuroeconomics of Flavor and Nutrition



The most important ultimate function of the human brain flavor system is making the right choices in consuming healthy or unhealthy food. The key to making these choices lies in the decision-making mechanisms of our brains, which only recently have begun to be recognized. Interest in these mechanisms has merged with the interests of economists, who for many years have realized that people make economic choices that are based on their value judgments about what they like. I first became aware of this when my father, Geoffrey Shepherd, wrote an article about it in 1956. This merging of interests of neuroscientists and economists has given rise to a new field called *neuroeconomics*, a term coined by Paul Glimcher in his book *Decisions, Uncertainty, and the Brain: The Science of Neuroeconomics*.

We have already met elements of the decision system in considering emotions and in the actions of dopamine on the subsystems we have studied thus far (chapter 19), as well as on the factors that lead to obesity (chapter 21). We bring them together here to enable us to enlarge the human brain flavor system to include the mechanisms that determine whether we eat in healthy, and flavor-fulfilling, ways.

Dopamine: Key to a Happy Life

One of the molecules that is key to how our brains work is the neurotransmitter *dopamine*, which was introduced when we discussed

emotions in chapter 19. The largest population of dopamine-containing neurons is in the midbrain—far away, you might think, from the highest levels of brain activity. However, from this vantage point these neurons send their axons throughout the brain. Some of them go to the striatum, a large region under the cerebral cortex that is involved in planning, initiating, and carrying out movements as well as in various motivational states; we have already met the striatum in chapter 19 as part of the system of habits for food cravings. Most people have heard about these dopamine cells because of their role in Parkinson's disease, in which the degeneration of these cells and their subsequent loss of input to the striatum results in progressive paralysis.

The other important concentration of dopamine neurons is located in what is called the *ventral tegmental area* (VTA). These cells connect widely in the brain. Especially relevant to the flavor system are parts of the striatum, the prefrontal cortex (including the orbitofrontal cortex), the insular cortex (where smell and taste are combined), the nucleus accumbens, the amygdala, and the hippocampus. These VTA-dopamine connections form what is called the *reward system* of the brain. The experiments providing evidence for this have been carried out in rats, monkeys, and humans and often involve the subjects working for rewards of fruit juice, so the subjects essentially are motivated by the images of rettronasal smell and flavor.

We have already met Wolfram Schultz in chapter 19 as a leader in studying these dopamine reward systems. In a typical experiment in his laboratory, a monkey explores for hidden food; when a hidden bit of cookie or another food is touched, the dopamine cells release a burst of impulses. In another type of experiment, the dopamine neurons fire a burst of impulses when the monkey is stimulated by the reward of water or fruit juice. The dopamine neurons fire to any rewarding stimulus (discriminating between the stimuli is done by the sensory systems). In his early experiments the cells did not respond to aversive stimuli, such as water that was too salty; the reward needed to be pleasurable. Recently some responses to aversive stimuli have also been found. Of special interest is the fact that dopamine neurons fire to conditioning stimuli, such as a light that signals a future reward. This means they are able to predict future rewards. This ability constitutes one of the highest cognitive functions of the brain. The dopamine neurons do this through their

modulation of the cells in the orbitofrontal cortex that are involved in planning future actions. Which brings us back to the human brain flavor system.

These functions modulated by dopamine are important for all sensory systems, but especially so for flavor. The dopamine fibers not only connect from the midbrain to the olfactory cortex, where they can modulate the formation of odor images and odor objects there, but also to the orbitofrontal cortex. In addition, in the olfactory bulb there are dopamine-containing interneurons (some of the periglomerular cells), so that dopamine can be involved in the shaping of the initial smell images in the glomerular layer. Another connection between smell and dopamine is found in the neurodegenerative diseases such as Parkinson's and Alzheimer's; an early sign of these diseases is a decline in smell sensitivity.

Through its role in reward systems in the brain, dopamine is also involved in the brain mechanisms underlying drug addiction. The way it works appears to be as follows. After dopamine is released to activate the reward neurons in the striatum and cerebral cortex, there are cell mechanisms for its reuptake to terminate its action. Cocaine blocks this reuptake, amplifying and prolonging dopamine's action, bringing on the addictive state. Some drugs also increase long-term potentiation at synapses where the excitatory neurotransmitter glutamate is released. Nicotine has been shown to have this effect. It also has a direct stimulatory effect on dopamine cells. There are thus multiple mechanisms for amplifying the reward system. Because of the inherent plasticity induced in brain cells by their activity, these actions tend to be self-prolonging. These addictive effects brought on by drug actions are present in food cravings, as we saw in chapter 19, and were a motivating hypothesis for the early study of food cravings. As we shall see, it is becoming an organizing principle for understanding overeating.

The Reticular System: Your USB Port

Because the dopamine cells have such widespread actions in the brain, it is important to know where they get their inputs. Some of them come from the same areas to which they project, completing feedback loops that can maintain their activity. The other main inputs come from the

core of the brain that is often called the *reticular system* because it is not a specific region but rather a kind of network of cells that stretches from the center of the brain stem into the depths of the forebrain. It is an ancient system, present in all vertebrates and expanded in the human. The cells have long dendrites, as if they are reaching out to receive and integrate many inputs from different brain regions. The key point is that their inputs come from within the brain, just as their outputs stay within the brain, so it is an entirely internal system.

This reticular system is the unknown workhorse of the brain. It is rather like the USB slot on your computer, ready to accept a wide range of input devices and connect them to the desired output. The inputs may come from the hypothalamus to stimulate or terminate feeding; they may signal different emotional or motivational states from the prefrontal cortex or the nucleus accumbens, a deep brain region or from different sensory systems, including those involved in flavor. The VTA neurons, with their own long dendrites, integrate these signals and transmit them through release of dopamine, in many cases back onto the same regions that have sent them their inputs. In this way, both the reticular system and the dopamine neurons are concerned with the significance and expectation of sensory inputs or motor outcomes rather than with discrimination among them. The fact that significance and expectation are embedded so deeply in our brains further explains how difficult it is to change the link between flavors and our cravings for them.

Brain Mechanisms for Making Food Choices

We are now in a position to incorporate all the elements of the human brain flavor system into the new field of neuroeconomics. This reflects the fact that economists have realized that the reason people attach economic value to a particular product is to be found not only in the product but even more so in the way an individual places personal value on the product—in essence, the way a person gives it a reward value. An example from recent studies illustrates this new field as it applies to decisions about flavors.

Todd Hare, Colin Camerer, and Antonio Rangel at the California Institute of Technology wished to know how we make choices, and postulated

that the brain has mechanisms for making optimal choices between alternatives. It had previously been shown that a value signal for making choices arises in the ventromedial area of the prefrontal cortex, in the frontal lobe, which as we have seen is concerned with higher cognitive functions. They hypothesized that this area must be under control by another area, the dorsolateral prefrontal cortex, which had been shown to be involved in various higher functions, including cognitive control of decision making. They were particularly interested in food choices, and set up experiments to study the brains of people on diets. Tests were first carried out to separate the subjects into two groups, those who demonstrated self-control and those who lacked self-control. The self-controllers chose foods that were healthy, the non-self-controllers chose foods that tended to be unhealthy.

The investigators then put the subjects in a brain scanner and carried out functional brain imaging while the subjects made their choices. They first found that activity in the ventromedial area was correlated with the subject's goal values, whether healthy or not. The activity was correlated with healthy ratings by the self-controllers but not by the non-self-controllers. The dorsolateral area was more active during successful self-control trials. And the dorsolateral and ventromedial areas were both active during self-control trials.

The authors make the interesting suggestion that the ventromedial area originally evolved to assign a short-term value to a food, such as flavor in this case, and the dorsolateral area developed subsequently to reflect long-term considerations, such as healthiness. The dorsolateral area has wide connections with other higher-cognitive brain areas, which the authors suggest may be why general intelligence and emotional control are involved in self-control in decision-making. In final summary, Hare, Camerer, and Rangel observe:

Lastly, an improved understanding of the neurobiology of self-control in decision-making will have applications to clinical practice in domains such as obesity and addiction, to economic and public policy analysis in problems such as sub-optimal savings and health behaviors, and to legal thinking about which criteria should be used in determining if an individual is in full command of his decision-making faculties and thus accountable to the law.

The Food Choice Control System

A synthesis of the brain systems involved in food choices has been made recently by Nora Volkow, Gene-Jack Wang, and Ruben Baler. Volkow has impeccable credentials for this task. She is a long-time student of drug addiction, as well as director of the National Institute on Drug Abuse (NIDA). As we saw in chapter 19, research on addiction is providing valuable insights into the brain mechanisms that are active in both drug craving and “images of desire” for food. This similarity has led Volkow in recent years to build on this background to propose a model for the different brain systems involved in food choice and healthy versus unhealthy eating (figure 22.1). This puts the basic elements of the model of the human brain flavor system presented in chapter 18 (see figure 18.2) into the more dynamic form of a control system.

The dynamic control model pictured in the figure consists of four main parts. It begins with *saliency*, a psychologist’s term for how strong and attractive a sensory stimulus is. Saliency includes the irresistible salty,

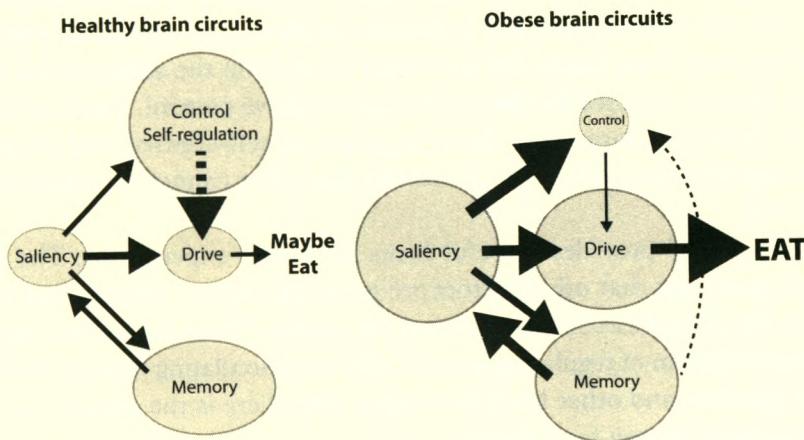


FIGURE 22.1 Schematic representation of the sensory control system in the human

This diagram was developed originally to depict the sensory control system as seen in drug addiction and is here applied to the control of eating.

(Adapted from N. D. Volkow, G.-J. Wang, and R. D. Baler, Reward, dopamine, and the control of food intake: Implications for obesity, *Trends in Cognitive Science* 15 [2011]: 37–45)

sugary, fatty, high-calorie density of fast foods; the smells of coffee and chocolate; and the balanced attractiveness of the flavors of traditional cuisines around the world. These reflect the array of sensory inputs shown in figure 18.2 as well as how much reward value they have as assessed by the brain mechanisms in the orbitofrontal cortex and related areas.

These inputs go to three main subsystems. One is the memory subsystem, which stores the conditioned preferences by learning of the individual. Second is the motivational drive subsystem that determines how much an individual desires or “craves” a kind of food. And third is the subsystem for inhibitory control, emotional regulation, and executive function, providing the top-down cognitive control of choice. Figure 22.1 shows that normally the executive function is strong. In the terms of the study by Hare, Camerer, and Rangel, people with this strong executive function are those with normal self-control.

By contrast, these systems and their interactions appear to be disrupted in obese individuals. As shown in figure 22.1, for them, saliency is powerful, in many cases overpowering, with strong inputs to all the systems. The learned memories of these overly attractive stimuli, the drive they elicit, and the input to the control subsystem are all increased. There is also a new direct input from the learned memories of the craved foods to the control subsystem. But in these individuals, the control subsystem is decreased. As a result, the increased drive from the salient stimuli is only weakly opposed by the inhibitory executive control. There is thus, in the terms of Hare and colleagues, a lack of self-control, and the person experiences a drive for the craved food that cannot be adequately resisted.

This model provides a useful focus for future experiments. The authors point out that other factors are involved, such as circuits that regulate mood and circuits for internal awareness. There is also the highly complex system of regulation of gut hormones, circulating levels of leptins and ghrelin, and other body hormones. And there is the critical role of language in human food choices.

We end by returning to our original question: what is it that makes the flavor of a given food irresistible? Recall the experiments on food cravings that we reviewed in chapter 19. In reviewing those studies in 2009,

Marci Pelchat notes: "Thus, this work supports the common substrate hypothesis for food and drug cravings. The prominent representation of memory and sensory integration structures in this study is consistent with the central role of sensory memory in the experience of food cravings. It is as if, when craving, one has a sensory template of what has to be eaten to satisfy the craving."

This brings us full circle back to the steps along the way we have covered of how the brain creates flavor: the sensory representation of odor images and odor objects—the "sensory template"—in memory circuits in the olfactory pathway; the integration with the other sensory representations in multiple areas of the cerebral cortex; the formation of images of desire by those interacting areas; and the magnification of those desires by activity in emotional circuits beyond the control by the decision-making centers of the brain. The diagrams of the human brain flavor action system (see figure 18.2) and of food addiction control (see figure 22.1) identify some of the hidden brain systems and their mechanisms that need to be taken into account in any public strategy to encourage healthful eating.