CHAPTER SIX

Motivation Explained: Ultimate and Proximate Accounts of Hunger and Appetite

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Contents

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Abstract

A theory of motivation is described in which rewards modulated by motivational states provide the goals for instrumental actions. The "ultimate" (evolutionary adaptive) value of the design principle is that genes specify the goals for actions, and not the actions themselves which can be learned. The "proximate" mechanisms underlying motivation are described with respect to the motivational system underlying hunger which modulates the appetite for the goal value of a food.

In primates, including humans, the primary taste cortex in the anterior insula provides separate and combined representations of the taste, temperature, and texture of food in the mouth independently of hunger and thus of reward value and pleasantness. One synapse on, in the orbitofrontal cortex, these sensory inputs are for some neurons combined by associative learning with olfactory and visual inputs, and these neurons encode food reward value in that they only respond to food when hungry, and in that activations correlate linearly with subjective pleasantness. Cognitive factors, including word-level descriptions, and selective attention to affective value, modulate the representation of the reward value of taste, olfactory, and flavor stimuli in the orbitofrontal cortex and a region to which it projects, the anterior cingulate cortex. These food reward representations are important in the appetite for food. Hunger and satiety signals reflecting many gastrointestinal and hormonal processes are integrated in the hypothalamus, and then modulate the reward value of food in the orbitofrontal cortex. Individual differences in these reward representations may contribute to obesity.

1. A THEORY OF MOTIVATION

1.1 Introduction and Aims

This article describes Rolls' theory of motivation, which encompasses both the ultimate and the proximal explanations of motivation, with special reference to the control of appetite, hunger, food reward, and the regulation of food intake.

Understanding the functions of motivation is important, not only for understanding the nature of motivation, but also for understanding the different brain systems involved in the different types of response that are produced by motivational states. Indeed, answers to "why" questions in nature (for example, "Why do we have motivation? What are the functions of motivation?") are important and are "ultimate" answers. So also are answers to "how" questions (for example, "How is motivation implemented in the brain? How do disorders of motivation arise and how can they be understood and treated?"), which are "proximate" or mechanistic answers. In fact, answers to proximate questions often suggest answers to ultimate questions, and this is the case in my exploration of the mechanisms for motivation and its functions.

In this article, the question of why we have motivation is a fundamental issue that I answer in terms of a Darwinian, functional, approach, producing the answer that motivations are states elicited to enable us by instrumental goal-directed learning to perform actions to obtain goals (rewards and punishers), and that this is part of an adaptive process by which genes can specify the behavior of the animal by specifying goals for behavior rather than fixed responses. I believe that this approach leads to a fundamental understanding of why we have motivation which is likely to stand the test of time, in the same way that Darwinian thinking itself provides a fundamental way of understanding biology and many "why" questions about life (Rolls, 2012c).

While considering "why" (or "ultimate") questions (which are important in their own right), it may be helpful to place into perspective the approaches taken to understanding the adaptive value of behavior (Tinbergen, 1963) that have led to sociobiology and evolutionary psychology (Buss, 2015). These approaches are relevant to understanding why we have motivation and emotion. "Adaptation" refers to characteristics of living organisms—such as their color, shape, physiology, and behavior—that enable them to survive and reproduce successfully in the environments in which they live (Dawkins, 1995).

Sociobiology and evolutionary psychology have sometimes been criticized as producing "just-so" stories in which the purported adaptive explanation for a behavior seems too facile and untestable (Gould & Lewontin, 1979), but we should note that there are rigorous approaches to testing evolutionary hypotheses for the adaptive value of a behavior or other characteristic (Buss, 2015; Dawkins, 1995). Thus adaptive accounts of behavior can be tested, and need not be "just-so" stories. Further, by no means does all behavior reflect optimal adaptation (Dawkins, 1982).

1.2 The Outline of a Theory of Motivation

I will first introduce the essence of the definition of motivation that I propose. **My definition of motivation is that motivational states are states that are present when rewards and punishers, that is, instrumental reinforcers, are the goals for action**. A reward is anything for which an animal (and this includes humans) will work. A punisher is anything that an animal will work to escape or avoid, or that will suppress actions on which it is contingent (Rolls, 2014). The force of "instrumental" in this definition is that the motivational states are seen as defining the goals for arbitrary behavioral actions, made to obtain the instrumental reinforcer. This is very different from classical conditioning, in which a response, typically autonomic, may be elicited to a stimulus without any need for an intervening state (Rolls, 2014). The motivational states modulate the reinforcement value of instrumental reinforcers with particular functions (Rolls, 2014).

An example of a motivational state might thus be a hunger state in which the animal will perform goal-directed actions to obtain the reinforcer or goal. Another example is that the omission or termination of a reward ("extinction" and "time out, " respectively) can produce a motivational state of frustration, in which the probability of the action may become reduced if no action is possible to regain the reward, or may increase if further motivated attempts are likely to lead to the reward (Rolls, 2014).

These examples show that the reinforcement contingency as well as the particular reinforcer or goal object (eg, food, water, aversive stimulation) lead to particular motivational states. The types of motivational state produced by different reinforcement contingencies are illustrated in Fig. 1. The diagram summarizes motivational states that might arise for one reinforcer as a result of different contingencies. Every separate reinforcer has the potential to operate according to contingencies such as these. Each different reinforcer will produce different motivational states, but the contingencies will operate as shown to produce different specific motivational

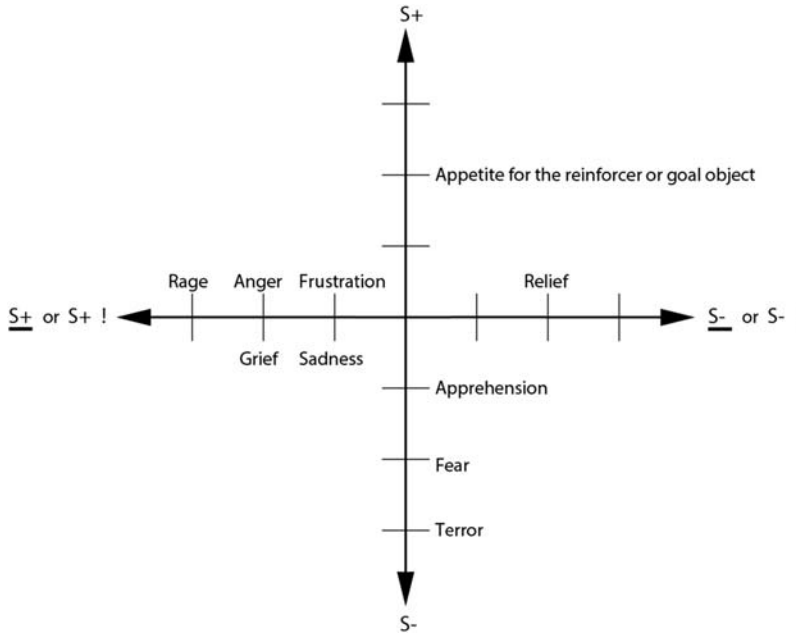

Figure 1 Some of the motivational states associated with different reinforcement contingencies are indicated. Intensity increases away from the centre of the diagram, on a continuous scale. The classification scheme shows how different motivational states created by the different reinforcement contingencies consist of being in a state that leads to (1) performing an action to obtain a reward (S+), (2) performing an action to escape from or avoid a punisher (S−), (3) performing an action, or not, because of the omission of a reward (S+) (extinction) or the termination of a reward (S + !) (time-out), and (4) performing an action, or not, because of the omission of a punisher (S−) (avoidance) or the termination of a punisher (S−!) (escape). Note that the vertical axis describes motivational states associated with the delivery of a reward (up) or punisher (down). The horizontal axis describes motivational states associated with the nondelivery of an expected reward (left) or the nondelivery of an expected punisher (right). The diagram summarizes motivational states that might arise for one reinforcer as a result of different contingencies. Every separate reinforcer has the potential to operate according to contingencies such as these. Each different reinforcer will produce different motivational states, but the contingencies will operate as shown to produce different specific motivational states for each different reinforcer.

states for each different reinforcer. Thus hunger might be present when the appetite is for the goal object of food, and thirst when the appetite is for the goal object of water. Definitions of reinforcers, and of the contingencies with which they operate, are elaborated by Rolls (2014).

We must be clear about the difference between motivation and emotion. According to Rolls' theory of emotion, emotion is the state that results from

having received, or not having received, the instrumental reinforcer, the goal object (Rolls, 2014). In contrast, motivation is the state when the instrumental reinforcer is being worked for, before the outcome stage, where the outcome is the delivery or not of the reinforcer. An important attribute of this theory of motivation and emotion is that the goal objects can be the same for motivation and emotion, simplifying the biological specification, with the difference being that motivation is the phase before the outcome, and emotion is the phase after the outcome. An additional property is that emotions, states occurring after the delivery or not of the reinforcer, can be motivating (Rolls, 2014). A good example is that if an expected reward is not obtained, then the frustrative nonreward can be motivating, and make the animal work harder to obtain the goal object (Rolls, 2014).

Reinforcers, that is rewards or punishers, may be unlearned or **primary reinforcers**, or learned, that is secondary reinforcers. An example of a primary reinforcer is pain, which is innately a punisher. The first time a painful stimulus is ever delivered, it will be escaped from, and no learning that it is aversive is needed. Similarly, the first time a sweet taste is delivered, it acts as a positive reinforcer, so it is a primary positive reinforcer or reward. Other stimuli become reinforcing by learning, because of their association with primary reinforcers, thereby becoming "secondary reinforcers." For example, the sight of a food that regularly precedes the flavor of the food can rapidly become a secondary reinforcer.

Some examples of primary reinforcers are provided in Table 1. All of the primary reinforcers or goal objects can elicit different, specific, motivational states. As these are primary reinforcers, they are likely to be gene-specified.

1.3 Motivational States Are States Elicited by Instrumental Reinforcers, and Are Different From Taxes, Approach Responses, and Classical Conditioning

1.3.1 Taxes

A simple design principle is to incorporate mechanisms for taxes into the design of organisms. Taxes consist at their simplest of orientation toward stimuli in the environment, for example, the bending of a plant toward light that results in maximum light collection by its photosynthetic surfaces. When just turning rather than locomotion is possible, such responses are called tropisms. With locomotion possible, as in animals, taxes include movements toward sources of nutrient, and movements away from hazards such as very high temperatures. The design principle here is

Table 1 Some primary reinforcers and the dimensions of the environment to which they are tuned

Taste	
Salt taste	Reward in salt deficiency
Sweet	Reward in energy deficiency
Bitter	Punisher, indicator of possible poison
Sour	Punisher
Umami	Reward, indicator of protein; produced by monosodium glutamate and inosine monophosphate
Tannic acid	Punisher; it prevents absorption of protein; found in old leaves; probably somatosensory not gustatory (Critchley & Rolls, 1996c)
Odor	
Putrefying odor	Punisher; hazard to health
Pheromones	Reward (depending on hormonal state)
Somatosensory	
Pain	Punisher
Touch	Reward
Grooming	Reward; to give grooming may also be a primary reinforcer.
Washing	Reward
Temperature	Reward if tends to help maintain normal body temperature; otherwise punisher
Visual	
Snakes, etc.	Punisher for, eg, primates
Youthfulness	Reward, associated with mate choice
Beauty, eg, symmetry	Reward

(*Continued*)

Table 1 Some primary reinforcers and the dimensions of the environment to which they are tuned—cont'd

Secondary sexual characteristics	Rewards
Face expression	Reward (eg, smile) or punisher (eg, threat)
Blue sky, cover, open space	Reward, indicator of safety
Flowers	Reward (indicator of fruit later in the season?)
Auditory	
Warning call	Punisher
Aggressive vocalization	Punisher
Soothing vocalization	Reward (part of the evolutionary history of music, which at least in its origins taps into the channels used for the communication of emotions)
Reproduction	
Courtship	Reward
Sexual behavior	Reward (different reinforcers, including a low waist-to-hip ratio, and attractiveness influenced by symmetry and being found attractive by members of the other sex)
Infant attachment to parents (love)	Reward (good for the infant's genes)
Crying of infant	Punisher to parents; produced to promote successful development
Mate guarding	Reward for a male to protect his parental investment. Jealousy results if his mate is courted by another male, because this may ruin his parental investment
Nest building	Reward (when expecting young)
Parental attachment (love)	Reward (good for the parent's genes both when the attachment is to the other parent or an infant)
Power, status, wealth, resources	Attractive to females, who may benefit from resources for their offspring. Attractive to males as they make males attractive to females.
Body size	Large in males may be attractive to females as a signal for the provision of protection and of the ability of her male offspring to compete for a mate. Small in females may be attractive to males as a neotenous sign of youth, and therefore fertility

Other	
Novel stimuli	Rewards (encourage animals to investigate the full possibilities of the multidimensional space in which their genes are operating)
Sleep	Reward; minimizes nutritional requirements and protects from danger
Altruism to genetic kin	Reward (kin altruism)
Altruism to other individuals	Reward while the altruism is reciprocated in a tit-for-tat reciprocation (reciprocal altruism). Forgiveness, honesty, and altruistic punishment are some associated heuristics. May provide underpinning for some aspects of what is felt to be moral.
Altruism to other individuals	Punisher when the altruism is not reciprocated
Group acceptance, reputation	Reward (social greeting might indicate this). These goals can account for why some cultural goals are pursued
Control over actions	Reward
Play	Reward
Danger, stimulation, excitement	Reward if not too extreme (adaptive because of practice?)
Exercise	Reward (keeps the body fit for action)
Mind reading	Reward; practice in reading others' minds, which might be adaptive
Solving an intellectual problem	Reward (practice in which might be adaptive)
Storing, collecting	Reward (eg, food)
Habitat preference, home, territory	Reward
Some responses	Reward (eg, pecking in chickens, pigeons; adaptive because it is a simple way in which eating grain can be programmed for a relatively fixed type of environmental stimulus)
Breathing	Reward

that animals have, through a process of natural selection, built receptors for certain dimensions of the wide range of stimuli in the environment, and have linked these receptors to response mechanisms in such a way that the stimuli are approached or escaped from.

1.3.2 Rewards and Punishers: Instrumental Goals for Action Toward Which Motivation Is Directed

As soon as we have approach to stimuli at one end of a dimension (eg, a source of nutrient) and away from stimuli at the other end of the dimension (in this case, lack of nutrient), we can start to wonder when it is appropriate to introduce the terms "rewards" and "punishers" for the stimuli at the different ends of the dimension. By convention, if an animal's response consists of a fixed response to obtain the stimulus (eg, locomotion up a chemical gradient), we shall call this a taxis not a reward. If fixed behavioral response or action pattern such as skeletomotor freezing and autonomic responses are elicited by a stimulus, they may be adaptive, but are essentially stimulus–response reflexes, with no need for an intervening state, such as the representation of a goal to be reached. On the other hand, if an arbitrary operant action (an instrumental action) can be performed by the animal in order to approach the stimulus, then we will call this rewarded behavior, and the stimulus that the animal works to obtain a reward, the goal for the action. The arbitrary operant response can be thought of as any arbitrary response the animal will perform to obtain the stimulus. It can be thought of as an action. This criterion, of an arbitrary operant response, is often tested by bidirectionality. For example, if a rat can be trained to either raise its tail, or lower its tail, in order to obtain a piece of food, then we can be sure that there is no fixed relationship between the stimulus (eg, the sight of food) and the response, as there is in a taxis. I, and a number of other authors, reserve the term "motivated behavior" for that in which an arbitrary operant action, an instrumental action, will be performed to obtain a reward or to escape from or avoid a punisher. If this criterion is not met, and only a fixed response can be performed, then the term "drive" can be used to describe the state of the animal when it will work to obtain or escape from the stimulus.

We can thus distinguish a first level of approach/avoidance mechanism complexity in a taxis, with a fixed response available for the stimulus, from a second level of complexity in which any arbitrary response (or action) can be performed, in which case we use the term reward when a stimulus is being approached, and punisher when the action is to escape from or avoid the stimulus.

The role of natural selection in this process is to guide animals to build sensory systems that will respond to dimensions of stimuli in the natural environment along which actions of the animals can lead to better survival to enable genes to be passed on to the next generation, which is what we mean by fitness. Fitness refers to the fitness of genes, but this must be measured by the effects that the genes have on the organism. The animals must be built by such natural selection to perform actions that will enable them to obtain more rewards; that is, to work to obtain stimuli that will increase their fitness. Correspondingly, animals must be built to perform actions that will enable them to escape from, or avoid (when learning mechanisms are introduced), stimuli that will reduce their fitness. There are likely to be many dimensions of environmental stimuli along which actions of the animal can alter fitness. Each of these dimensions may be a separate reward–punisher dimension. An example of one of these dimensions might be food reward. It increases fitness to be able to sense nutrient need, to have sensors that respond to the taste of food, and to perform behavioral responses to obtain such reward stimuli when in that need or motivational state. Similarly, another dimension is water reward, in which the taste of water becomes rewarding when there is body fluid depletion (Rolls, 2005).

One aspect of the operation of these reward–punisher systems that these examples illustrate is that with very many reward–punisher dimensions for which actions may be performed, there is a need for a selection mechanism for actions performed to these different dimensions. In this sense, rewards and punishers provide a common currency that provides one set of inputs to action selection mechanisms. Evolution must set the magnitudes of each of the different reward systems so that each will be chosen for action in such a way as to maximize overall fitness. Food reward must be chosen as the aim for action if some nutrient depletion is present, but water reward as a target for action must be selected if current water depletion poses a greater threat to fitness than does the current degree of food depletion. This indicates that for a competitive selection process for rewards, each reward must be carefully calibrated in evolution to have the right value on a common scale for the selection process (but not converted into a common currency) (Rolls, 2014). Other types of behavior, such as sexual behavior, must be performed sometimes, but probably less frequently, in order to maximize fitness (as measured by gene transmission into the next generation).

There are many processes that contribute to increasing the chances that a wide set of different environmental rewards will be chosen over a period of

time, including not only need-related satiety mechanisms that reduce the rewards within a dimension (such as hunger signals described later), but also sensory-specific satiety mechanisms, which facilitate switching to another reward stimulus (sometimes within and sometimes outside of the same main dimension), and attraction to novel stimuli. Attraction to novel stimuli, ie, finding stimuli rewarding, is one way that organisms are encouraged to explore the multidimensional space within which their genes are operating. The suggestion is that animals should be built to find somewhat novel stimuli rewarding, for this encourages them to explore new parts of the environment in which their genes might do better than others' genes. Unless animals are built to find novelty somewhat rewarding, the multidimensional genetic space being explored by genes in the course of evolution might not find the appropriate environment in which they might do better than others genes (Rolls, 2014).

1.3.3 Habit or Stimulus–Response Learning

In this second level of complexity, involving reward or punishment, learning may occur. If an organism performs trial and error responses, and as the result of performing one particular response is more likely to obtain a reward, then the response may become linked by a learning process to that stimulus as a result of the reward received. The reward is said to reinforce the response to that stimulus, and we have what is described as stimulus–response or habit learning. The reward acts as a positive reinforcer in that it increases the probability of a response on which it is made contingent. A punisher reduces the probability of a response on which it is made contingent. It should be noted that this is an operational definition, and that there is no implication that the punisher feels like anything in particular—the punisher just has, in the learning mechanism, to reduce the probability of responses followed by the punisher. Stimulus–response or habit learning is typically evident after overtraining, and once habits are being executed, the behavior becomes somewhat independent of the reward value of the goal, as shown in experiments in which the reward is devalued. This is described in more detail in the section 1.3.6 *Wanting and Liking*.

1.3.4 Instrumental, Action–Outcome, Goal-Directed, Learning

When behavior is under control of the goal, the reward or punisher, then we call this motivated behavior. A test of whether the behavior is under the control of the goal is reward devaluation. For example, if humans and other animals are fed to satiety with a food, they show sensory-specific satiety for

the food, rate its subjective pleasantness as zero, and are no longer motivated to obtain and ingest it. The motivation for other foods not eaten to satiety usually remains (see the section *Sensory-Specific Satiety*). The hallmark of a devaluation experiment showing that a behavior is under the control of the goal and therefore qualifies for being described as 'motivated' is that when the goal is devalued, the human or other animal will not perform an instrumental action to obtain it the first time that the stimulus is presented (see the section *Wanting versus liking*).

Two stages of learning may be involved in such goal-controlled instrumental learning. Rewards and punishers provide the basis for guiding behavior within a dimension, and for selecting the dimension toward which action should be directed.

The first stage of the learning is stimulus–reinforcer association learning, in which the reinforcing value of a previously neutral, eg, visual or auditory, stimulus is learned because of its association with a primary reinforcer, such as a sweet taste or a painful touch. This learning is of an association between one stimulus, the conditioned or secondary reinforcer, and the primary reinforcer, and is thus stimulus–stimulus association learning. This stimulus–reinforcer learning can be very fast, in as little as one trial. For example, if a new visual stimulus is placed in the mouth and a sweet taste is obtained, a simple approach response such as reaching for the object will be made on the next trial. Moreover, this stimulus–reinforcer association learning can be reversed very rapidly. For example, if subsequently the object is made to taste of salt, then approach no longer occurs to the stimulus, and the stimulus is even likely to be actively pushed away. This process leads to representations of expected value in the orbitofrontal cortex (Rolls, 2014).

The second process or stage in this type of learning is instrumental learning of an action (or "operant response") made in order to obtain the stimulus now associated with reward (or avoid the stimulus associated by learning with the punisher). This is action–outcome learning (implemented in brain regions such as the cingulate cortex (Grabenhorst & Rolls, 2011; Rolls, 2014; Rushworth, Noonan, Boorman, Walton, & Behrens, 2011)). The outcome could be a primary reinforcer, but often involves a secondary reinforcer learned by stimulus–reinforcer association learning. The action–outcome learning may be much slower, for it may involve trial and error learning of which action is successful in enabling the animal to obtain the stimulus now associated with reward or avoid the stimulus now associated with a punisher. However, this second stage may be greatly speeded if an operant response or strategy that has been learned previously to obtain a

different type of reward (or avoid a different punisher) can be used to obtain (or avoid) the new stimulus now known to be associated with reinforcement. It is in this flexibility of the response that two-factor learning has a great advantage over stimulus–response learning. The advantage is that any response (even, at its simplest, approach or withdrawal) can be performed once an association has been learned between a stimulus and a primary reinforcer. This flexibility in the response is much more adaptive (and could provide the difference between survival or not) than no learning, as in taxes, or stimulus–response learning. The different processes that are involved in instrumental learning are described in more detail by Rolls (2014).

Another key advantage of this type of two-stage learning is that after the first stage the different rewards and punishers available in an environment can be compared in a selection mechanism, using the common scale of different rewards and punishers for the comparison and selection process (Rolls, 2014). In this type of system, the many dimensions of rewards and punishers are again the basis on which the selection of a behavior to perform is made (Rolls, 2014).

1.3.5 Gene-Specified Rewards and the Mechanisms of Evolution

Part of the process of evolution can be seen as identifying the factors or dimensions that affect the fitness of an animal, and providing the animal with sensors that lead to rewards and punishers that are tuned to the environmental dimensions that influence fitness. The example of sweet taste receptors being set up by evolution to provide reward when physiological nutrient need is present has been mentioned previously.

We can ask whether there would need to be a separate sensing mechanism tuned to provide primary (unlearned) reinforcers for every dimension of the environment to which it may be important to direct behavior (the behavior has to be directed to climb up the reward gradient to obtain the best reward, or to climb a gradient up and away from punishers). It appears that there may not be. For example, in the case of the so-called specific appetites, for perhaps a particular vitamin lacking in the diet, it appears that a type of stimulus–reinforcer association learning may actually be involved, rather than having every possible flavor set up to be a primary reward or punisher. The way that this happens is by a form of association learning. If an animal deficient in one nutrient is fed a food with that nutrient, it turns out that the animal "feels better" some time after ingesting the new food, and associates this "feeling better" with the taste of that particular food. Later, that food will be chosen. The point here is that the first time

the animal is in the deficient state and tastes the new food, that food may not be chosen instead of other foods. It is only after the postingestive conditioning that, later, that particular food will be selected (Rozin & Kalat, 1971). Thus in addition to a number of specific primary (unlearned) reward systems (eg, sweet taste for nutrient need, salt taste for salt deficiency, pain for potentially damaging somatosensory stimulation), there may be great opportunity for other arbitrary sensory stimuli to become conditioned rewards or punishers by association with some quite general change in physiological state. The implication here is that a number of bodily signals can influence a general bodily state, and we learn to improve the general state, rather than to treat the signal as a specific reinforcer that directs us to a particular goal. Another example might be social reinforcers. It would be difficult to build in a primary reinforcer system for every possible type of social reinforcer. Instead, there may be a number of rather general primary social reinforcers, such as acceptance within a group, approbation, greeting, face expression, and pleasant touch, which are among the primary rewards; and by association with these primary rewards, other stimuli can become secondary social reinforcers.

To help specify the way in which stimulus—reinforcer association learning operates, a list of what may be in at least some species primary reinforcers is provided in Table 1. The reader will doubtless be able to add to this list, and it may be that some of the reinforcers in the list are actually secondary reinforcers. The reinforcers are categorized where possible by modality, to help the list be systematic. Possible dimensions to which each reinforcer is tuned are suggested.

In my theory, there may be a set of approximately 100 gene-specified primary reinforcers of the type described in Table 1. Each primary reinforcer accounts for a motivational state in which the reward is the target of an instrumental action, and for the emotional state that is produced when the reward is or is not received. These motivational and emotional states must all be specific; for example, hunger must increase food reward but not water reward. These reward value systems must be modulated by the correct selective signals; for example, sensors of metabolic state that relate to hunger must increase the reward value of food but not of water. In so doing, there must be mechanisms to lead animals, when in a motivational state, to navigate and perform appropriate actions to find a specific reward (Deutsch, 1960). The reward is produced by the sensory input produced by taste, smell, flavor, touch, sight, and sound, etc., and not by a reduction in the motivational signal. Some of the evidence for this is that very small

sensory inputs, such as a drop of food, act as powerful rewards, but reducing hunger by placing food into the stomach produces little reward (Rolls, 2014). Consistent with this, reducing the firing of hunger neurons has only a minor rewarding effect (Sternson, 2013), so reducing hunger or more generally motivation does not normally drive instrumental behavior. In the reward-based motivational system that I describe, each reward must be scaled to a similar range, so that the different rewards are selected at least sometimes by competing in a decision-making process, so that each reward can contribute to survival and reproductive success (Rolls, 2014). Motivational behavior can be seen from this approach as an animal operating with a set of initially gene-specified goals for actions (though subject to learned reevaluation) which compete in a high-dimensional space of rewards for a decision to be taken about which is most rewarding at the time, depending on modulators such as hunger signals, sensory-specific satiety, etc. (Rolls, 2014). The decision taken will also reflect the costs of the actions required to obtain the different rewards (Rolls, 2014). Evidence about how the underlying mechanisms operate is described in *Emotion and Decision-Making Explained* (Rolls, 2014).

1.3.6 Wanting Versus Liking and Goal-Directed Motivational Behavior

Rolls' theory of motivation holds that each gene-specified reward is a goal for action, that is, accounts for motivation; and also, when the reward is received, it generates emotion (Rolls, 2014). An important attribute of these theories of motivation and emotion is that the same specification of a goal object, a reward, perhaps genetically or by stimulus–reward learning, accounts for both the motivation, which has to be produced if the animal is ever to seek the reward, and the emotion, which is associated with the reward when it is received. This makes for great economy in evolution, for genes are needed to specify goal objects, and in doing this, have to produce both working to obtain those goal objects ("wanting") and the emotional state when the goal object is received or not received (Rolls, 2014).

It is useful in this context to discuss an apparent dissociation between "wanting" and "liking" (or "desire" versus "pleasure") that has been raised (Berridge, 1996; Berridge & Robinson, 1998; Berridge, Robinson, & Aldridge, 2009). "Wanting" or conditioned "incentive salience" effects are used to describe classically conditioned approach behavior to rewards (Berridge & Robinson, 1998, 2003), and this learning is implemented via

the amygdala and ventral striatum, is under control of dopamine (Cardinal, Parkinson, Hall, & Everitt, 2002), and contributes to addiction (Robinson & Berridge, 2003). Conditioned "incentive salience" effects can influence instrumental responses made, for example, to obtain food.

A first point is that Berridge and Robinson (1998) suggest that "liking" can be measured by orofacial reflexes such as ingesting sweet solutions or rejecting bitter solutions. There is evidence that brain opioid systems are involved in influencing the palatability of and hedonic reactions to foods, in that humans report a reduction in the pleasantness of sucrose solution following administration of naltrexone which blocks opiate receptors, but can still discriminate between sucrose solutions (Gosnell & Levine, 2009; Stice, Figlewicz, Gosnell, Levine, & Pratt, 2013). One problem here is that orofacial reflexes may reflect brain stem mechanisms that are not at all closely related to the reward value of food as reflected in instrumental actions performed to obtain food. Some of the evidence for this is that these responses occur after decerebration, in which the brain stem is all that remains to control behavior (Grill & Norgren, 1978) (with consistent evidence from anencephalic humans (Steiner, Glaser, Hawilo, & Berridge, 2001)).

A second point is that normally the rated reward value or pleasantness given in humans to food is closely related to instrumental actions performed to obtain food, as shown by the close relation between pleasantness ratings ("liking") by humans given to a food in a sensory-specific satiety experiment, and whether that food is subsequently eaten in a meal ("wanting") (Rolls, Rowe, et al., 1981).

Third, a confusion may arise when a stimulus–response habit is formed by overlearning, and persists even when the reward is devalued by, for example, feeding to satiety. This persistence of stimulus–response habits after reward devaluation should not necessarily be interpreted as "wanting" when not "liking," for it may just reflect the operation of a stimulus–response habit system that produces responses after overlearning without any guidance from reward, pleasantness, and liking (Cardinal et al., 2002; Rolls, 2014). Indeed, I emphasize that after overtraining, responses may become inflexibly linked to stimuli, and the goals, and the reward value of the goals, may no longer be directly influencing behavior in an ongoing way. If behavior becomes overlearned and a habit or stimulus–response connection is built up by another brain system (such as the basal ganglia), then animals may make automatic responses that are not goal-directed. There has been confusion in the literature caused by overlooking this point

(Berridge & Robinson, 1998; Berridge et al., 2009). The fact that behavior can become stimulus–response and no longer under the control of the goal need not surprise us. Normally, and certainly during learning before habits set in, we want a goal, and when we get the goal we like it: goal stimuli normally specify what is wanted, and what is liked. Indeed, my theory is that normally we want because we like. This is inherent in my theory, for the genes that make a stimulus (such as a sweet taste) rewarding (ie, wanted, a goal for action) also make the stimulus liked (ie, accepted, with a subjective correlate of pleasure, pleasantness, and affective liking).

My approach is that I believe that liking, defined by pleasantness ratings of stimuli, is normally very closely related to wanting, that is being willing to perform behavior (instrumental actions) to obtain a reward of the pleasant stimulus (Rolls, 2014). Thus motivational behavior is normally (when not overlearned) controlled by reward stimuli or goals (unless the behavior is overlearned), and motivational state (eg, hunger) modulates the reward value of unconditioned and conditioned stimuli such as the taste and sight of food. Thus normally, liking a goal object and wanting it are different aspects of how reward systems control instrumental behavior, and this follows from the approach to gene-specified goal or value representations which in a unifying way account for wanting a goal, and liking the goal object when it is obtained (Rolls, 2014).

Nevertheless, it is possible to dissociate the brain mechanisms involved in "wanting" and "liking" experimentally, with the classically conditioned "incentive salience" stimuli that influence approach and instrumental actions and which influence "appetitive" behavior, implemented in part separately from the reward systems that are activated by a primary reinforcer such as the taste of food during "consummatory" behavior. In a sense, the "incentive salience" effects require learning of expected value to predict primary rewards and punishers, and then to influence behavior, and thus require additional brain mechanisms to those involved in representing primary rewards and punishers.

2. THE MECHANISMS OF HUNGER AND THE APPETITE FOR FOOD

In the remainder of this article, I consider the proximate processes, the mechanisms, that underlie an example of motivated behavior, hunger, and the appetite for food. I show how taste, olfactory, food texture, and visual inputs are processed in the brain, how a representation of reward value is

produced and is related to subjective pleasure, how cognition and selective attention influence this food reward value-related processing, how this reward is affected by nutritional signals of hunger and satiety, how this reward value acts as the signal for appetite for food and eating, and how these sensory-related reward signals can override nutritional requirements to contribute to overeating and obesity.

The concept here is that food reward is a goal that normally drives appetite and eating, and it is therefore important to understand the brain mechanisms involved in food reward in order to understand the control of appetite and food intake (Rolls, 2014, 2015a, 2015b). It is normally the case that motivated behavior is performed for the reward or goal, and it is only when a habit or stimulus–response behavior becomes established that eating is no longer under the control of the reward (Berridge et al., 2009); so normally goal-directed "liking" predicts motivation or "wanting" (Rolls, 2014, 2015b).

Emphasis is placed on research in primates and humans, because there is evidence that the rodent taste and food reward systems operate somewhat differently (Rolls, 2014, 2015a, 2015b). In brief, the taste system is different in rodents in that there is a pontine taste area which then projects subcortically, but in primates there is no pontine taste area and cortical processing is performed first (Fig. 3B). Second, in rodents, the taste and olfactory systems are modulated peripherally (in the nucleus of the solitary tract and the olfactory bulb, respectively (Rolls, 2015b; Pager, Giachetti, Holley, & Le Magnen, 1972; Palouzier-Paulignan et al., 2012)) by hunger so that reward is represented peripherally and is entangled with sensory processing, whereas in primates and humans food perception is separated from its reward value, as described later (Fig. 3B). A perceptual correlate of this is that when humans feed to satiety, the intensity of the flavor changes very little, whereas the pleasantness of the flavor decreases to zero (Rolls & Rolls, 1997; E.T. Rolls, Rolls, & Rowe, 1983), showing that in humans, perceptual representations of taste and olfaction are kept separate from hedonic representations. This is adaptive, in that we do not go blind to the sight, taste, and smell of food after eating it to satiety, and can therefore still learn about where food is located in the environment even when we are not hungry (Rolls, 2014). Third, the orbitofrontal cortex is very little developed in rodents (with only an agranular part) (Wise, 2008), yet is one of the major brain areas involved in taste and olfactory processing, and emotion and motivation, in primates, including humans (Rolls, 2014). These findings make the rodent taste and olfactory system a poor model of neural food reward

processing in humans, and for that reason emphasis is placed here on discoveries in primates and humans (Rolls, 2014, 2015a, 2015b).

3. TASTE, OLFACTORY, AND ORAL TEXTURE PROCESSING IN THE PRIMATE, INCLUDING HUMAN, BRAIN

3.1 Pathways

Diagrams of the taste and related olfactory, somatosensory, and visual pathways in primates are shown in Figs. 2 and 3. The multimodal convergence that enables single neurons to respond to different combinations of taste, olfactory, texture, temperature, and visual inputs to represent different flavors produced often by new combinations of sensory input, and where reward is represented, are themes that will be addressed.

3.2 The Insular Primary Taste Cortex

3.2.1 Neuronal Responses to Taste

The primary taste cortex in the primate anterior (granular) insula and adjoining frontal operculum contains not only taste neurons tuned to sweet, salt, bitter, sour (Rolls & Scott, 2003; Scott & Plata-Salaman, 1999; Scott, Yaxley, Sienkiewicz, & Rolls, 1986a; Yaxley, Rolls, & Sienkiewicz, 1990), and umami as exemplified by monosodium glutamate (Baylis & Rolls, 1991; Rolls, Critchley, Wakeman, & Mason, 1996), but also other neurons that encode oral somatosensory stimuli including viscosity, fat texture, temperature, and capsaicin (Verhagen, Kadohisa, & Rolls, 2004). Some neurons in the primary taste cortex respond to particular combinations of taste and oral texture stimuli, but macaque insular taste cortex neurons do not respond to olfactory stimuli or visual stimuli such as the sight of food (Verhagen et al., 2004).

Neurons in the insular and frontal opercular primary taste cortex do not represent the reward value of taste, that is the appetite for a food, in that their firing is not decreased to zero by feeding the taste to satiety (Rolls, Scott, Sienkiewicz, & Yaxley, 1988; Yaxley, Rolls, & Sienkiewicz, 1988).

In macaques, neural processing peripheral to the primary taste cortex is consistent with this, with taste responses found in the rostral part of the nucleus of the solitary tract (Scott, Yaxley, Sienkiewicz, & Rolls, 1986b) that are not influenced by feeding to satiety (Yaxley, Rolls, Sienkiewicz, & Scott, 1985).

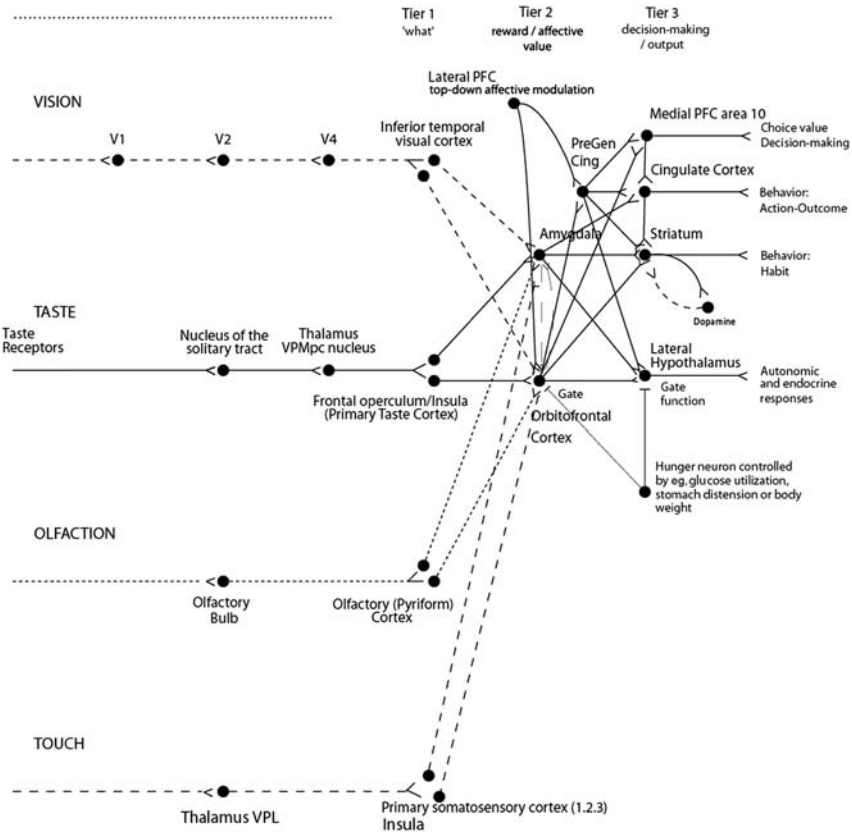

Figure 2 Schematic diagram showing some of the gustatory, olfactory, visual, and somatosensory pathways to the orbitofrontal cortex, and some of the outputs of the orbitofrontal cortex, in primates. The secondary taste cortex and the secondary olfactory cortex are within the orbitofrontal cortex. *V1*, primary visual cortex; *V4*, visual cortical area V4; *PreGen Cing*, perigenual cingulate cortex. "Gate" refers to the finding that inputs such as the taste, smell, and sight of food in some brain regions only produce effects when hunger is present (Rolls, 2014). Tier 1: the column of brain regions including and below the inferior temporal visual cortex represents brain regions in which "what" stimulus present is made explicit in the neuronal representation, but not its reward or affective value which are represented in the next tier of brain regions (Tier 2), the orbitofrontal cortex and amygdala, and in the anterior cingulate cortex. In Tier 3 areas beyond these such as medial prefrontal cortex area 10, choices or decisions about reward value are taken (Rolls, 2008b, 2014; Rolls & Deco, 2010). Top-down control of affective response systems by cognition and by selective attention from the dorsolateral prefrontal cortex is also indicated. *Medial PFC area 10*, medial prefrontal cortex area 10; *VPMpc*, ventralposteromedial thalamic nucleus, the thalamic nucleus for taste.

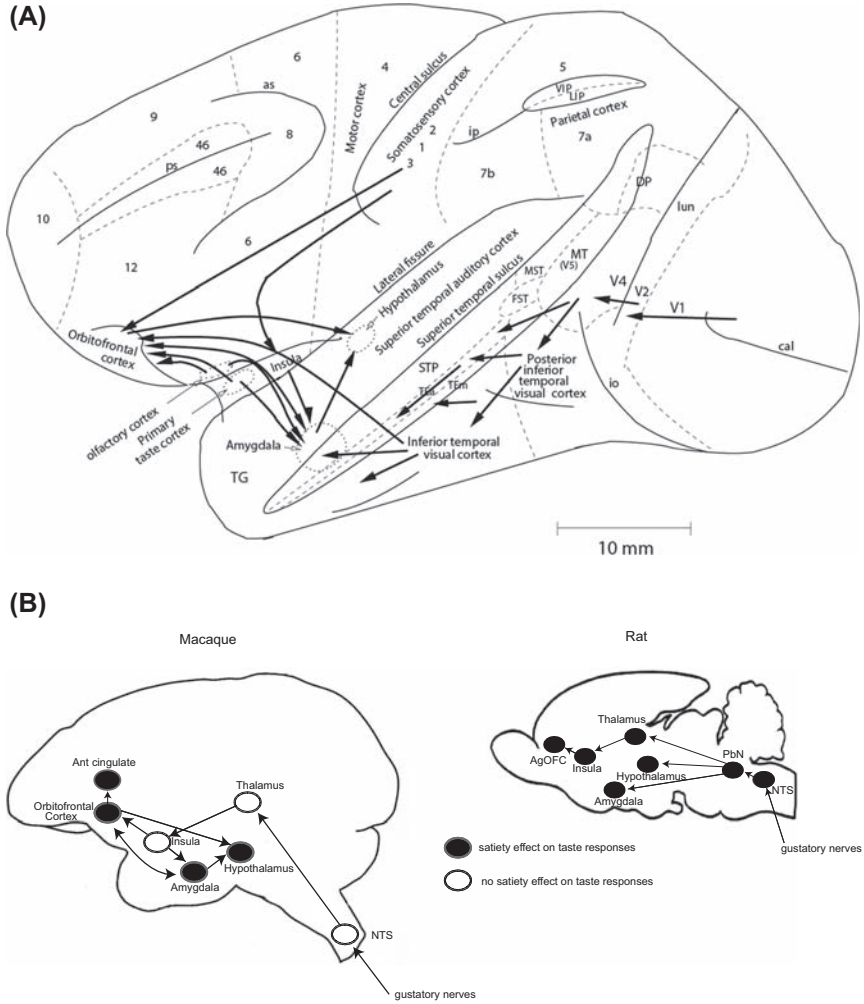

Figure 3 (A) Some of the pathways involved in processing food-related stimuli are shown on this lateral view of the primate brain (macaque). Connections from the primary taste and olfactory cortices to the orbitofrontal cortex and amygdala are shown. Connections are also shown in the "ventral visual system" from V1 to V2, V4, the inferior temporal visual cortex, etc., with some connections reaching the amygdala and orbitofrontal cortex. In addition, connections from the somatosensory cortical areas 1, 2, and 3 that reach the orbitofrontal cortex directly and via the insular cortex, and that reach the amygdala via the insular cortex, are shown. *as*, arcuate sulcus; *cal*, calcarine sulcus; *cs*, central sulcus; *lf*, lateral (or Sylvian) fissure; *lun*, lunate sulcus; *ps*, principal sulcus; *io*, inferior occipital sulcus; *ip*, intraparietal sulcus (which has been opened to reveal some of the areas it contains); *sts*, superior temporal sulcus (which has been opened to reveal some of the areas it contains); *AIT*, anterior inferior temporal cortex; *FST*, visual motion processing area; *LIP*, lateral intraparietal area; *MST*, visual motion processing area; *MT*, visual motion processing area (also called V5); *PIT*, posterior inferior temporal cortex;

3.2.2 Activations of the Insular Taste Cortex in Humans

In humans it has been shown in neuroimaging studies using functional magnetic resonance imaging (fMRI) that taste activates an area of the anterior insula/frontal operculum, which is probably the primary taste cortex (de Araujo, Kringelbach, Rolls, & McGlone, 2003; Grabenhorst & Rolls, 2008; O'Doherty, Rolls, Francis, Bowtell, & McGlone, 2001; Small, 2010; Small et al., 1999). This is generally found at coordinates between Y = 10 and Y = 20. This is illustrated in Fig. 4, which also illustrates activations to taste stimuli in the orbitofrontal cortex, which is probably the secondary taste cortex (de Araujo, Kringelbach, Rolls, & McGlone, 2003; Francis et al., 1999; O'Doherty et al., 2001; Rolls, 2015b), and the anterior cingulate cortex. We pioneered the use of a tasteless control with the same

STP, superior temporal plane; *TA*, architectonic area including auditory association cortex; *TE*, architectonic area including high order visual association cortex, and some of its subareas TEa and TEm; *TG*, architectonic area in the temporal pole; *V1—V4*, visual areas V1—V4; *VIP*, ventral intraparietal area; *TEO*, architectonic area including posterior visual association cortex. The numerals refer to architectonic areas, and have the following approximate functional equivalence: 1,2,3, somatosensory cortex (posterior to the central sulcus); 4, motor cortex; 5, superior parietal lobule; 7a, inferior parietal lobule, visual part; 7b, inferior parietal lobule, somatosensory part; 6, lateral premotor cortex; 8, frontal eye field; 12, part of orbitofrontal cortex; 46, dorsolateral prefrontal cortex. (B) Taste pathways in the macaque and rat. In the *macaque*, gustatory information reaches the nucleus of the solitary tract (NTS), which projects directly to the taste thalamus (ventral posteromedial nucleus, pars parvocellularis, VPMpc) which then projects to the taste cortex in the anterior insula (Insula). The insular taste cortex then projects to the orbitofrontal cortex and amygdala. The orbitofrontal cortex projects taste information to the anterior cingulate cortex. Both the orbitofrontal cortex and the amygdala project to the hypothalamus (and to the ventral striatum). In macaques, feeding to normal self-induced satiety does not decrease the responses of taste neurons in the NTS or taste insula (and by inference not VPMpc) (see text). In the *rat*, in contrast, the NTS projects to a pontine taste area, the parabrachial nucleus (PbN). The PbN then has projections directly to a number of subcortical structures, including the hypothalamus, amygdala, and ventral striatum, thus bypassing thalamocortical processing. The PbN in the rat also projects to the taste thalamus (VPMpc), which projects to the rat taste insula. The taste insula in the rat then projects to an agranular orbitofrontal cortex (AgOFC), which probably corresponds to the most posterior part of the primate OFC, which is agranular. (In primates, most of the orbitofrontal cortex is granular cortex, and the rat may have no equivalent to this (Passingham & Wise, 2012; Rolls, 2014, 2015b; Small & Scott, 2009; Wise, 2008).) In the rat, satiety signals such as gastric distension and satiety-related hormones decrease neuronal responses in the NTS (see text), and by inference therefore in the other brain areas with taste-related responses, as indicated in the figure.

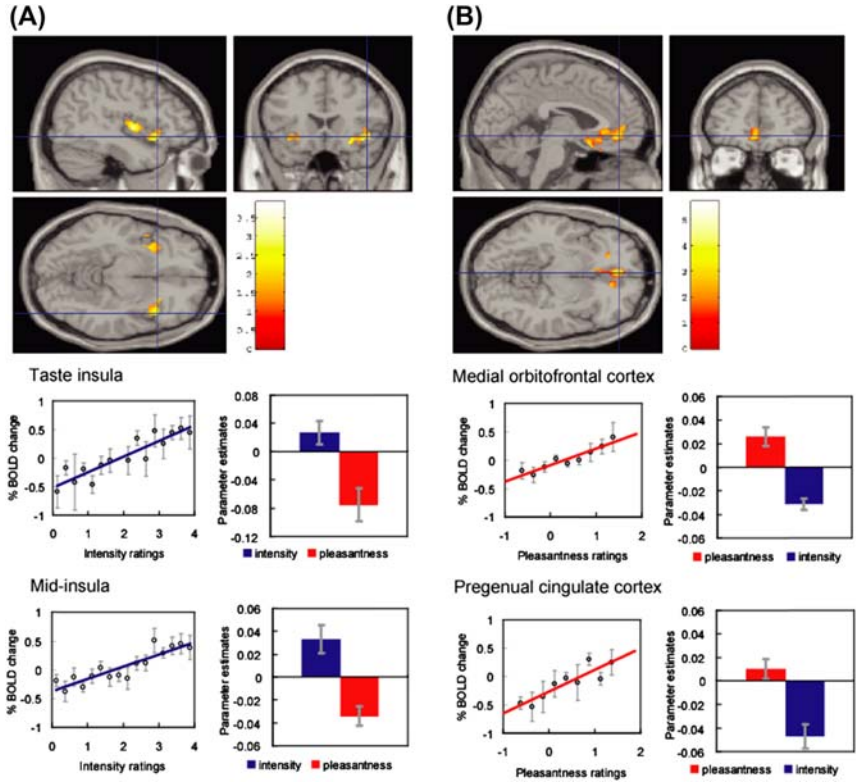

Figure 4 Effect of paying attention to the pleasantness versus the intensity of a taste stimulus, monosodium glutamate. (A) Top: A significant difference related to the taste period was found in the taste insula at [42 18 −14] (indicated by the cursor) and in the mid-insula at [40 −2 4]. Middle: Taste insula. Right: The parameter estimates (mean ± sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the taste insula. Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate. Bottom: Mid-insula. Right: The parameter estimates (mean ± sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the mid-insula. Left: The correlation between the intensity ratings and the activation (% BOLD change) at the specified coordinate. The taste stimulus, monosodium glutamate, was identical on all trials. (B) Top: A significant difference related to the taste period was found in the medial orbitofrontal cortex at [−6 14 −20] (toward the back of the area of activation shown) and in the perigenual cingulate cortex at [−4 46 −8] (at the cursor). Middle: Medial orbitofrontal cortex. Right: The parameter estimates (mean ± sem across subjects) for the activation at the specified coordinate for the conditions of paying attention to pleasantness or to intensity. The parameter estimates were significantly different for the orbitofrontal cortex. Left: The correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate. Bottom: perigenual cingulate cortex. Conventions as above. Right: The parameter estimates were significantly different for the perigenual cingulate cortex. Left: The correlation between the pleasantness ratings and the activation (% BOLD change) at the specified coordinate. The taste stimulus, 0.1 M monosodium glutamate, was identical on all trials. *Grabenhorst, F., & Rolls, E.T. (2008). Selective attention to affective value alters how the brain processes taste stimuli.* European Journal of Neuroscience, 27*(3), 723−729. Copyright (2008), with permission from John Wiley & Sons.*

ionic constituents as saliva (de Araujo, Kringelbach, Rolls, & McGlone, 2003; O'Doherty et al., 2001), as water can activate some neurons in cortical taste areas (Rolls, Yaxley, & Sienkiewicz, 1990) and can activate the taste cortex (de Araujo, Kringelbach, Rolls, & McGlone, 2003). The insular primary taste cortex is activated by oral temperature (Guest et al., 2007). In the mid-insular cortex, there is a somatosensory representation of oral texture (de Araujo & Rolls, 2004), which might be unpleasant, and this region can sometimes be activated by taste stimuli as illustrated in Fig. 4. If the insular taste cortex in humans is activated by odors, this may be because of taste recalled through back-projection pathways (Rolls, 2016a) from the more anterior agranular insular cortex, which is multimodal (de Araujo, Rolls, Kringelbach, McGlone, & Phillips, 2003), or from the orbitofrontal cortex.

The primary taste cortex in the anterior (granular) insula of humans represents the identity and intensity of taste (Rolls, 2015a, 2015b) in that activations there are linearly correlated with the subjective intensity of the taste; and were not found to decrease in the insular taste cortex after feeding to satiety (Kringelbach, O'Doherty, Rolls, & Andrews, 2003). In contrast, the orbitofrontal and anterior cingulate cortex represent the reward value of taste, in that activations there correlate with the subjective pleasantness of taste (Grabenhorst & Rolls, 2008; Grabenhorst, Rolls, & Bilderbeck, 2008; Fig. 4); and in that activations in the orbitofrontal cortex decrease when humans are fed to satiety (Kringelbach et al., 2003). The texture-related unpleasantness of some oral stimuli is represented in frontal opercular areas that are close to the insular taste cortex (Rolls, Kellerhals, & Nichols, 2015).

3.3 The Pyriform Olfactory Cortex

In humans, the pyriform (primary olfactory) cortex is activated by olfactory stimuli (Gottfried, 2010; Rolls, Kringelbach, & de Araujo, 2003; Sobel et al., 2000). Activations in the pyriform cortex are correlated with the intensity of odors and not their pleasantness (Rolls, Kringelbach, et al., 2003). In addition, feeding to satiety has not been shown to reduce the activations of the pyriform cortex to odors, though satiety does reduce activations of the orbitofrontal cortex to food-related odors (O'Doherty et al., 2000) and to flavors that include taste and olfactory components (Kringelbach et al., 2003). These findings provide evidence that the human pyriform cortex is involved in representing the intensity and identity of odors, but not their reward value or pleasantness.

3.4 The Secondary Taste and Olfactory Cortex in the Orbitofrontal Cortex, and the Representation of Reward Value

3.4.1 Neuronal Responses to Taste

A secondary cortical taste area in primates was discovered by Rolls and colleagues (Rolls, Sienkiewicz, & Yaxley, 1989; Rolls et al., 1990; Thorpe, Rolls, & Maddison, 1983) in the orbitofrontal cortex, extending several millimeter in front of the primary taste cortex. This is defined as a secondary cortical taste area, for it receives direct inputs from the primary taste cortex, as shown by a combined neurophysiological and anatomical pathway tracing investigation (Baylis, Rolls, & Baylis, 1995). Different neurons in this region respond not only to each of the four classical prototypical tastes—sweet, salt, bitter, and sour (Kadohisa, Rolls, & Verhagen, 2005a; Rolls, 1997; Rolls, Verhagen, & Kadohisa, 2003; Rolls et al., 1990; Verhagen, Rolls, & Kadohisa, 2003)—but also to umami tastants such as glutamate (which is present in many natural foods such as tomatoes, mushrooms, and human milk (Baylis & Rolls, 1991)) and inosine monophosphate (which is present in meat and some fish such as tuna (Rolls, Critchley, Wakeman, et al., 1996)). This evidence, taken together with the identification of glutamate taste receptors (Maruyama, Pereira, Margolskee, Chaudhari, & Roper, 2006; Zhao et al., 2003), leads to the view that there are five prototypical types of taste information channels, with umami contributing, often in combination with corresponding olfactory inputs (McCabe & Rolls, 2007; Rolls, 2009b; Rolls, Critchley, Browning, & Hernadi, 1998), to the flavor of protein. In addition, other neurons respond to water (Rolls et al., 1990), and others to somatosensory stimuli including astringency as exemplified by tannic acid (Critchley & Rolls, 1996c) and capsaicin (Kadohisa, Rolls, & Verhagen, 2004; Rolls, Verhagen, et al., 2003).

Some of the coding principles are illustrated by the two neurons shown in Fig. 5. The two neurons each have their independent tuning to the set of stimuli. It is this independent tuning or coding with sparse distributed representations that underlies the ability of the brain to represent the exact nature of a stimulus or event, and this applies to taste in addition to other sensory modalities including smell (Rolls, 2015b, 2016a; Rolls, Critchley, & Treves, 1996; Rolls, Critchley, Verhagen, & Kadohisa, 2010; Rolls & Treves, 2011). This tuning also provides a foundation for the implementation of sensory-specific satiety (Rolls, 2014, 2015b). Taste responses are found in a large mediolateral extent of the orbitofrontal cortex (Critchley & Rolls, 1996c; Pritchard et al., 2005; Rolls, 2008a, 2015b; Rolls & Grabenhorst, 2008).

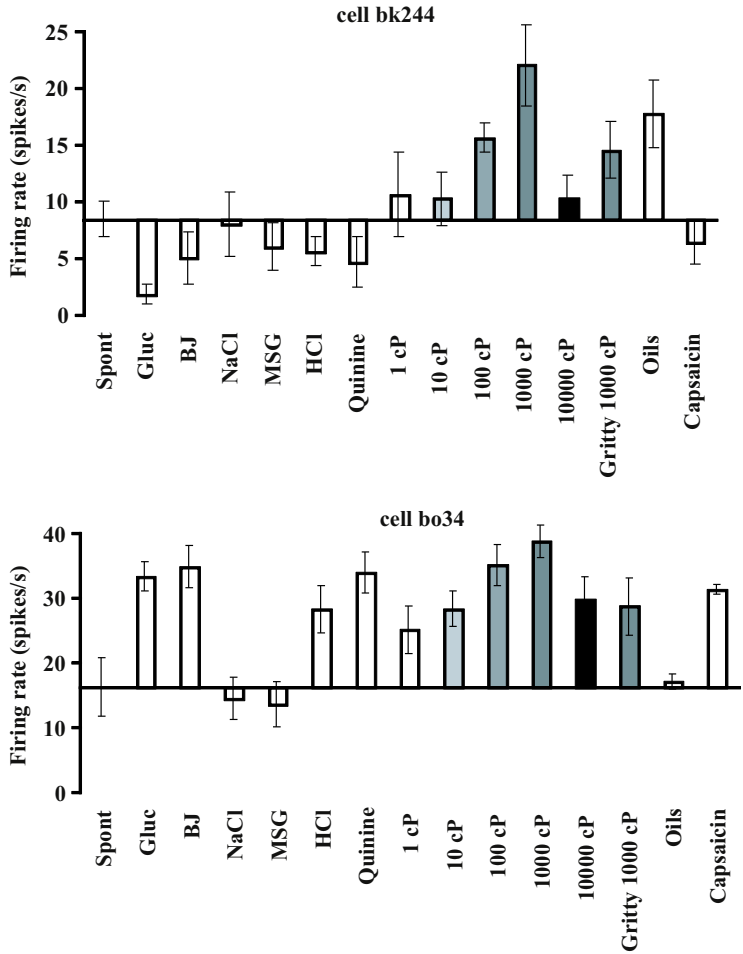

Figure 5 Independent coding of food-related stimuli shown by the responses of two orbitofrontal cortex neurons to taste and oral somatosensory inputs. Above. Firing rates (mean ± sem) of viscosity-sensitive neuron bk244 which did not have taste responses, in that it did not respond differentially to the different taste stimuli. The firing rates are shown to the viscosity series (carboxymethylcellulose 1−10,000 centiPoise, to the gritty stimulus (1000 cP carboxymethylcellulose with Fillite microspheres), to the taste stimuli 1 M glucose (Gluc), 0.1 M NaCl, 0.1 M MSG, 0.01 M HCl, and 0.001 M QuinineHCl, and to fruit juice (BJ). *Spont*, spontaneous firing rate. Below. Firing rates (mean ± sem) of viscosity-sensitive neuron bo34 which had responses to some taste stimuli and had no response to the oils (mineral oil, vegetable oil, safflower oil, and coconut oil, which have viscosities that are all close to 50 cP). The neuron did not respond to the gritty stimulus in a way that was unexpected given the viscosity of the stimulus, was taste tuned, and did respond to capsaicin. *Rolls, E. T., Verhagen, J. V., & Kadohisa, M., (2003). Representations of the texture of food in the primate orbitofrontal cortex: neurons responding to viscosity, grittiness and capsaicin.* Journal of Neurophysiology, 90*(1), 3711−3724. Copyright (2003), with permission from John Wiley & Sons.*

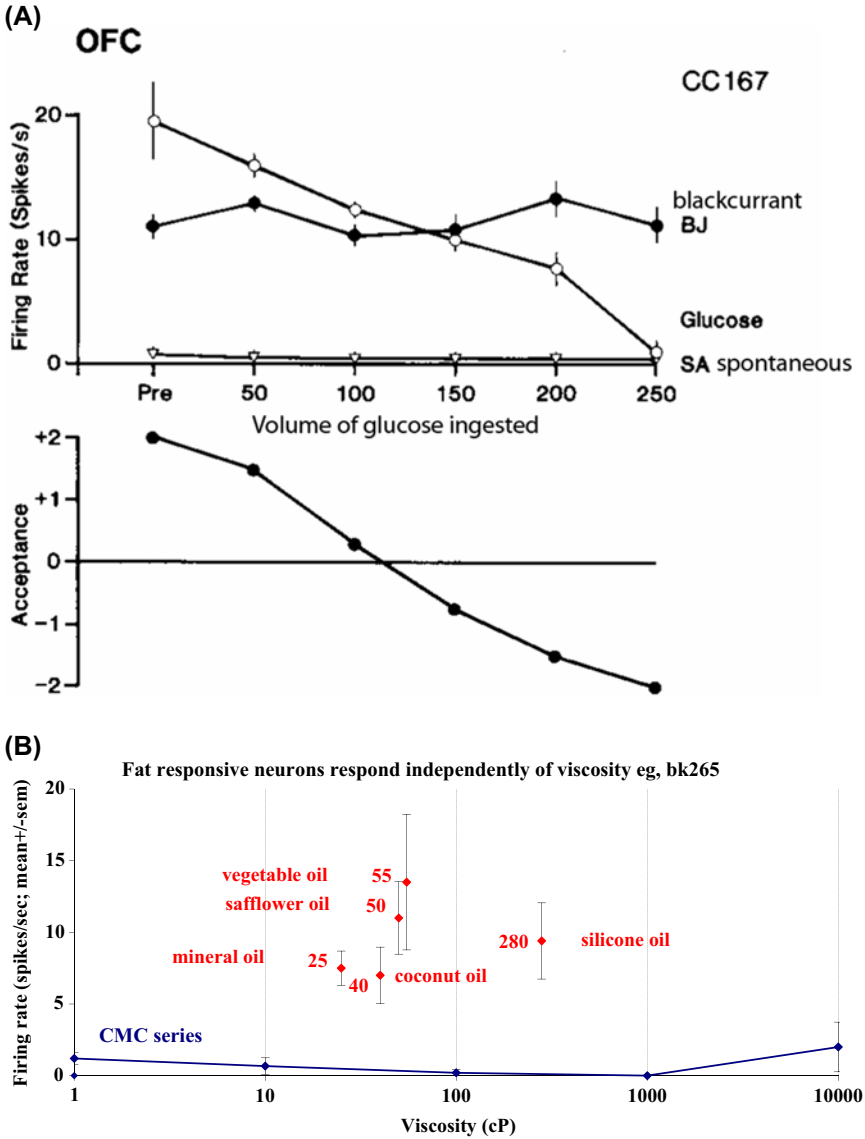

Figure 6 (A) The effect of feeding to satiety with glucose solution on the responses (firing rate ±s.e.m.) of a neuron in the orbitofrontal (secondary taste) cortex to the taste of glucose (*open circles*) and of blackcurrant juice (BJ). The spontaneous firing rate is also indicated (SA). Below the neuronal response data, the behavioral measure of the acceptance or rejection of the solution on a scale from +2 (strong acceptance) to −2 (strong rejection) is shown. The solution used to feed to satiety was 20% glucose. The monkey was fed 50 ml of the solution at each stage of the experiment as indicated along the abscissa, until he was satiated as shown by whether he accepted or rejected

The majority of these orbitofrontal cortex neurons have their responses to taste and/or olfactory stimuli modulated by hunger (Critchley & Rolls, 1996a). This is illustrated in Fig. 6, and described in more detail in the section "Reward value in the orbitofrontal cortex."

3.4.2 Activations of the Orbitofrontal Cortex in Humans to Taste Stimuli

Different regions of the human orbitofrontal cortex can be activated by pleasant (sucrose or glucose) or aversive (eg, quinine or sodium chloride) taste stimuli (O'Doherty et al., 2001; Zald, Hagen, & Pardo, 2002; Zald, Lee, Fluegel, & Pardo, 1998). Umami taste stimuli, of which an exemplar is monosodium glutamate (MSG), and which capture what is described as the taste of protein, activate the insular (primary), orbitofrontal (secondary), and anterior cingulate (tertiary (Rolls, 2008a)) taste cortical areas (de Araujo, Kringelbach, Rolls, & Hobden, 2003; Rolls, 2009b).

3.4.3 Neuronal Responses to Odors in the Primate Orbitofrontal Cortex

Some primate orbitofrontal cortex neurons respond well to olfactory stimuli (Critchley & Rolls, 1996b; Rolls, Critchley, Mason, & Wakeman, 1996; Rolls, Critchley, et al., 2010). For many of these neurons, the response is related to tastes (Critchley & Rolls, 1996b) and can be learned by olfactory-to-taste association learning (Rolls, Critchley, Mason, et al., 1996), providing evidence that the orbitofrontal cortex can remap odors from the

the solution. Pre is the firing rate of the neuron before the satiety experiment started. (B) A neuron in the primate orbitofrontal cortex responding to the texture of fat in the mouth independently of viscosity. The cell (bk265) increased its firing rate to a range of fats and oils (the viscosity of which is shown in centipoise). The information that reaches this type of neuron is independent of a viscosity sensing channel, in that the neuron did not respond to the methyl cellulose (CMC) viscosity series. The neuron responded to the texture rather than the chemical structure of the fat in that it also responded to silicone oil ($Si(CH_3)_2O)_n$) and paraffin (mineral) oil (hydrocarbon). Some of these neurons have taste inputs. *Reproduced from Rolls, E.T., Sienkiewicz, Z. J., & Yaxley, S. (1989). Hunger modulates the responses to gustatory stimuli of single neurons in the caudolateral orbitofrontal cortex of the macaque monkey,* European Journal of Neuroscience, 1*(1), 53–60, Copyright 1989 with permission from John Wiley & Sons.; Rolls, E. T., Verhagen, J. V., & Kadohisa, M., (2003). Representations of the texture of food in the primate orbitofrontal cortex: neurons responding to viscosity, grittiness and capsaicin.* Journal of Neurophysiology, 90*(1), 3711–3724. Copyright (2003), with permission from John Wiley & Sons.*

olfactory gene-specified representation (Buck & Axel, 1991; Mombaerts, 2006) into a representation where the "meaning" in terms of the association of the odor with other stimuli is paramount. Flavors are built by learning in the orbitofrontal cortex as combinations of taste and olfactory inputs, with oral texture also often being a component (Rolls, Critchley, Mason, et al., 1996). The olfactory-to-taste association learning is slow, however, taking 30–60 trials to reverse, so that flavor representations are somewhat stable (Rolls, Critchley, Mason, et al., 1996). The representation of information by primate orbitofrontal cortex neurons (Rolls, Critchley, & Treves, 1996) is approximately independent by different neurons, in that the information increases approximately linearly with the number of neurons (Rolls, Critchley, et al., 2010).

Many primate olfactory orbitofrontal neurons encode the reward value of odor, not only in that their responses often reflect the taste primary reinforcer with which an odor is associated (Critchley & Rolls, 1996b; Rolls, Critchley, Mason, et al., 1996), but also in that their activity is decreased in a sensory-specific satiety way by feeding a particular food to satiety (Critchley & Rolls, 1996a) (see the section "Reward value in the orbitofrontal cortex").

3.4.4 Olfactory Representations in the Human Orbitofrontal Cortex

In humans, there is strong and consistent activation of the orbitofrontal cortex by olfactory stimuli (Francis et al., 1999; Rolls, Kringelbach, et al., 2003; Zatorre, Jones-Gotman, Evans, & Meyer, 1992). This region represents the reward value and pleasantness of odor, as shown by a sensory-specific satiety experiment with banana versus vanilla odor (O'Doherty et al., 2000), and these reward-specific activations have been confirmed by Gottfried et al. (personal communication and (Gottfried, 2015; Howard, Gottfried, Tobler, & Kahnt, 2015)), who also showed that activations in the pyriform (primary olfactory) cortex were not decreased by odor devaluation by satiety. Further, pleasant odors tend to activate the medial, and unpleasant odors the more lateral, orbitofrontal cortex (Rolls, Kringelbach, et al., 2003), adding to the evidence that it is a principle that there is a hedonic map in the orbitofrontal cortex, and also in the anterior cingulate cortex, which receives inputs from the orbitofrontal cortex (Grabenhorst & Rolls, 2011; Rolls, 2014; Rolls & Grabenhorst, 2008). The primary olfactory (pyriform) cortex represents the identity and intensity of odor in that activations there correlate with the subjective intensity of the odor, and the orbitofrontal and anterior cingulate cortex represent the reward value of odor, in that activations there

correlate with the subjective pleasantness (medially) or unpleasantness (laterally) of odor (Grabenhorst & Rolls, 2011; Grabenhorst, Rolls, Margot, da Silva, & Velazco, 2007; Rolls, 2014; Rolls & Grabenhorst, 2008; Rolls, Grabenhorst, & Franco, 2009; Rolls, Grabenhorst, Margot, da Silva, & Velazco, 2008; Rolls, Kringelbach, et al., 2003).

3.4.5 The Texture of Food Including Fat Texture

3.4.5.1 Viscosity, Particulate Quality, and Astringency

Some orbitofrontal cortex neurons have oral texture—related responses that encode parametrically the viscosity of food in the mouth (shown using a methyl cellulose series in the range 1—10,000 centiPoise), and other neurons independently encode the particulate quality of food in the mouth (Rolls, Verhagen, et al., 2003). Somatosensory signals that transmit information about capsaicin (chilli) and astringency are also reflected in neuronal activity in these cortical areas (Critchley & Rolls, 1996c; Kadohisa et al., 2004; Kadohisa et al., 2005a).

3.4.5.2 Oral Fat Texture

Texture in the mouth is an important indicator of whether *fat* is present in a food, which is important not only as a high value energy source, but also as a potential source of essential fatty acids. In the orbitofrontal cortex, Rolls, Critchley, Browning, Hernadi, and Lenard (1999) have found a population of neurons that responds when fat is in the mouth. The fat—related responses of these neurons are produced at least in part by the texture of the food rather than by receptors sensitive to certain chemicals, in that such neurons typically respond not only to foods such as cream and milk containing fat, but also to paraffin oil (which is a pure hydrocarbon) and to silicone oil ($(Si(CH_3)_2O)_n$). Moreover, the texture channels through which these fat-sensitive neurons that are activated are separate from viscosity-sensitive channels, in that the responses of these neurons cannot be predicted by the viscosity of the oral stimuli (as illustrated in Fig. 6B; Rolls, 2011b; Verhagen et al., 2003). The responses of these oral fat-encoding neurons are not related to free fatty acids such as linoleic or lauric acid (Kadohisa et al., 2005a; Rolls, 2011b; Verhagen et al., 2003), and the fat responsiveness of these primate orbitofrontal cortex neurons is therefore not related to fatty acid sensing (Gilbertson, 1998; Gilbertson, Fontenot, Liu, Zhang, & Monroe, 1997), but instead to oral texture sensing (Rolls, 2011b, 2012b). The hypothesis is that in rodents, with relatively high concentrations of lingual lipase, a fatty acid responsive "taste" receptor might provide evidence

about the presence of fat in the mouth (Gilbertson, 1998; Gilbertson et al., 1997). There is less lingual lipase in primates, and the neuronal responses to fat placed in the mouth in macaques are fast (Verhagen et al., 2004, 2003) so that the intervention of digestion by a salivary enzyme is unlikely to be the main mechanism that detects fat in the mouth. Moreover, oils that have the same texture as fat but that contain no fat, such as silicone and paraffin oil, activate the neurons in macaques that respond to fat in the mouth. This has important implications for the development of foods with the mouth feel of fat, but low-energy content (Rolls, 2011b, 2012b). A few neurons do have responses to linoleic and/or lauric acid, but these neurons do not respond to fat in the mouth, and may reflect the bad taste that rancid fats may have because of their free fatty acids (Rolls, 2011b; Verhagen et al., 2003). Some of the fat texture—related orbitofrontal cortex neurons do though have convergent inputs from the chemical senses, in that in addition to taste inputs, some of these neurons respond to the odor associated with a fat, such as the odor of cream (Rolls et al., 1999).

Feeding to satiety with fat (eg, cream) decreases the responses of these fat-responsive neurons to zero on the food eaten to satiety. This provides evidence that these neurons encode the reward value of fat in the mouth, but if the neuron receives a taste input from, for example, glucose taste, that is not decreased by feeding to satiety with cream (Rolls et al., 1999).

3.4.5.3 Oral Temperature

In addition, we have shown that some neurons in the insular cortex, orbitofrontal cortex, and amygdala reflect the temperature of substances in the mouth, and that this temperature information is represented independently of other sensory inputs by some neurons, and in combination with taste or texture by other neurons (Kadohisa et al., 2004, 2005a; Kadohisa, Rolls, & Verhagen, 2005b; Verhagen et al., 2004). Somatosensory signals that transmit information about capsaicin (chilli) are also reflected in neuronal activity in these brain areas (Kadohisa et al., 2004, 2005a). Activations in the human orbitofrontal and insular taste cortex also reflect oral temperature (Guest et al., 2007).

3.4.5.4 Activations in Humans

The viscosity of food in the mouth is represented in the human primary taste cortex (in the anterior insula), and also in a mid-insular area that may not be primarily taste cortex, but which represents oral somatosensory stimuli (de Araujo & Rolls, 2004). Oral viscosity is also represented in the human

orbitofrontal and perigenual cingulate cortices, and it is notable that the perigenual cingulate cortex, an area in which many pleasant stimuli are represented, is strongly activated by the texture of fat in the mouth and also by oral sucrose (de Araujo & Rolls, 2004). We have shown that the pleasantness and reward value of fat texture is represented in the mid-orbitofrontal and anterior cingulate cortex, where activations are correlated with the subjective pleasantness of oral fat texture (Grabenhorst, Rolls, Parris, & D'Souza, 2010; Rolls, 2009b, 2010). This provides a foundation for future studies of whether activations in the fat reward system are heightened in people who tend to become obese (Rolls, 2012d). Interestingly, high fat stimuli with a pleasant flavor increase the coupling of activations between the orbitofrontal cortex and somatosensory cortex, suggesting a role for the somatosensory cortex in processing the sensory properties of food in the mouth (Grabenhorst & Rolls, 2014).

3.4.6 Convergence of Olfactory, Taste, and Visual Inputs in the Orbitofrontal Cortex

3.4.6.1 Neuronal Activity

Taste and olfactory pathways are brought together in the orbitofrontal cortex where flavor is formed by learned associations at the neuronal level between these inputs (see Fig. 2; Critchley & Rolls, 1996b; Rolls & Baylis, 1994; Rolls, Critchley & Treves, 1996). Visual inputs also become associated by learning in the orbitofrontal cortex with the taste of food to represent the sight of food and contribute to flavor (Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983). Olfactory-to-taste associative learning by these orbitofrontal cortex neurons may take 30–40 trials to reverse in an olfactory-to-taste discrimination task, and this slow learning may help to make a flavor stable (Rolls, Critchley, Mason, et al., 1996). Olfactory neurons are found in a considerable anterior–posterior extent of the primate orbitofrontal cortex, extending far into areas 11 and 14 (Critchley & Rolls, 1996a, 1996b; Rolls & Baylis, 1994; Rolls, Critchley, Mason, et al., 1996; Rolls, Critchley & Treves, 1996), and are not restricted to a posterior region as some have thought (Gottfried & Zald, 2005).

Visual-to-taste association learning and its reversal by neurons in the orbitofrontal cortex can take place in as little as one trial (Deco & Rolls, 2005; Rolls, Critchley, Mason, et al., 1996; Thorpe et al., 1983). This has clear adaptive value in enabling particular foods with a good or bad taste to be learned and recognized quickly, important in foraging and in food selection for ingestion. The visual inputs reach the orbitofrontal cortex

from the inferior temporal visual cortex, where neurons respond to visual objects independently of their reward value (eg, taste) as shown by satiety and reversal learning tests (Rolls, 2008b, 2012a; Rolls, Judge, & Sanghera, 1977). The visual-to-taste associations are thus learned in the orbitofrontal cortex (Rolls, 2014). These visual—taste neurons thus respond to expected value (Rolls, 2014).

Different neurons in the orbitofrontal cortex respond when a visually signaled expected taste reward is not obtained, that is, to negative reward prediction error (Rolls, 2014; Rolls & Grabenhorst, 2008; Thorpe et al., 1983). There is evidence that dopamine neurons in the ventral tegmentum respond to positive reward prediction error (Schultz, 2007), and as such, they do not respond to taste reward (Rolls, 2014). The inputs to the dopamine neurons may originate from structures such as the orbitofrontal cortex, where expected value, reward outcome (eg, taste), and negative reward prediction error are represented (Rolls, 2014).

3.4.6.2 Taste—Olfactory Convergence Shown by Activations in Humans

Taste and olfactory conjunction analyses, and the measurement of supraadditive effects that provide evidence for convergence and interactions in fMRI investigations, show convergence for taste (sucrose) and odor (strawberry) in the orbitofrontal and anterior cingulate cortex, and activations in these regions are correlated with the pleasantness ratings given by participants (de Araujo, Rolls, et al., 2003; Small & Prescott, 2005; Small et al., 2004). These results provide evidence on the neural substrate for the convergence of taste and olfactory stimuli to produce flavor in humans, and where the pleasantness of flavor is represented in the human brain (Rolls, 2014, 2015b). The first region where the effects of this olfactory—taste convergence are found is in an agranular part of what cytoarchitecturally is the insula (Ia) that is topologically found in the posterior orbitofrontal cortex, though it is anterior to the insular taste cortex, and posterior to the granular orbitofrontal cortex (de Araujo, Rolls, et al., 2003; Rolls, 2015a, 2015b).

McCabe and Rolls (2007) have shown that the convergence of taste and olfactory information in the orbitofrontal cortex appears to be important for the delicious flavor of umami. They showed that when glutamate is given in combination with a consonant, savory, odor (vegetable), the resulting flavor can be much more pleasant than the glutamate taste or vegetable odor alone, and that this reflected activations in the perigenual cingulate cortex and medial orbitofrontal cortex. The principle is that certain sensory combinations can produce very pleasant food stimuli, which may of course be

important in driving food intake; and that these combinations are formed in the brain far beyond the taste or olfactory receptors (Rolls, 2009b).

O'Doherty et al. (2002) showed that visual stimuli associated with the taste of glucose activate the orbitofrontal cortex and some connected areas, consistent with the primate neurophysiology. Simmons, Martin, and Barsalou (2005) found that showing pictures of foods, compared to pictures of places, can also activate the orbitofrontal cortex. Similarly, the orbitofrontal cortex and connected areas were also found to be activated after presentation of food stimuli to food-deprived subjects (Wang et al., 2004).

3.4.7 Reward Value in the Orbitofrontal Cortex

The visual and olfactory as well as the taste inputs represent the reward value of the food, as shown by sensory-specific satiety effects (Critchley & Rolls, 1996a; see Fig. 6A).

The modulation of the reward value of a sensory stimulus such as the taste of food by motivational state, for example, hunger, is one important way in which motivational behavior is controlled (Rolls, 2014, 2015b). The subjective correlate of this modulation is that food tastes pleasant when hungry, and tastes hedonically neutral when it has been eaten to satiety. Following Edmund Rolls' discovery of sensory-specific satiety revealed by the selective reduction in the responses of lateral hypothalamic neurons to a food eaten to satiety (Rolls, 1981; Rolls, Murzi, Yaxley, Thorpe, & Simpson, 1986), it has been shown that this is implemented by neurons in a region that projects to the hypothalamus, the orbitofrontal (secondary taste) cortex, for the taste, odor, and sight of food (Critchley & Rolls, 1996a; Rolls, 2015b; Rolls et al., 1989). Consistent changes are found in humans (Kringelbach et al., 2003), and this study provided evidence that the subjective pleasantness of the flavor of food, and sensory-specific satiety, are represented in the human orbitofrontal cortex.

This evidence shows that the reduced acceptance and reward value of food that occurs when food is eaten to satiety, the reduction in the pleasantness of its taste and flavor, and the effects of variety to increase food intake (Hetherington, 2007; B.J. Rolls, Rolls, & Rowe, 1983; Rolls, Rolls, Rowe, & Sweeney, 1981; Rolls, Rowe, & Rolls, 1982; Rolls, Rowe, et al., 1981; Rolls, Van Duijvenvoorde, & Rolls, 1984; B.J. Rolls, Van Duijenvoorde, & Rowe, 1983; Rolls & Rolls, 1977, 1982, 1997), are produced in the primate orbitofrontal cortex, but not at earlier stages of processing, including the insular-opercular primary taste cortex (Rolls et al., 1988; Yaxley et al., 1988) and the nucleus of the solitary tract (Yaxley et al., 1985), where the

responses reflect factors such as the intensity of the taste, which is little affected by satiety (Rolls & Grabenhorst, 2008; E.T. Rolls, Rolls, et al., 1983). The orbitofrontal cortex provides an implementation of sensory-specific satiety (probably by adaptation of the synaptic afferents to orbitofrontal cortex neurons with a time-course of the order of the length of a course of a meal). In addition, it is likely that visceral and other satiety-related signals reach the orbitofrontal cortex (as indicated in Fig. 2) from the nucleus of the solitary tract, via thalamic, insular visceral cortex, and possibly hypothalamic nuclei, and there modulate the representation of food, resulting in an output that reflects the reward (or appetitive) value of each food (Rolls, 2014, 2015b).

3.4.8 The Neuroeconomics of Food Reward Value in the Orbitofrontal Cortex

The reward value representations in the primate orbitofrontal cortex of taste, olfactory, and flavor stimuli are appropriate for economic decision-making in a number of ways (Rolls, 2014, 2015b). First, the responses of orbitofrontal cortex neurons reflect the quality of the commodity or "good" (eg, the sight or taste of food) multiplied by the amount available (Padoa-Schioppa, 2011; Padoa-Schioppa & Assad, 2006). In humans, activations in the orbitofrontal cortex reflect the "subjective value" of foods (where "subjective value" in economics refers strictly to what is chosen by a subject rather than to conscious subjective pleasantness (Rolls, 2014, 2015b)), assessed in a task in which the value is measured by choices between different foods and different amounts of money (Plassmann, O'Doherty, & Rangel, 2007). Moreover these neurons reflect the value of reward stimuli, and not actions made to obtain them (Padoa-Schioppa & Assad, 2006; Rolls, 2014; Rolls et al., 1990; Thorpe et al., 1983; Verhagen et al., 2003).

3.4.9 Representations in the Orbitofrontal Cortex of Reward Value on a Common Scale but Not in a Common Currency

For decision-making, it is important that representations of reward value are on a common scale (so that they can be compared), but are not in a common currency of general reward value, for the specific reward must be represented to guide actions (Rolls, 2014, 2015b). To investigate whether specific reward representations are on a common scale of reward value, we performed an fMRI study in which we were able to show that even fundamentally different primary rewards, taste in the mouth and warmth on the hand, produced activations in the human orbitofrontal cortex that were scaled to

the same range (Grabenhorst, D'Souza, Parris, Rolls, & Passingham, 2010). Further fMRI studies are consistent with this (Levy & Glimcher, 2012). These reward value representations in the orbitofrontal cortex are thus in a form suitable for making decisions about whether to, for example, choose and eat a particular food, with the decision-making mechanisms now starting to be understood (Grabenhorst & Rolls, 2011; Rolls, 2014, 2015b; Rolls & Deco, 2010; Rolls, Grabenhorst, & Deco, 2010a, 2010b; Rolls, Grabenhorst, & Parris, 2010).

3.5 The Amygdala

The amygdala is a structure in the temporal lobe with somewhat similar connections to the orbitofrontal cortex (see Fig. 2). The amygdala has been present in evolution for much longer than the primate orbitofrontal cortex, and appears to differ from the orbitofrontal cortex in that it cannot implement one-trial, rule-based, visual discrimination reversal when the taste or flavor associated with the visual stimulus is reversed (Rolls, 2014). The primate amygdala contains neurons that respond to taste and oral texture (Kadohisa et al., 2005a, 2005b; Sanghera, Rolls, & Roper-Hall, 1979; Scott et al., 1993). Some neurons respond to visual stimuli associated with reinforcers such as taste, but do not reflect the reinforcing properties very specifically, do not rapidly learn and reverse visual-to-taste associations, and are much less affected by reward devaluation by feeding to satiety than are orbitofrontal cortex neurons (Kadohisa et al., 2005a, 2005b; Rolls, 2014; Sanghera et al., 1979; Wilson & Rolls, 2005; Yan & Scott, 1996). The primate orbitofrontal cortex appears to be much more closely involved in flexible (rapidly learned, and affected by reward devaluation) reward representations than is the primate amygdala (Rolls, 2014).

Fat texture, oral viscosity, and temperature, for some neurons in combination with taste, and also the sight and smell of food, are represented in the macaque amygdala (Kadohisa et al., 2005a, 2005b; Rolls, 2000; Rolls & Scott, 2003). Interestingly, the responses of these amygdala neurons do not correlate well with the preferences of the macaques for the oral stimuli (Kadohisa et al., 2005a), and feeding to satiety does not produce the large reduction in the responses of amygdala neurons to food (Rolls, 2000; Rolls & Scott, 2003; Yan & Scott, 1996) that is typical of orbitofrontal cortex neurons.

We found activation of the human amygdala by the taste of glucose (Francis et al., 1999). Extending this study, O'Doherty et al. (2001) showed that the human amygdala was as much activated by the affectively pleasant

taste of glucose as by the affectively negative taste of NaCl, and thus provided evidence that the human amygdala is not especially involved in processing aversive as compared to rewarding stimuli. Zald et al. (2002, 1998) also showed that the human amygdala responds to aversive (eg, quinine) and to sucrose taste stimuli.

Rolls (2014) has compared and contrasted the roles of the orbitofrontal cortex versus the amygdala.

3.6 The Anterior Cingulate Cortex: A Tertiary Taste Cortical Area

The orbitofrontal cortex, including the extensive areas where the taste neurons noted as discussed earlier are found, projects to the perigenual cingulate cortex area 32 (Carmichael & Price, 1996; see Figs. 2 and 3). In human imaging studies it has been shown that reward-related stimuli, such as the taste of sucrose and the texture of oral fat, activate the perigenual cingulate cortex (de Araujo & Rolls, 2004; Grabenhorst & Rolls, 2011; Rolls, 2005, 2009a; Rolls & Grabenhorst, 2008). In recordings made in the primate perigenual cingulate cortex, we (Rolls, Gabbott, Verhagen, and Kadohisa; see Rolls (2008a)) showed that neurons can respond to taste and related food texture stimuli such as glucose, fruit juice, and cream, to monosodium glutamate, and to quinine, and that such neurons show a sensory-specific decrease in the response to the taste of glucose after feeding to satiety with glucose (Rolls, 2008a). Our hypothesis is that the outcomes, the rewards and punishers, are represented in the anterior cingulate cortex because it is involved in action—outcome learning (Grabenhorst & Rolls, 2011; Rolls, 2008a, 2009a, 2014; Rushworth et al., 2011).

3.7 Hypothalamus

The orbitofrontal cortex and amygdala project to the hypothalamus, which is implicated in the control of food intake (Rolls, 2014). The primate lateral hypothalamus contains taste-responsive neurons, which only respond to food when hunger is present, and indeed reflect sensory-specific satiety (Rolls, 1981; Rolls et al., 1986). The lateral hypothalamus also contains neurons that respond to the sight of food, and they also only respond to food when hunger is present, that is, when the food is rewarding (Burton, Rolls, & Mora, 1976; Mora, Rolls, & Burton, 1976; Rolls, 1981, 2014; Rolls, Burton, & Mora, 1976; Rolls et al., 1986; Rolls, Sanghera, & Roper-Hall, 1979). The traditional view of the hypothalamus is that it integrates many of the hormonal and nutritional signals that control appetite (Morton,

Meek, & Schwartz, 2014; Suzuki, Simpson, Minnion, Shillito, & Bloom, 2010; Woods, 2013) (see Section 5), but this neurophysiological evidence shows that the hypothalamus is also involved in the reward signals from taste, olfaction, and vision that need to be interfaced to hunger and satiety signals (Rolls, 2014).

3.8 Striatum

The primate ventral striatum and adjoining part of the head of the caudate nucleus receive connections from the orbitofrontal cortex and amygdala (Haber & Knutson, 2009; Rolls, 2014). Consistent with this, some neurons in these striatal regions respond to the taste, flavor, and/or sight of food (Rolls, 2014; E.T. Rolls, Thorpe, & Maddison, 1983; Rolls & Williams, 1987; Strait, Sleezer, & Hayden, 2015; Williams, Rolls, Leonard, & Stern, 1993).

These taste and related inputs to the basal ganglia may be involved in stimulus–response habit formation, with the taste and other reinforcers helping to stamp in the connections between environmental stimuli and behavioral responses that cooccur just prior to receiving a reinforcer such as the taste, flavor, or sight of food (Rolls, 2014). Perhaps as part of this functionality, incentive stimuli such as food can have effects on behavior that are mediated through the striatum (Everitt & Robbins, 2013; Smith & Robbins, 2013). The hypothesis that there is less D2 receptor binding in the dorsal striatum of the obese and that this system contributes to human obesity (Volkow, Wang, Tomasi, & Baler, 2013) has been questioned (Cosgrove, Veldhuizen, Sandiego, Morris, & Small, 2015). There are smaller BOLD responses in the dorsal striatum to palatable food with increasing body mass index, with the reduced striatal response being interpreted as a consequence of the reduced incentive value of food in the overweight. There is in contrast a positive relation of D2/D3 receptor binding to body mass index, and this is not associated with the change in the BOLD response (Cosgrove et al., 2015).

The striatum receives a dopaminergic input that it has been suggested is a positive reward prediction error signal (Schultz, 2013), though there may be too much diversity in the activity of dopamine neurons for this to apply in a simple way (Bromberg-Martin, Matsumoto, & Hikosaka, 2010; Rolls, 2014). Moreover, there is no evidence that the dopamine neurons encode a specific reward signal (for example, for the taste of food versus the texture of fat) in the way that is required to account for the control of goal-directed rewarded behavior and that is present in the primate orbitofrontal cortex

(Rolls, 2014). Further, the activity of ventral striatal neurons appears to be more influenced by orbitofrontal cortex types of signals rather than by positive reward prediction error signals (Strait et al., 2015). The role of the striatum and dopamine in the control of behavior is considered in more detail elsewhere (Rolls, 2014).

4. FURTHER IMAGING STUDIES ON REWARD VALUE REPRESENTATIONS IN HUMANS

4.1 Top-Down Cognitive Effects on Taste, Olfactory, and Flavor Processing

To what extent does cognition influence the hedonics of food-related stimuli, and how far down into the sensory system does the cognitive influence reach? We found that the activation of a standard test odor (isovaleric acid combined with cheddar cheese odor, presented orthonasally using an olfactometer) was paired with a descriptor word on a screen, which on different trials was "Cheddar cheese" or "Body odor." Participants rated the affective value of a standard test odor, isovaleric acid, as significantly more pleasant when labeled "Cheddar cheese" than when labeled "Body odor," and these effects reflected activations in the medial orbitofrontal cortex and perigenual cingulate cortex (de Araujo, Rolls, Velazco, Margot, & Cayeux, 2005). The implication is that cognitive factors can have profound effects on our responses to the hedonic and sensory properties of food, in that these effects are manifest quite far down into sensory and hedonic processing (in the orbitofrontal cortex, see Fig. 2), so that hedonic representations of odors are affected (de Araujo et al., 2005).

Similar cognitive effects and mechanisms have now been found for the taste and flavor of food, where the cognitive word-level descriptor was, for example, "rich delicious flavor" and activations to flavor were increased in the orbitofrontal cortex and regions to which it projects including the perigenual cingulate cortex and ventral striatum, but were not influenced in the insular primary taste cortex where activations reflected the intensity (concentration) of the stimuli (Grabenhorst, Rolls, & Bilderback, 2008; see Fig. 7). Cognitive factors can also influence the release of the hunger-related hormone ghrelin (Crum, Corbin, Brownell, & Salovey, 2011). If self control of reward-related processing is required, the dorsolateral prefrontal cortex may be involved in the attentional and related aspects of the processing (Hare, Camerer, & Rangel, 2009; Rolls, 2014).

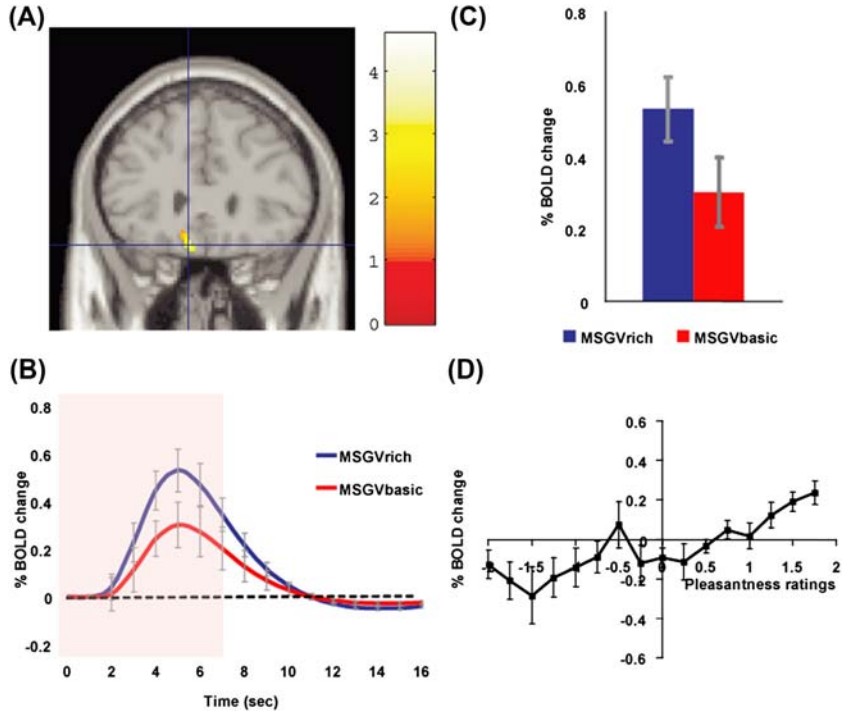

Figure 7 Cognitive modulation of flavor reward processing in the brain. (A) The medial orbitofrontal cortex was more strongly activated when a flavor stimulus was labeled "rich and delicious flavor" (MSGVrich) than when it was labeled "boiled vegetable water" (MSGVbasic) ([-8 28 -20]). (The flavor stimulus, MSGV, was the taste 0.1 M MSG + 0.005 M inosine 5′monophosphate combined with a consonant 0.4% vegetable odor.) (B) The timecourse of the BOLD signals for the two conditions. (C) The peak values of the BOLD signal (mean across subjects ± sem) were significantly different. (D) The BOLD signal in the medial orbitofrontal cortex was correlated with the subjective pleasantness ratings of taste and flavor, as shown by the SPM analysis, and as illustrated (mean across subjects ± sem). *Grabenhorst, F., & Rolls, E.T. (2008). Selective attention to affective value alters how the brain processes taste stimuli.* European Journal of Neuroscience, *27(3), 723–729. Copyright (2008), with permission from John Wiley & Sons.*

4.2 Effects of Top-Down Selective Attention to Affective Value Versus Intensity on Representations of Taste, Olfactory, and Flavor Processing

We have found that with taste, flavor, and olfactory food–related stimuli, selective attention to pleasantness modulates representations in the orbitofrontal cortex, whereas selective attention to intensity modulates activations

in areas such as the primary taste cortex (see Fig. 4; Ge, Feng, Grabenhorst, & Rolls, 2012; Grabenhorst & Rolls, 2008, 2010; Luo, Ge, Grabenhorst, Feng, & Rolls, 2013; Rolls, 2013; Rolls et al., 2008).

This differential biasing of brain regions engaged in processing a sensory stimulus depending on whether the cognitive demand is for affect-related versus more sensory-related processing may be an important aspect of cognition and attention which has implications for how strongly the reward system is driven by food, and thus for eating and the control of appetite (Grabenhorst & Rolls, 2008, 2011; Rolls, 2012d, 2014; Rolls et al., 2008). The top-down modulations of processing have many implications for investigations of taste, olfactory, and other sensory processing, and for the development of new food products.

4.3 Individual Differences in the Reward System

An important hypothesis is that different humans may have reward systems that differ in how strongly their reward systems are activated, driven by the sensory and cognitive factors that make taste, olfactory, and flavor stimuli attractive. In a test of this, we showed that activations to the sight and flavor of chocolate in the orbitofrontal and perigenual cingulate cortex were much higher in chocolate cravers than noncravers (Rolls & McCabe, 2007), though there were no differences at the level of the insular taste cortex. This provides evidence that differences in specific reward systems, and not necessarily in earlier sensory processing, can lead to individual differences in behavior to taste, olfactory, and flavor stimuli. This is consistent with the hypothesis that part of the way in which evolution results in effective specific reward systems is by utilizing natural variation in these reward systems, and selecting for reward systems that lead to reproductive success (Rolls, 2014). This concept that individual differences in responsiveness to food reward are reflected in brain activations in regions related to the control of food intake (Beaver et al., 2006; Rolls & McCabe, 2007) may provide a way for understanding and helping to control food intake and obesity (Rolls, 2012d, 2014).

4.4 Age-Related Differences in Food Reward Representations

There are age-related differences in the acceptability of different foods. For example, children may not take readily to a wide range of vegetables, yet find sweet foods palatable (Birch, 1999; Hetherington, Cecil, Jackson, & Schwartz, 2011). Adults may find a wide range of foods pleasant. As people

age, smell and even taste may become less sensitive and this may contribute to the changes in eating that can occur in aging (Jacobson, Green, & Murphy, 2010). In an examination of the neural mechanisms underlying these age-related differences in the acceptability of different flavors and foods with three age groups (21, 41, and 61 years), we found that orange was liked by all age groups, while vegetable juice was disliked by the young, but liked by the elderly (Rolls et al., 2015). In the insular primary taste cortex, the activations to these stimuli were similar in the three age groups, indicating that the differences in liking for these stimuli between the three groups were not represented in this first stage of cortical taste processing. In the supracallosal anterior cingulate cortex, where unpleasant stimuli are represented, there was a greater activation to the vegetable than to the orange stimuli in the young but not in the elderly. In the amygdala (and orbitofrontal cortex), where the activations were correlated with the pleasantness of the stimuli, there was a smaller activation to the vegetable than to the orange stimuli in the young but not in the elderly. Thus age differences in the activations to different flavors can, in some brain areas where olfactory, taste, and flavor stimuli are represented in terms of their hedonic value, be related to, and probably cause, the differences in pleasantness of foods as they differ for people of different ages (Rolls et al., 2015).

5. BEYOND REWARD VALUE TO DECISION-MAKING

Representations of the reward value of food and their subjective correlate the pleasantness of food, are fundamental in determining appetite and processes such as food-related economic decision-making (Padoa-Schioppa, 2011; Padoa-Schioppa & Cai, 2011; Rolls, 2014). But after the reward evaluation, a decision has to be made about whether to seek for and consume the reward. We are now starting to understand how the brain makes decisions as described in *The Noisy Brain* (Rolls & Deco, 2010) and *Emotion and Decision-Making Explained* (Rolls, 2014), and this has implications for whether a reward of a particular value will be selected (Deco, Rolls, Albantakis, & Romo, 2013; Grabenhorst & Rolls, 2011; Rolls, 2008b, 2011a, 2014; Rolls & Deco, 2010; Rolls & Grabenhorst, 2008).

A tier of processing beyond the orbitofrontal cortex, in the medial prefrontal cortex area 10, becomes engaged when choices are made between odor stimuli based on their pleasantness (Grabenhorst, Rolls, & Parris, 2008; Rolls et al., 2010a, 2010b; Rolls, Grabenhorst, et al., 2010)

(tier 3 in Fig. 2). For example, activations in this area are larger when humans make a decision about which of two odors they prefer, compared to only rating the odors on a continuous scale of reward value (Grabenhorst, Rolls, & Parris, 2008).

6. HORMONAL SIGNALS RELATED TO HUNGER AND SATIETY, AND THEIR EFFECTS ON THE HYPOTHALAMUS

There are many peripheral signals including hormonal signals that are produced when food is eaten, and some of these influence hunger and satiety by their direct or indirect effects on hypothalamic nuclei (Begg & Woods, 2013; Morton et al., 2014; Woods & Begg, 2015). These hunger/satiety signals modulate the reward value of food, that is, when hunger is present the reward value of food is high, and when satiety is present the reward value of food is low or zero. To produce this modulation of reward value, it is likely that these hypothalamic hunger/satiety signals reach the primate, including human orbitofrontal cortex, where they modulate neuronal responsiveness to taste, olfactory, flavor, and visual stimuli produced by food to produce the food reward signal present in orbitofrontal cortex neurons. Some of the effects of these hunger/satiety signals on the hypothalamus are now summarized with reference to Fig. 8. We start with the hormone leptin, with some of the findings as follows (Campfield, Smith, Guisez, Devos, & Burn, 1995; van der Klaauw & Farooqi, 2015; Morton et al., 2014).

Leptin or OB protein is the hormone encoded by the mouse ob gene (here ob stands for obesity). Genetically obese mice that are double recessive for the ob gene (ie, obob mice) produce no leptin. Leptin reduces food intake in wild-type (lean) mice (who have genes that are OBOB or OBob so that they produce leptin) and in obob mice (showing that obob mice have receptors sensitive to leptin). The satiety effect of leptin can be produced by injections into the brain. Leptin does not produce satiety (reduce food intake) in another type of genetically obese mouse designated dbdb. These mice may be obese because they lack the leptin receptor or mechanisms associated with it. Leptin has a long time-course: it fluctuates over 24 h, but not in relation to individual meals. Leptin concentration may correlate with body weight/adiposity, consistent with the possibility that it is produced by fat cells, and can signal the total amount of body fat.

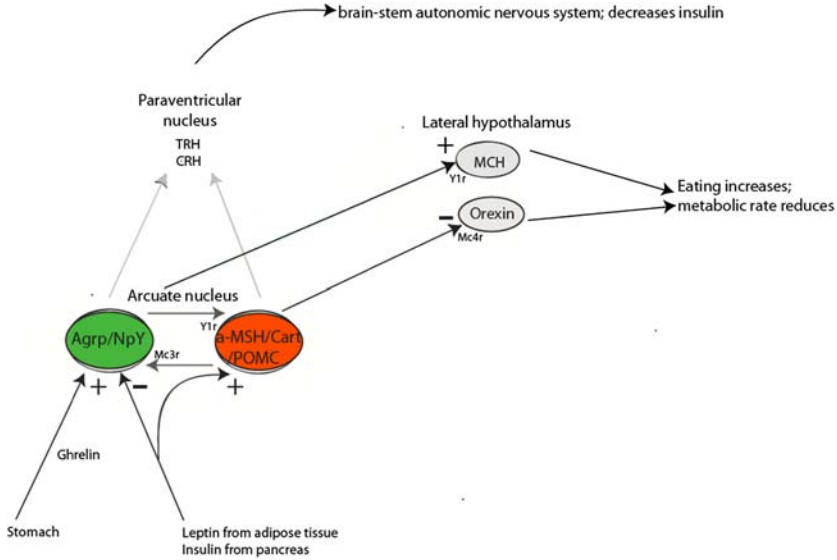

Figure 8 Effects of peripheral hunger- and satiety-related signals on some of the neurochemically identified feeding-related neurons of the hypothalamus, including neurons in the arcuate, lateral hypothalamic, and paraventricular nuclei. The Agrp/NpY neurons contain neuropeptide Y and agouti-related peptide, and have hunger-related activity and effects (green (gray in print versions)). The α-MSH/CART/POMC neurons contain α-melanocyte-stimulating hormone, cocaine- and amphetamine-regulated transcript, and pro-opiomelanocortin, and have satiety-related activity and effects (red (dark gray in print versions)). *TRH*, thyrotropin-releasing hormone; *CRH*, corticotrophin-releasing hormone; *MCH*, melanin-concentrating hormone; +, excitatory; −, inhibitory.

A hypothesis consistent with these findings is that leptin is produced in proportion to the amount of body fat, and that this is a signal that influences how much food is eaten. Although this is an interesting mechanism implicated in the long-term control of body weight, it appears that most obesity in humans cannot be accounted for by malfunction of the leptin system, for even though genetic malfunction of this system can produce obesity in humans, such genetic malfunctions are very rare (van der Klaauw & Farooqi, 2015). It is found that obese people generally have high levels of leptin, so leptin production is not the problem, and instead leptin resistance (ie, insensitivity) may be somewhat related to obesity, with the resistance perhaps related in part to smaller effects of leptin on the arcuate nucleus NpY/Agrp neurons. However, there is now evidence that the leptin system may contribute to hunger only as a result of nutrition being poor, when

leptin may be reduced and hunger is produced (van der Klaauw & Farooqi, 2015).

We now broaden the approach to include other hormones and signals, and summarize how they influence brain systems involved in appetite control (Morton et al., 2014), which, as shown here, act through modulating food reward (Fig. 8).

In the lateral hypothalamus there are melanin-concentrating hormone (MCH) and orexin-producing neurons, and an increase in their activity increases food intake and decreases metabolic rate (Fig. 8). These neurons are activated by neuropeptide Y (NpY), itself a potent stimulator of food intake, produced by neurons in the arcuate nucleus, a hypothalamic nucleus in the ventromedial hypothalamic region. The arcuate NpY neurons also release agouti-related peptide (Agrp), itself a potent stimulator of food intake. One of the signals that activates NpY/Agrp neurons is ghrelin, a hunger-hormone produced by the stomach (Morton et al., 2014; Muller et al., 2015; Fig. 8). NpY/Agrp neurons increase their firing rates during fasting, and are inhibited by leptin (Morton et al., 2014), so may be thought of as signaling hunger.

Leptin also inhibits the lateral hypothalamic orexin-producing neurons that are linked to eating, and these are two ways in which leptin may decrease feeding (Morton et al., 2014). Leptin can also reduce feeding by activating the α-MSH/CART/POMC "satiety" neurons in the arcuate nucleus shown in Fig. 8 (POMC is pro-opiomelanocortin). CART (cocaine- and amphetamine-regulated transcript), produced by these "satiety" neurons, reduces hunger (ie, is anorexigenic or increases satiety), and so does α-melanocyte-stimulating hormone (α-MSH) produced by the same neurons (Morton et al., 2014; Fig. 8). Consistent with this, the (very rare) humans with clear genetic dysfunctions of the leptin receptor systems may show overeating and obesity which is treatable by leptin, and approximately 4% of obese people have deficient (MC4) receptors for melanocyte-stimulating hormone (MSH; van der Klaauw & Farooqi, 2015). Also consistently, a very rare mutation in the gene encoding POMC in humans results in low MSH levels and obesity (van der Klaauw & Farooqi, 2015).

The paraventricular nucleus contains the anorectic thyrotropin-releasing hormone (TRH) and corticotrophin-releasing hormone (CRH). Destruction of the paraventricular nucleus causes hyperphagia and obesity. A number of hormones released when food enters the gut also influence food intake, and act via effects on the hypothalamus and on brain stem areas such as the nucleus of the solitary tract, which contains a brain stem relay

of afferents from the gut. These hormones include glucagon-like peptide-1 (GLP-1), cholecystokinin (CCK), pancreatic polypeptide (PP), peptide YY (PYY), and oxyntomodulin (Hussain & Bloom, 2013; Price & Bloom, 2014). The afferents from the gut convey effects of gastric distension which is essential for satiety (Gibbs, Maddison, & Rolls, 1981; Rolls, 2014), and of taste and other receptors in the gut which probably contribute to satiety. The visceral part of the nucleus of the solitary tract projects to visceral parts of the parabrachial nucleus (Beckstead, Morse, & Norgren, 1980), which then sends projections to the thalamus (the rostral nontaste part of the VPMpc, which in turn projects to the visceral part of the insula), the lateral hypothalamus, and the central nucleus of the amygdala (Pritchard, Hamilton, & Norgren, 2000). The projection to the central nucleus of the amygdala has now been genetically identified in mice and implicated as a pathway involved in satiety (Carter, Soden, Zweifel, & Palmiter, 2013).

These findings show that many hormones and other signals that influence hunger, satiety, and body weight act on the hypothalamus, but do not address how these effects in the hypothalamus influence the reward value of the sensory stimuli produced by food to influence appetite and food intake. That is likely to occur as a result of these hunger and satiety signals influencing taste and flavor neurons in the primate including the human orbitofrontal cortex. These orbitofrontal cortex neurons are then likely to relay the resulting food reward value signal to the lateral hypothalamus, where neurons are found that respond to food reward, in particular to the sight and taste of food when hunger is present (Burton et al., 1976; Rolls, 2014; Rolls et al., 1979).

7. POSTINGESTIVE EFFECTS OF NUTRIENTS INCLUDING CONDITIONED APPETITE AND SATIETY

Oral signals of taste, texture, and temperature, and retronasally sensed olfactory effects, implement the hedonic reward value of food, with subjective pleasantness correlated with activations in the OFC and ACC. Animals, including humans, work to obtain small quantities of these oral signals. Food placed directly into the gut or provided intravenously does not produce immediate unconditioned reward with small quantities (Nicolaidis & Rowland, 1977; Sclafani, Ackroff, & Schwartz, 2003). That is, a reduction in hunger produced by directly placing food into the gut and bypassing taste and smell is not very rewarding. Consistent with this, turning off hunger-related Agrp neurons in the arcuate nucleus of the hypothalamus is not a

good reward for instrumental behavior, though it can produce some conditioned preferences for foods or places with which the hunger reduction is associated (Sternson, 2013).

Food sensed in the gut after ingestion can produce conditioned (learned) appetite or preference for a food, and can also produce conditioned satiety (Booth, 1985). This was demonstrated by David Booth, who fed two groups of participants either high-energy sandwiches with flavor 1 or low-energy sandwiches with flavor 2. After several days with this pairing, when medium energy sandwiches were provided, participants ate more of those with flavor 2, as it had previously been paired with low-energy nutrition sensed after ingestion. This demonstrates how postingestive signals can influence humans' flavor preferences by postingestive learning of the association between the flavor and its nutritional including energy content. It is important to bear in mind these conditioned appetite and satiety effects when designing low-energy foods, for postingestive conditioning is likely to produce some compensation by increasing the amount eaten of such foods.

There is considerable interest in how signals sensed in the gut contribute to these postingestive effects of nutrients. When ingested food reaches the GI tract, it produces satiety by producing gastric distension and stimulation of intestinal hormone release (as shown by the absence of satiety in sham feeding when food drains from a gastric or duodenal cannula in primates (Gibbs et al., 1981). The results with the duodenal cannula open show that the gastric distension only occurs if food enters the duodenum where it activates gut receptors so causing closing of the pyloric sphincter. This is probably an unconditioned satiety effect produced by gastric distension and intestinal hormonal release (Seeley, Kaplan, & Grill, 1995). If the distension is reduced at the end of a meal, then feeding resumes very quickly, typically within 1 min, in primates (Gibbs et al., 1981; Rolls, 2014). In addition to unconditioned effects of food in the gut, there are also conditioned effects whereby the metabolic and other nutritive consequences of the ingestion of a flavor can influence the reward value of the flavor later, in, for example, conditioned appetite (Booth, 1985), sometimes referred to as appetition (Sclafani, 2013). Some of the mechanisms involved in conditioned appetite are described next.

When food enters the gastrointestinal (GI) tract it activates a wide range of gut receptors including gut taste receptors, which stimulate locally the release of peptides such as CCK, PYY, ghrelin, and GLP-1 from endocrine cells (Depoortere, 2014; Kokrashvili, Mosinger, & Margolskee, 2009a, 2009b; Margolskee et al., 2007), which play a crucial role in the regulation

of food intake (Hussain & Bloom, 2013; Parker, Gribble, & Reimann, 2014; Price & Bloom, 2014). Sugar delivered into the GI tract acts through sodium-glucose transporters (SGLTs) to stimulate the release of GLP-1 (Depoortere, 2014). In contrast, glucose transporter type2 (GLUT2) is not involved in the release of GLP-1 (Depoortere, 2014). Activation of T2R bitter receptors in the GI tract can lead to the release of CCK or PYY, which can influence vagal afferents (Behrens & Meyerhof, 2011). Gut receptors for other nutrients such as amino acids and fatty acids have been identified. For example, GPRC6A and CaSR are for amino acids and FFARs for fatty acids (Berthoud, 2008; Depoortere, 2014; Rasoamanana, Darcel, Fromentin, & Tome, 2012). These receptors are involved in the secretion of peptide hormones such as GLP-1, CCK, and PYY (Berthoud, 2008; Depoortere, 2014; Rasoamanana et al., 2012). These peptide hormones may act both peripherally and centrally to influence processes in the gut and in the brain.

Conditioned taste aversions (CTAs) involve associative learning between oral and visceral stimuli (Scott, 2011). For example, a novel taste solution (CS) followed by aversive malaise (US) will not be ingested afterward, although the taste solution was rewarding before the conditioning. The acquisition of this conditioning depends on the insular cortex in rats, but changes then occur in the nucleus of the solitary tract (which will influence activity in all rodent taste areas), and the CTA thereafter no longer requires the presence of the insula (Scott, 2011).

Conditioned taste preferences depend on visceral signals generated by specific nutrients that are components of the unconditioned stimulus (Ackroff & Sclafani, 2014; Sclafani, 2013). The conditioning can be fast in rodents, apparently influencing appetite for a flavor stimulus such as cherry versus grape within 15 min (Sclafani, 2013; Zukerman, Ackroff, & Sclafani, 2011). The post-oral effect of sugars apparently does not require T1R2 + T1R3 sweet taste receptors in the gut in that flavor preference was still conditioned to intragastric infusion of sucrose in T1R3 knockout mice (Sclafani, Glass, Margolskee, & Glendinning, 2010). Glucose is more effectively absorbed in the intestine than the hepatic portal system for glucose-conditioned flavor preferences (Ackroff, Yiin, & Sclafani, 2010). Furthermore, a humoral pathway is involved in post-oral glucose conditioning since visceral deafferentiation does not impair glucose-conditioned flavor preferences (Sclafani et al., 2003). Glucose infusion produces stronger flavor conditioning effects than fructose in rats and mice, even though the fructose is metabolized (Ackroff, Touzani, Peets, & Sclafani, 2001; Sclafani & Ackroff, 2012; Sclafani, Fanizza, & Azzara, 1999), and the same applies to

the reinforcing effects of intragastric infusions measured by operant behavior (Sclafani & Ackroff, 2015). This indicates that metabolism per se is not part of the sensing mechanism for flavor conditioning to gut signals. In addition, the three sodium-glucose transporter SGLT1 ligands: glucose, a nonmetabolizable glucose analog α-methyl-D-glucopyranoside (MDG), and galactose, all conditioned significant CS+ preferences; with the SGLT3 ligands (glucose, MDG) producing the strongest preferences (Zukerman, Ackroff, & Sclafani, 2013). Fructose, which is not a ligand for SGLTs, fails to stimulate CS+ intake or preference (Zukerman et al., 2013). MDG acts through SGLT1/3 in that intragastric infusion of MDG with a SGLT1/3 antagonist, phloridzin, blocked MDG appetition. However, phloridzin alone has only minimal effects on glucose-induced appetition. Instead, glucose-induced appetition is blocked by phloridzin and phloretin (a glucose transporter type2 (GLUT2) antagonist) (Zukerman et al., 2013). Taken together, these findings suggest that humoral signals generated by intestinal SGLT1 and SGLT3, and to a lesser degree, GLUT2, mediate post-oral sugar appetition in mice. The MDG results indicate that sugar metabolism is not essential for the post-oral intake-stimulating and preference-conditioning actions of sugars in mice (Zukerman et al., 2013). Rapid effects have also been described after intragastric infusion of fat emulsion (Tellez et al., 2013) which are mediated in part by intestinal fatty acid sensors (GPR40, GPR120) (Sclafani, Zukerman, & Ackroff, 2013). Interestingly, nondeprived and sated animals can still acquire strong conditioned flavor preferences (Sclafani, 2013).

Most of the previously mentioned studies have been on conditioned preferences produced by food in the GI tract. It will be of interest in future research to analyze, in addition, how visceral signals can produce conditioned satiety for the flavor with which they are paired. It would be of interest to develop our understanding of conditioned satiety, for this may be relevant to food intake control and its disorders.

8. RELEVANCE TO THE CONTROL OF FOOD INTAKE AND OBESITY AND CONCLUSION

These investigations show that a principle of brain function is that representations of the reward/hedonic value and pleasantness of sensory, including food-related, stimuli are formed separately from representations of what the stimuli are and their intensity. The pleasantness/reward value is represented in areas such as the orbitofrontal cortex and perigenual

cingulate cortex, and it is here that hunger/satiety signals modulate the representations of food to lead to a representation of reward value. The satiety signals that help in this modulation may reach the orbitofrontal cortex from the hypothalamus, and in turn, the orbitofrontal cortex projects to the lateral hypothalamus where neurons are found that respond to the sight, smell, and taste of food if hunger is present (Burton et al., 1976; Rolls, 1981, 2014; Rolls et al., 1976; Rolls & Grabenhorst, 2008). We have seen earlier some of the principles that help to make the food pleasant, including particular combinations of taste, olfactory, texture, visual, and cognitive inputs. Applications of this approach to motivation to understanding the overeating in obesity are described elsewhere (Rolls, 2014, 2016b; see Fig. 9).

In this paper, a theory of motivation has been advanced. This is a development from Rolls' theory of emotion (Rolls, 2014). Many further aspects of how motivation of other type operates have been described elsewhere, including for thirst (Rolls, 2005), for sexual behavior (Rolls, 2014), and other types of motivation (Rolls, 2012c). Moreover, the relation between

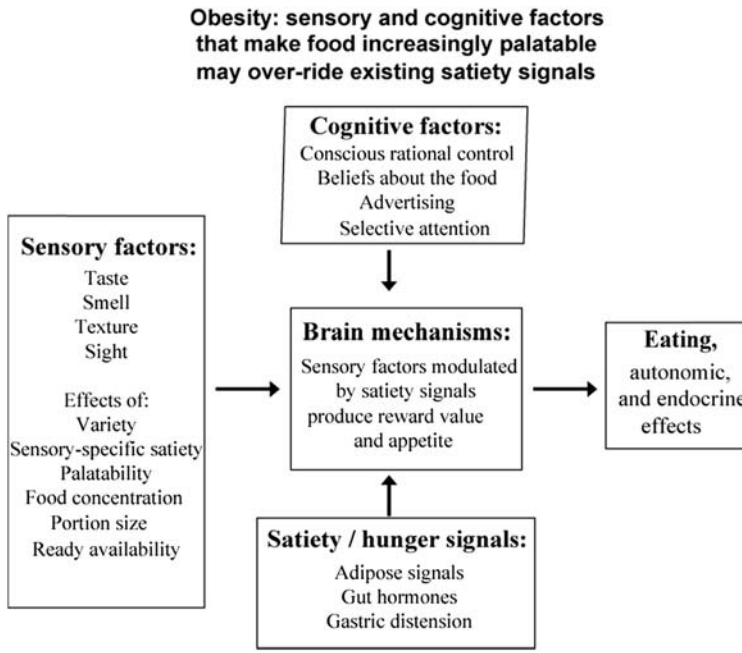

Figure 9 Schematic diagram to show how sensory factors interact in the orbitofrontal cortex with satiety signals to produce the hedonic, rewarding value of food, which leads to appetite and eating. Cognitive and attentional factors directly modulate the reward system in the brain.

motivation, emotion, and rewards, and the underlying mechanisms, has been analyzed further elsewhere (Rolls, 2014).

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