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Food Reward: Brain Substrates of Wanting and Liking

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BERRIDGE, K.C. *Food reward: brain substrates of wanting and liking.* NEUROSCI BIOBEHAV REV **20**(1) 1–25, 1996. — What are the neural substrates of food reward? Are reward and pleasure identical? Can taste pleasure be assessed in animals? Is reward necessarily conscious? These questions have re-emerged in recent years, and there is now sufficient evidence to prompt re-examination of many preconceptions concerning reward and its relation to brain systems. This paper reviews evidence from many sources regarding both the psychological structure of food reward and the neural systems that mediate it. Special attention is paid to recent evidence from "taste reactivity" studies of affective reactions to food. I argue that this evidence suggests the following surprising possibilities regarding the functional components and brain substrates of food reward. (1) Reward contains distinguishable psychological or functional components—"liking" (pleasure/palatability) and "wanting" (appetite/incentive motivation). These can be manipulated and measured separately. (2) Liking and wanting have separable neural substrates. Mediation of liking related to food reward involves neurotransmitter systems such as opioid and GABA/benzodiazepine systems, and anatomical structures such as ventral pallidum and brainstem primary gustatory relays. Mediation of wanting related to food reward involves mesotelencephalic dopamine systems, and divisions of nucleus accumbens and amygdala. Both liking and wanting arise from vastly distributed neural systems, but the two systems are separable. (3) Neural processing of food reward is not confined to the limbic forebrain. Aspects of food reward begin to be processed in the brainstem. A neural manipulation can enhance reward or produce aversion but no single lesion or transection is likely abolish all properties of food reward. (4) Both wanting and liking can exist without subjective awareness. Conscious experience can distort or blur the underlying reward processes that gave rise to it. Subjective reports may contain false assessments of underlying processes, or even fail at all to register important reward processes. The core processes of liking and wanting that constitute reward are distinct from the subjective report or conscious awareness of those processes.

Food intake Palatability Affect Reward Pleasure Appetite Taste Lateral hypothalamus
Dopamine Nucleus accumbens Amygdala Benzodiazepine

INTRODUCTION

> "...It is time that we again address questions of sensation, feeling, and affect in humans, and animals as well, and ask about the biological basis of hedonic experience." [Eliot Stellar, in The Physiological Mechanisms of Motivation (D. Pfaff, ed.), p. 378.]

IT SEEMS axiomatic that we want the rewards we like, and like the rewards we want. Yet while this is usually the case, recent evidence indicates that wanting and liking do not always go together. Liking corresponds closely to the concept of palatability; wanting, by comparison, corresponds more closely to appetite or craving. Evidence is mounting that wanting and liking have separable underlying brain substrates. Under some circumstances, especially after particular brain manipulations, they may actually change in opposite directions. Since most of the literature relevant to wanting and liking in food reward has come from animal studies, it will be essential to consider here how these processes have been assessed in the past, and which measures assess each process best. It will also be important to consider how these processes, as assessed in animals, relate to aspects of reward in humans.

In this paper, I intend to address five basic questions that seem important concerning our understanding of food reward. These are:

(1) What should we look for in definitions of palatability or food reward?
(2) Where in the brain is food reward?
(3) What is the relation of liking to wanting within reward?
(4) What are the brain substrates of wanting and liking?
(5) How does human subjective experience relate to these reward processes?

Issues of Definition

Hunger and satiety are often conceived in terms of physiological signals that reflect homeostatic states. We operationalize them behaviorally in animal studies

by parameters such as intake amount, rates and pattern. But many neuroscientists and psychologists, like many people in general, tend to define reward in terms of how it "feels" (at least whenever reward is meant as something more than Skinnerian reinforcement, which by itself fails to cover many aspects of behavioral reward). We may operationalize food reward for animal studies in measures such as food preference, operant responses, and affective taste reactivity patterns. Still, many consider these measures to be less revealing of the process they measure—subjective reward—than behavioral measures for other psychological constructs (hunger, satiety, memory, etc.). Thus it is not uncommon to encounter assertions such as "Only in humans *who can say what they feel* can we directly study reward" (e.g., 28,132). The intuitive plausibility of that position is self-evident, but it is not without difficulties. By equating reward with consciousness, the field has been led into puzzles—can non-human animals, incapable of verbal reports, be demonstrated to have affect? If preference and intake are the sole measures of food reward for animals, then are reward concepts for animals necessarily circular (i.e., inferred on the basis of intake and instrumental performance, but unsubstantiated apart from such measures)? Can reward be studied at all in animals?

These puzzles arise if we identify reward with our own subjective experience. But if reward processes can exist apart from subjective experience, as I will argue below, then the puzzles are predicated upon a wrong assumption. It may be that both reward processes and their neural substrates can be studied independently of subjective experience (85,106). This is not to deny the importance of subjective experience, but it draws a line between it and the fundamental processes of reward that are reflected, albeit with some distortion, in subjective experience. It converts the question from "how can one study neural substrates of a conscious process (reward) in animals?" into the pair of questions' "leaving consciousness momentarily aside, how can one study fundamental neural processes of reward (in animals)," and then later, "how do these fundamental processes relate to consciousness (which can be studied in humans)?"

If reward is not to be defined solely as subjective experience then how should we define it? Behavioral neuroscience is perhaps accustomed to insist on full definitions of a concept before studying it empirically. The importance of defining scientific concepts in a clear fashion cannot be disputed. But I suggest we do more harm than good to our search for understanding if we demand a complete definition of reward before we enter into its study. This amounts to a plea against the premature definition of reward. Although postponing definition has its own dangers, it may still be the most prudent course for several reasons. Our definitions may change—even drastically—as we learn more about a phenomenon. We can lock ourselves into unproductive habits of thought by too strict an insistence on prior definition, and adequate definitions have to be built empirically, step by step, which takes time. This means we must be willing to tolerate a "minimal definition" of skeletal properties of reward processes early on, and to work gradually toward more complete understanding.

Minimal Defining Properties of Food Reward

One well-established property with which to begin a minimal definition is that food reward is not simply a physical property of a taste stimulus itself (even though the palatability of novel sweets and bitters may be heavily biased by their physical stimulus properties). Palatability, or the hedonic component of food reward, instead results from a central integrative process that can incorporate aspects not only of the taste, but of the physiological state and of the individual's associative history.

Although reward and hunger have often been conceived as quite different in nature, and arising from different sensory receptor sources, the dichotomy between hunger and reward is by no means absolute. Cabanac has captured the interdependence between the two in his concept of alliesthesia—a change in the pleasantness of a constant physical stimulus as a consequence of a change in physiological state (26,27). The pleasantness of taste changes with physiological need or satiety. In a sense, it is a "response" by the brain to a configuration of physiological stimuli and associative cues, as well as to the taste itself.

Another established property is that food reward, like other rewards, is as much an incentive process as it is a process of drive reduction. Food reward is focused upon the taste, smell, sight, and feel of food and of the act of eating. Physiological deficit cues act largely by modulating the value of incentive stimuli and their representations, not by directly activating or reinforcing behavior themselves (17,141). For a full discussion of the evidence regarding incentive vs. drive processes in reward, the reader is referred to (141). My intention here is to accept that food reward is largely an incentive process, and to proceed to its constituents and controls.

Reward as Cause

A consequence of the tendency to define subjective experience as the *sine qua non* of reward has led some in the field of behavioral neuroscience to view it with suspicion as a cause for behavior. If palatability is an essentially conscious phenomenon, then can it be said to be causal in the same sense as a neural stimulus?

This problem like others is made less difficult if we make a distinction between subjective experience and the fundamental underlying processes of reward. By focusing upon the fundamental processes, one can use reward as a causal concept just as any other central state, irrespective of the causal properties of consciousness. Toates makes this argument explicitly: "Whether, for example, the energy-depleted rat has a conscious sensation of pleasure on making contact with a sucrose solution is perhaps an interesting philosophical speculation but not one that need worry us unduly. However, what is crucial is the need to postulate a central state that (a) depends upon both incentive and nutrient level; and (b) plays a role in keeping the rat

going at licking the sucrose in the face of other competing potential candidates for behavioral control" (142). The existence of this state produces consequences in both neural systems and behavioral output. Its use as a cause does not require us to know the concomitant conscious experience of these processes—which is a matter for separate study—as long as other indicators of reward states can be monitored, nor does it require a definitive answer to the question of the causal properties of consciousness.

Reward can be causal in the same sense as any "software" state—it creates conditions that potentiate coordinated sets of behaviors, cognitive strategies, etc. Many authors have pointed to the central neural state to act as a "common currency" to coordinate the pursuit of beneficial events. As Toates quotes Cabanac (28) "Pleasure opens an infinite register of new responses. Indeed it is far more simple to maximize pleasure than to accumulate within the CNS an infinite number of instinctual responses." Similar arguments regarding the causal properties of reward states have been made by several other biopsychologists (e.g., 45,132,138,139,141).

Where in the Brain is Food Reward?

The stream of taste sensation ascends through the brain in a bifurcating pathway (86,88,97,98). A classic sensory path is traced upward from the nucleus of the solitary tract in the medulla oblongata, pausing first, in rodents at least, within the hindbrain pons at the parabrachial nuclei (89). The pons sends dual projections to the forebrain. One pathway travels via a gustatory relay in the ventroposteriormedial thalamus and thence to gustatory cortex. A parallel secondary branch from the brainstem solitary nucleus ascends to limbic forebrain sites in the hypothalamus, substantia innominata, and amygdala. Traditionally, sensory aspects of taste processing have been viewed to be processed in the brainstem–thalamus–cortex path. Food reward, on the other hand, has been viewed traditionally as arising from operations performed within forebrain structures along a limbic path (e.g., 97).

But a classification of food reward as originating solely in forebrain limbic structures is too strong. For example, gustatory neurons in a limited region of the orbitofrontal cortex of the macaque monkey show declines in activity rates to preferred tastes as satiety ensues (109), reflecting an incorporation of food reward into at least this late stage of thalamocortical gustatory processing. There is also good evidence that evaluation of taste reward may begin before the bifurcation into thalamocortical vs. limbic paths, even within the nucleus of the solitary tract and parabrachial nucleus of the brainstem. For example, Scott and his colleagues have shown the neuronal coding of taste stimuli in the nucleus of the solitary tract of the medulla to be altered, at least in some species, by several manipulations that change the palatability of a taste, such as associative aversion conditioning (32). Associative aversion conditioning transforms the electrophysiological response elicited from the rat's

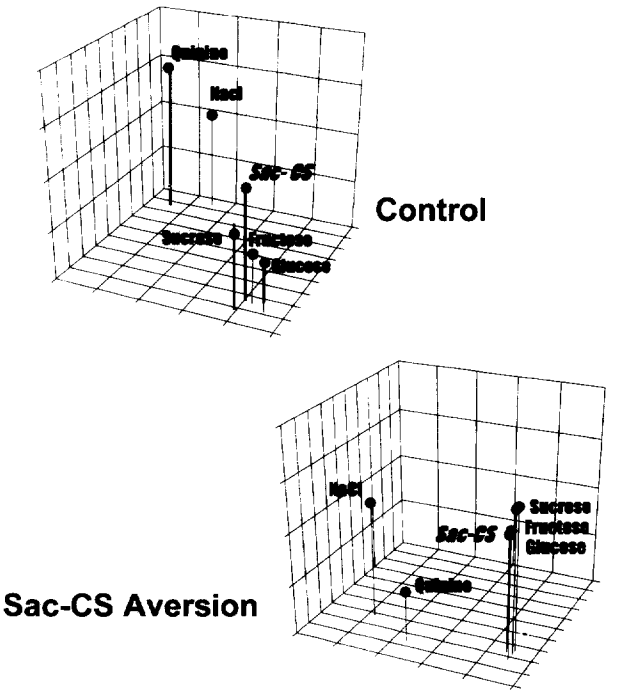

FIG. 1. Reorganization of neuronal taste coding within the brainstem nucleus of the solitary tract by a shift in reward. Upper panel represents the relative similarity of neuronal responses elicited by various taste stimuli from gustatory neurons of rats. Lower panel represents the reorganization of neuronal responses to the same taste stimuli after saccharin (conditioned stimulus—CS) was paired associatively with illness. [Modified from (32).]

nucleus of the solitary tract by the taste of associatively-paired saccharin from a sweet-typical pattern into one that resembles the normal response to bitter quinine (Fig. 1). A possible interpretation of this observation is that the brainstem gustatory neurons that participate in this shift actually code the "palatability" of the taste stimulus instead of the sweet/bitter "sensory" qualities that we usually assign to brainstem sensory relay nuclei. The idea that taste palatability is evaluated to a significant degree within the brainstem is supported by the ability of decerebrate animals and anencephalic human infants, which lack both higher pathways, to show positive or negative affective reactions to appropriate tastes (61,64,130,131). Further evidence for the idea that subtle aspects of taste reward are processed at an early stage before the signal leaves the hindbrain comes from observations that a primary consequence of parabrachial lesions, early in the brainstem stream, is to eliminate the capacity to develop associative taste aversions, while producing only minor effects on discrimination among taste sensory quality (52,105,127). In summary, the forebrain has no monopoly on reward aspects of taste processing—palatability has already begun to be coded neurally before taste leaves the hindbrain.*

This conclusion, if true, poses puzzles for how we understand the relative coding of taste sensory quality and palatability. Which neurons in the rat nucleus of the solitary tract code taste sensory quality, and which code palatability? Although some brainstem neurons

may code palatability more than sensory quality, surely they cannot all do so. It would be logically impossible for all gustatory neurons to be transformed by conditioned taste aversions. If that were so, the sensory coding of the particular taste would be unrecognizable as the conditioned stimulus the next time it was encountered. The hallmark of a conditioned aversion after all is that it is associative—specific to the paired taste—and the paired taste needs to be recognized when it occurs again. Recognition requires coding constancy. A sweet taste does not become transformed into a bitter sensation by associative aversion learning. It remains that particular sweet taste, and is recognized as such, but with altered palatability. As yet we have little understanding of how both sensory quality and affective palatability could co-exist and be coded simultaneously by neurons in the same primary relay nucleus, such as the nucleus of the solitary tract. But knowing only what we do, we can already conclude that the neural origin of food reward is not segregated to the limbic system. Food reward begins in the brainstem, and the forebrain exerts powerful descending influences on the evaluations that are made there (60).

Components of Food Reward: Appetite (Wanting) vs. Palatability (Liking)

To distinguish between appetite and palatability means to distinguish between the disposition to eat and the sensory "pleasure" of actually eating [for a similar distinction, see (20,107)]. This is a distinction between motivation and affect. Are all changes in appetite due to or accompanied by a change in palatability? Are none? Several investigators have pointed out that a confound for the study of palatability and appetite in animals is that we generally assess whether food is liked by asking whether and how much it is eaten (e.g., 22,71,104,107). This equates wanting food—the disposition to eat or appetite—with liking food—sensory pleasure or palatability.

If the equivalence of wanting and liking were always valid, then measures of one would indeed constitute measures of the other. Identity between the two might also mean that the separate concepts were redundant. On the other hand, if the equation of "wanting" = "liking" is not always valid, then we need ways to identify each process. Only if we can identify them separately can we study the conditions under which the two co-vary together and those under which they do not, and only then can we hope to identify their respective neural substrates.

Before going further, I should explain my use of wanting and liking. These are useful but dangerous words to use regarding the fundamental processes that mediate food reward. "Wanting" and "liking," as common language words, are useful because they more immediately convey a distinction between affect and incentive than psychological terms such as appetite and palatability, motivation and affect, or incentive salience and sensory pleasure. In my experience, they are so much more effective than other words at communicating this distinction between palatability and appetite that without them I fear the point would be missed. But their familiarity and intuitive comprehension also carry two disadvantages. First, the colloquial words carry meanings from everyday usage that may not apply to the actual processes themselves (for example, that we are consciously aware of when they occur—this is not necessarily true, as I will argue below). Second, the actual processes these words refer to may involve aspects that are simply missed by the ordinary meanings of the words (for example, that the process of wanting depends crucially on the neural modulation of the incentive salience of perceptions and representations, in part via mesotelencephalic dopamine projections). They are at best a first step along the way to a better understanding of the psychological structure of reward. But as a first approximation, they are helpful to convey to a reader the distinction between affective processes of palatability/pleasure/displeasure (liking), on the one hand, and the non-affective but still motivational processes of appetite that translate affect into action (wanting), on the other.

Behavioral Measures of Reward

Traditional measures of food reward in animals, based on intake, preference, or operant tasks, all depend in some sense on an active, instrumental "reaching out" to the reward. They measure actions that are performed in order to obtain the next reward, whether the action be pressing a bar, reaching for the

*In primates, changes in gustatory neuron activity may possibly be restricted to the forebrain. For example, the alterations in gustatory nucleus of the solitary tract activity found in rodents, correlated with changes in reward produced by alliesthesia or associative learning, have not been observed in monkeys (32,81,160). However, only "weak" manipulations of palatability have so far been tested. The effect of stronger manipulations on solitary nucleus activity, such as associative taste aversions or sodium appetite, have not been examined in primates. But if the anatomical distinction between species is real, it may be viewed as a quantitative difference in the encephalization of gustatory processing (70,139). By this view, the evolution of extensive cortical processing in primates has invaded the autonomy originally possessed by brainstem circuits, and has transferred some forms of integration from brainstem to forebrain.

An interesting aspect of brainstem taste processing is that decebrate rats, which lack a forebrain, are not capable of altering their behavioral affective reactions on the basis of the taste aversion conditioning (62), but do alter their electrophysiological response of neurons in the nucleus of solitary tract (NST) to the paired taste similarly to intact animals (121). What does this mean? One possibility is that the NST electrophysiological change is a partial alteration in palatability evaluation expressed by behavioral affective reactions, but is insufficient by itself in the absence of addtional associative-based direction provided by the forebrain. Another possibilty is that electrophysiological change, which appears to reflect primarily an early peak of action potentials on the onset of quinine and the illness-paired taste, is essentially an "alerting reaction" that may help trigger associative-based changes in palatabilty (and which does imply a degree of recognition competence from the brainstem), but is not after all a palatability shift in itself. The possibility is supported by recent observations by the Scott laboratory that the NST electrophysiological change persists even after a conditioned aversion has been extinguished (Professor T. Scott, personal communication). A third alternative, which may be least likely, is that NST electrophysiological change is indeed a palatability shift, but that palatability is also processed in parallel by another brainstem circuit, and that in decebrates these parallel circuits fail to transfer information to output systems of motor control (see discussion of "nonaffective interpretations" of taste reactivity).

next pellet, or simply initiating the next bite of an external food. Even consummatory actions, such as a bite or lick, have an appetitive/instrumental aspect when the goal object is external and when the action is instrumental in capturing it (126). Instrumental aspects are the focus of almost all traditional behavioral measures of reward.

A great deal of thought and clever experimentation has gone into separating reward factors that influence these measures from performance factors such as motor coordination, fatigue, and general arousal (e.g., 135). For food reward, many sophisticated techniques have been developed to differentiate among multiple controls of ingestion such as taste, postingestive feedback, perfomance factors, etc. They include sham-feeding paradigms, which peel satiety feedback away from initial taste assessment and, more recently, "curve-shift" paradigms adopted from brain stimulation reward studies (44,148,149). Such techniques can be used to distinguish changes in reward from sensorimotor/arousal factors that alter instrumental performance, and they allow comparison of the magnitude of different types of reward (33).

The perfection of sophisticated analyses for instrumental behavior has provided powerful tools for examining how neural manipulations change an animal's wanting for reward. The reader may refer to excellent existing reviews that summarize current understanding of the brain mechanisms of traditional measures of food reward (e.g., 69,126,133,135). Instrumental behavior has also been used to infer changes in liking, on the assumption that changes in the degree to which an incentive is pursued (wanted) invariably reflects changes in the hedonic pleasure of that incentive object (the degree to which it is liked). No doubt the assumption that wanting reflects liking is often true. But it is important to note that there is no independent evidence for it in most studies of food reward or its neural controls.

Affective Reactions and Palatability

In the past 10 years, increasing evidence has emerged that raises the possibility that the assumption that "wanting" = "liking" is wrong—at least under some conditions. In the remainder of this paper, I wish to focus on studies that reveal a difference between wanting and liking. This evidence has come primarily from "taste reactivity" studies of affective reaction patterns elicited by the taste of food. Taste reactivity is a distinctly different measure of food reward. Affective reactions are engendered by a food reward that has been immediately experienced, whereas other types of reward-related behavior are directed toward capturing the next food target. I will argue that affective taste reactivity measures primarily reflect food liking or palatability, whereas instrumental behavior reflects wanting or appetite.

Affective reactions are distinctive, species-typical patterns of responses (Fig. 2). When a sweet or bitter taste is placed in the mouth of a human infant, stereotyped facial expressions can be observed, as demonstrated by Steiner (130,131). A sweet or mildly salty taste elicits a mild rhythmic smacking, slight protrusions of the tongue, a relaxed expression accompanied sometimes by a slight upturn of the corners of the mouth. A bitter, sour, or very salty taste elicits a grimace, a turning away, a gape or gagging movement as though to push out the offending taste, and a pushing away with the hands. No observer would question that these reactions reflect an evaluation in some sense of taste palatability.

If a similar taste is given to a chimpanzee, or to an old world monkey, corresponding facial reactions can be observed. These reactions are not identical to the human infant's, but a marked similarity of pattern can be observed across species, becoming gradually less similar as phylogenetic distance increases (129). Affective reactions to tastes are not exclusive to primates. Rats, which evolved as omnivores like us, and which naturally sample and evaluate a wide variety of foods—again like many primates—similarly display distinctively different patterns of facial and forelimb actions to sweet vs. bitter tastes (63). As shown originally by Grill and Norgren, sweet tastes elicit rhythmic mouth movement and tongue protrusions that are visible at the front of the mouth, distinctive lateral tongue protrusions that emerge at the side of the mouth and sweep back along the lips, and prolonged lapping at a target. Bitter tastes elicit gapes, rearing, shakes of the head, wiping of the face with the forelimbs and shaking of the paws (Fig. 2).

In all cases, the observed behaviors are affective reactions, in Epstein's sense: "discernible and recognizable patterns of responding ...richly complex and sufficiently diversified to express a variety of internal states" (45). They express an involuntary, immediate evaluation of the taste along dimensions of positive/negative acceptability. The nature of this affective evaluation has proved to be complex, hierarchical and multiply influenced by psychological as well as physiological factors. Affective patterns of taste reactivity in the rat have been studied by my laboratory partly in the hope that they provide a way of examining the controls and neural substrates of basic affect.

Use of affective reactions as measures to study the neural control of hedonic processes is based on the supposition that the neural and psychological mechanisms which evaluate taste acceptability in the rat overlap with those that form the core of affective evaluations experienced by humans as subjective palatability. That does not mean that palatability in rat and human are identical, in either mechanism or product. But evolution has produced different mammalian brains by a conservative process of modifying basic organization rather than creating entirely different circuits for different species. The similarity of reaction pattern across species, together with the similarity of brain systems, gives ground for hope that insight into human affect can be furthered by understanding the affective reactions of animals.

Evidence to support the hypothesis that the liking of taste palatability as experienced by humans overlaps with affective taste reactivity patterns of rats has come from comparisons of the factors that control them.

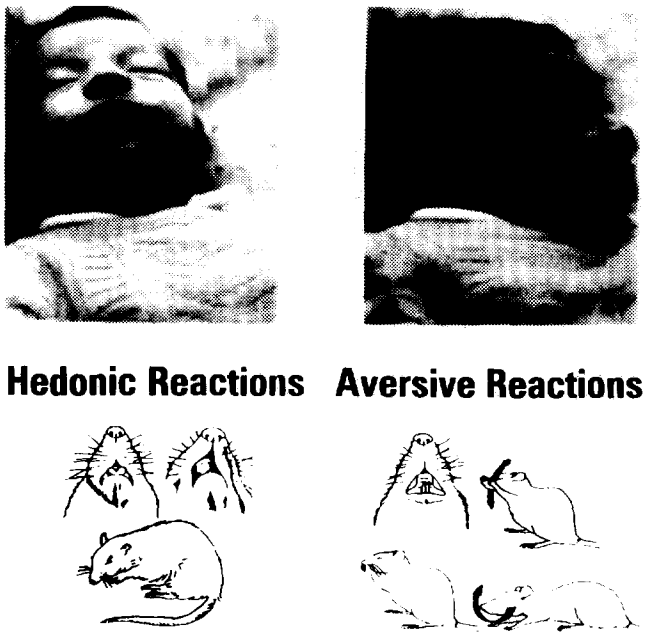

FIG. 2. Affective reactions to taste. Hedonic reaction of a 3-week old infant to a sweet solution (left: 1 M sucrose) vs. aversive reaction to an unpleasantly salty solution (right: 0.15 M NaCl) are shown in videotape frames at top. Various hedonic and aversive reactions of rats, which would be elicited by the same tastes, are drawn below. Hedonic reactions include tongue protrusions, lateral tongue protrusions and paw licks. Aversive reactions include gapes, headshakes, face/paw wipes and forelimb flails. Infant video from unpublished observations collected by G. Harris, D. Booth and K. Berridge at the University of Birmingham, England [following Steiner (130,131)]. Rat drawings of taste reactivity components follow Grill and Norgren (63).

Over the past 20 years, it has become very clear that many if not most manipulations that influence human perceptions of palatability also influence the affective reaction patterns of rats. Like human subjective perceptions of palatability, affective taste reactivity patterns of animals are modulated by the kinds of physiological states and psychological associations that change affect. For example, for humans, the perceived palatability of a taste can be altered by caloric hunger and satiety, sensory-specific satiety, specific appetites such as salt hunger, associative aversions established by taste–illness pairings, etc. (e.g., 4,27,28,73,80,108, 110). These same manipulations alter the affective patterns of rat taste reactivity components in ways that parallel human reports (e.g., 7,9,29,41,62,96,99). Affective taste reactivity patterns are also altered by many neural and pharmacological manipulations that are difficult to study in humans, but that might be expected to produce changes in taste affect based on current understanding of brain function, such as lesions of the primary gustatory pathway, ventral forebrain damage, opioid agents, etc. (e.g., 38,42,51,53,64,93,134). Although intake and palatability are often correlated, some situations can pull taste reactivity patterns apart from voluntary intake. Just as humans sometimes deliberately abstain from pleasant foods, rats can also be induced to suppress intake without altering affective reactions to palatability, by such psychological procedures as taste–shock pairing (96). A growing number of neural manipulations have also been shown to dissociate intake from affective patterns of taste reactivity (15,16,38,54,122), adding further support to the argument that hedonic and aversive patterns of rat taste reactivity reflect an affective evaluation rather than the decision to ingest.

Caveats and Alternatives to Palatability Interpretation of Affective Taste Reactivity Patterns

The claim that affective taste reactivity patterns measure evaluations of palatability is meant in a limited sense. There are several potential interpretations of my claim that I do not intend. These are described below in response to particular objections that I anticipate might be raised. Also, several nonaffective alternative views of taste reactions may occur to the reader. However, close inspection of the most commonly suggested alternatives shows them to be implausible, and I will briefly summarize why this is so.

Objection 1. All affect is not alike. Do I mean to imply that palatability for humans involves nothing more than is seen in rat taste reactivity measures? No. I do not mean that rat affective reaction patterns and human subjective reports reflect an identical process. Food reward is not a single process or an all or none phenomenon. It can exist in graded (and degraded) degrees. Palatability as assessed by taste reactivity is not identical to the full phenomenon of palatability in humans, though it may reflect a process that is at the core of human affect. By itself this process does not constitute subjective affect or even all aspects of nonsubjective affect. But the core process in rats and humans is highly similar in expression and in many factors that control it. Presumably it may also be similar in the organization of its underlying neural substrates.

Objection 2. Palatability is not behavior. Do I mean to suggest that palatability may be defined in terms of taste reactivity? Again, no. Affective patterns of taste reactivity reflect underlying assessments of palatability but they do not define it. Palatability or liking is the psychological/neural process that we wish to understand—it is not a pattern of actions. Taste reactivity gives an indication of underlying processes, just as do other behavioral measures, such as human subjective report, or as do neural measures, such as electrophysiological or neurochemical activity. Every indicator is subject to distortion, and must be interpreted with care by the observer. For taste reactivity patterns, as complex motor responses, the chief sources of distortion arise from sensorimotor factors, which I have discussed elsewhere (12), which can be avoided by careful attention to the pattern of activation across behavioral components.

Objection 3. Brainstem responses are reflexive, not affective. Doesn't the brainstem origin of these motor patterns rule them out as measures of palatability? Once again, no. Brainstem motor generation does not signify a separation of these patterns from affective processes of the forebrain. Some have been tempted to dismiss affective reaction patterns as mere "brainstem reflexes" because anencephalic human infants and

decerebrated rats, both of which possess an intact hindbrain and midbrain but lack virtually all forebrain structures, are capable of generating positive and negative reactions appropriately to sweet or bitter tastes (64,130). This conclusion wrongly assumes that behavior falls into one of two exclusive categories—forebrain affective pattern or mere brainstem reflex. Strict dichotomies between complex psychological functions of the forebrain and simple sensorimotor functions of the brainstem have been known to be too simplistic ever since the work of Jackson (70). The truth is that complex brain functions arise from subsystems that are distributed anatomically but connected together, and that often manifest strong hierarchical organization. A complex function such as affect cannot be assigned to a single neural division. The motor patterns of taste-elicited affective reactions are generated by the brainstem, and can be elicited by a limited range of natural stimuli. But, by illustrative comparison, all the movements of human speech are similarly controlled directly by the brainstem, and anencephalic infants vocalize to a range of stimuli. This does not mean that human speech is a brainstem reflex, and it does not mean that taste reactivity patterns are brainstem reflexes, when a forebrain is present and attached. The forebrain's role in human speech is not revealed by the occurrence of any particular sound; all sounds can be generated by brainstem connections to the vocal apparatus. Instead high-level control is revealed by the pattern of vocalization imposed by descending forebrain inputs. Similarly for affective expressions of taste reactivity, descending forebrain signals are crucial to the modulation of many patterns of response. For example, the forebrain is required for the reversal of affective reaction from hedonic to aversive to a sweet taste that is produced by an associative taste aversion. The forebrain of a normal rat hierarchically overrules, on the basis of associative pairing with illness, the positive evaluation programmed into the brainstem. Decerebrate rats are incapable of this hierarchical change in the pattern of reaction, regardless of their associative experience (62). Similarly, brainstem evaluations can be unconditionally biased toward positive or negative reaction patterns by forebrain manipulations ranging from opioid microinjections in the nucleus accumbens or hypothalamus (95) to destruction of zones or small areas of the telencephalon (38,51,64,134). All such observations indicate that the control of affective reaction patterns, in humans and animals that possess forebrains, are under the constant hierarchical control of descending forebrain influences. Affective reactions are generated by a distributed neural system. They cannot be considered to be "mere brainstem reflexes" when emitted by an individual that also possesses a forebrain.

At the same time, the studies of anencephalics and decerebrates do reveal an important brainstem contribution to affective evaluations that needs to be recognized—within the context of a hierarchical systems view of brain organization. If the neural system is changed by decerebration or by other massive neural intervention, then the function carried out by the system will be altered too. The process possessed by the decerebrate is not normal palatability (nor for that matter would be the experience of palatability possessed by an isolated forebrain, if it were possible to examine it), but still it is an integral element, a core component, of the system as a whole.

Are there plausible alternative interpretations for taste reactivity patterns other than as affective? Consider how else they might be interpreted. Several alternative interpretations can be evaluated: first, that positive or negative reactions are merely fixed reflexes to taste; second, that affective reactions are necessary correlates of swallowing and ingestion (i.e., a redundant measure of the decision to ingest); and third, that affective reactions indeed reflect a complex evaluation, but one that is nonetheless unconnected to "real" affect.

But the fixed reflex alternative is weakened by demonstrations that reaction patterns to a given stimulus can be reversed by physiological and psychological manipulations (e.g., 7,9,23,41,62,96). The correlate of ingestion alternative is weakened by demonstrations that taste reactivity patterns can be dissociated both from voluntary ingestion of ordinary foods and from "intraoral intake" of infused solutions by brain manipulations discussed below [e.g., (15,16,122); see (12) for more discussion]. The remaining alternative that taste reactivity patterns reflect a sophisticated evaluation that integrates taste, physiological state and associative learning factors to produce a positive or negative reaction, but one which is entirely separate from the process that mediates palatability, is possible but implausible. According to this alternative, the outcomes of two parallel evaluations are often the same, but this similarity is coincidental, and not due to overlap between the two. Although this alternative is logically admissible, it faces two difficulties. First, it is difficult to say what the purpose of such a separate non-palatability evaluation might be. Yet presumably it must serve some purpose related to evolutionary pressures or it would not have been selected as an adaptation that remains today. Second, it is improbable that a single brain would duplicate the presumably massive neural circuitry needed to integrate gustatory, physiological and associative factors together in two separate systems (one for taste reactivity and the other for palatability), unless there were a truly compelling need. Duplication of such evaluations would be too expensive, in terms of the neural processing needed to accommodate it. There is no evident pressure that would account for duplication, and there is no evidence from studies of brain mechanisms of palatability or taste reactivity to support it. This alternative can therefore be regarded as less plausible than the affective hypothesis that these reaction patterns reflect core evaluations of palatability. I will adopt this interpretation as a working hypothesis, and proceed to examine the implications that arise from it.

Manipulations that Alter Food Liking and Wanting Together

For most common manipulations of food reward, liking and wanting components change together (e.g.,

Fig. 3). All of the manipulations described above alter human palatability in conjunction with desire to eat: caloric hunger and satiety; the specific salt appetite induced by sodium deficiency; sensory-specific satiety; learned taste aversions and preferences; etc. Several neural manipulations similarly change liking and wanting components of food reward together, and will be discussed briefly. These include lesions of the ventral pallidum/substantia innominata, and administration of agonists for opioid and benzodiazepine/GABA neurotransmitter systems.

Aphagia and Aversion After Ventral Pallidum/Substantia Innominata Lesions

Aphagia is a famous consequence of damage to or near the lateral hypothalamus (LH) (140). Even excitotoxin lesions that kill LH neurons, which spare fibers of passage, produce aphagia that may last for weeks. But aversion is not a necessary consequence of hypothalamic lesions that produce aphagia. Schallert and Whishaw (114) noted that only anterior electrolytic lesions of the hypothalamus produce aversive affective reactions to the presentation of food. Posterior LH lesions produced aphagia, but animals with those lesions seemed to ignore, rather than reject, the food. Electrolytic lesions of the LH traditionally have been large, and damage has extended outside of the LH itself. In a dissertation completed in my laboratory, Howard Casey Cromwell discovered that the crucial site for lesion-induced aversion lies dorsal and anterior to the lateral hypothalamus, outside the hypothalamus itself (38). Cromwell applied the taste reactivity method to aphagia and aversion produced by small excitotoxin lesions, and combined this with a new stereological procedure adapted for the purpose of mapping neuronal death—a modification of the fractionator method of Gundersen and colleagues (65). The modified fractionator procedure allows precise quantification of cell loss and identification of the boundaries of an excitotoxin lesion. The results of this mapping study showed that aversion was produced only by neuron death within a 1 x 1 x 0.5 mm site in the ventral pallidum (substantia innominata) (Fig. 4). Damage exceeding 70% neuron loss in this bilateral site produced both aphagia and aversion. By contrast, lesions outside the site produced only aphagia without aversion. Damage restricted to the lateral hypothalamus itself never produced aversion, even if LH damage exceeded 70% neuron loss.

The circuitry necessary for manifestation of normal hedonic reactions thus appears to be contained near the hypothalamus but outside it. Earlier studies that reported aversive reactions to food after large electrolytic LH lesions may actually have intruded into this crucial ventral pallidal site, which lies at the immediate anterodorsolateral border of the lateral hypothalamus itself. It is somewhat surprising that damage only to this site should cause alterations in affective reaction to food reward. After all, electrophysiological studies have identified neurons apparently responding to taste palatability within the lateral hypothalamus itself (e.g., 25,109,120). From the neuroanatomical point of view, gustatory projections to the crucial site are not at all outstanding compared to adjacent forebrain sites (87) (although no anatomical study has yet been directed explicitly toward this site). Why should there appear to be equally dense gustatory representation in nearby areas? Perhaps LH neurons monitor palatability, but are not necessary for generating normal hedonic evaluations. Or perhaps LH neurons participate in translating core evaluations into other functions (e.g., instrumental behavior, subjective experience, etc.).

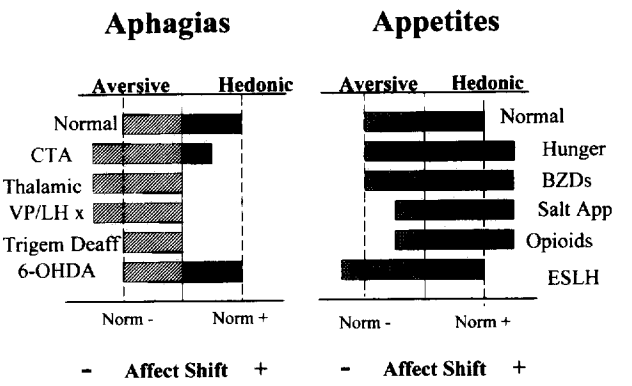

FIG. 3. Summary of affective routes for various appetites and aphagias. Changes in taste pleasure and aversion, revealed by analyses of affective reactions, produced by various manipulations that induce either appetite (right) or aphagia (left). Appetite: although all appetites appear similar by measures of wanting, they are mediated by very different changes in palatability. Compared to normal taste affect, both caloric hunger and benzodiazepine-induced feeding involve enhanced hedonic reactions but do not diminish aversion. Both sodium appetite and opioid-induced feeding enhance hedonic reactions while simultaneously diminishing aversion. By contrast, feeding elicited by electrical stimulation of the lateral hypothalamus occurs without a hedonic enhancement (or even in spite of enhanced aversion). Aphagia: suppression of intake induced by taste aversion conditioning, "thalamic" transection (removal of telencephalon), and ventral pallidal damage produced by lateral hypothalamic lesions, are all accompanied by enhanced aversion and suppressed hedonic reactions. Suppression of appetite by trigeminal deafferentation, conversely, involves only hedonic suppression without a change in aversion. Aphagia induced by 6-OHDA destruction of mesotelencephalic dopamine systems occurs in the absence of any change in taste liking. Based on data from (5,7–9,14–16,42,64).

Even the neurons of the "crucial site" in the ventral pallidum/innominata are not essential in one sense to normal core evaluations of liking. Decerebrate rats show positive reactions to sucrose, although they lack the "crucial site," but decerebrates also lack the rest of the forebrain (e.g., 64). However, the loss of this relatively anterior site alone, in conjunction with the preservation of an as yet unidentified forebrain substrate, appears to lead to the potentiation of aversion. This may also account for the exaggerated aversion of detelencephalic ("thalamic") rats observed by Grill and Norgren (64), which lack all forebrain structures above the diencephalon. If so, then the function of the ventral pallidal "crucial aversion site" (38) might actually be to amplify hedonic evaluations, rather than to mediate aversion. The enhanced aversion produced by its removal, when other forebrain structures remain behind, could then be interpreted as a disinhibition effect (60).

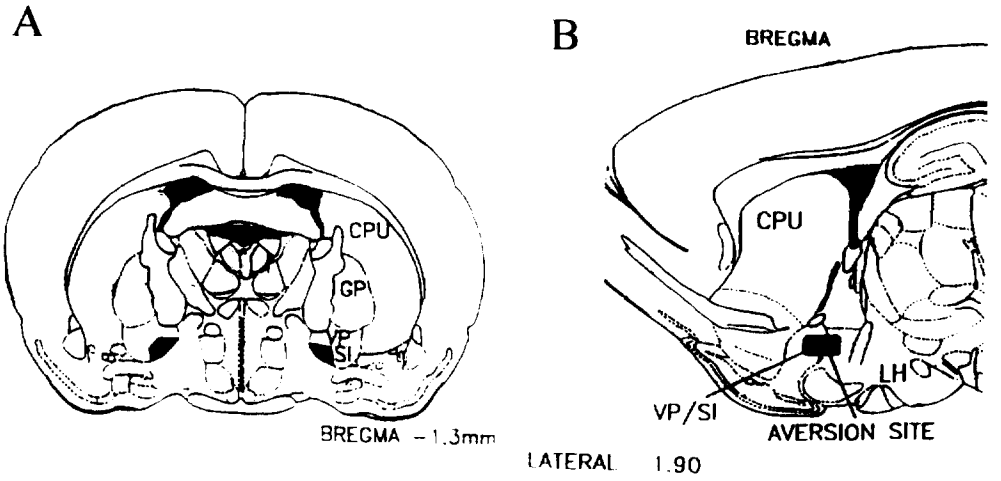

FIG. 4. Crucial site for lesion-induced aversion. The small site within the ventral pallidum in which neuron death (70% or more) produces enhanced aversion to food. Site boundaries were mapped using the modified fractionator procedure in a taste reactivity study. Damage outside of the site produces only aphagia without aversion. [Modified from Cromwell and Berridge (38).]

Opioid Enhancement of Liking and Appetite

Morphine and other opioid agonists stimulate feeding under some conditions when injected systemically, or when microinjected centrally into brain sites such as the nucleus accumbens, paraventricular hypothalamus, amygdala, or tegmentum (2,36,56,128, 158). Morphine also alters affective patterns of taste reactivity components. Systemic morphine suppresses aversive reactions to quinine and potentiates hedonic reactions to sucrose (42,93). In studies in my laboratory aimed at identifying the brain substrate involved in opioid hedonic enhancement, Susana Peciña has found that intracranial microinjections of morphine into the nucleus accumbens or paraventricular nucleus of the hypothalamus enhance hedonic taste reactivity patterns to sucrose [(95) and unpublished observations]. It cannot yet be stated with certainty whether hedonic enhancement results from opioid activation within those sites themselves or through diffusion elsewhere. Similarly, it is not yet clear whether opioid hedonic enhancement can be elicited from "all" the brain structures in which opioid agonists evoke feeding, or whether some opioid systems evoke feeding by a separate psychological process. However, from the evidence available to date, it appears that at least for certain opioid circuits, most likely contained within the forebrain, opioid agonist drugs do indeed induce feeding at least in part by enhancing the liking component of food reward. Similar conclusions have been suggested by others on the grounds that opioid antagonists may possibly suppress human ratings of food pleasantness [(43,47); but see (66)].

Benzodiazepine/GABA Enhancement of Liking and Appetite

Benzodiazepine agonists, which potentiate $GABA_A$ neurotransmission, similarly induce feeding in many situations [e.g., (34,35,37,155)]. There are substantial grounds for believing that such feeding is due specifically to activation of a process relevant to normal appetite, rather than to other famous benzodiazepine effects such as anxiety reduction or sedation (12,34–37). Benzodiazepine agonists accordingly enhance hedonic affective reactions to sweet and other tastes in a receptor-specific fashion (14,91,143,144). Thus, activation of benzodiazepine-related circuits, like activation of opioid circuits, appears to stimulate feeding at least in part by enhancing a liking component of food reward. In contrast to opioid action, however, studies of the neural substrate of benzodiazepine hedonic enhancement indicate that the benzodiazepine effect is due primarily to circuits in the brainstem rather than the forebrain. In normal rats, microinfusions of diazepam are more effective at enhancing hedonic reactions when delivered to the hindbrain 4th ventricle than when delivered to forebrain lateral ventricles (12,94). Further, benzodiazepines potentiate positive reactions even in mesencephalic decerebrate rats (6), supporting the conclusion that the relevant taste circuits modulate the palatability component of food reward at a brainstem stage of the neural hierarchy.

Neural Dissociations of Wanting and Liking in Food Reward

How do wanting and liking components of reward relate to each other? According to most contemporary models of incentive motivation, wanting and liking are essentially two aspects of the same process—incentive value (Fig. 5A) (17,141). By these views, rewards are liked and wanted to the same degree. A change in one necessarily implies a change in the other. But taste reactivity studies indicate that under some conditions "wanting" may change independently of "liking" or vice versa (Figs 4 and 5B). The most dramatic category of manipulations that appear to change wanting rather than liking are those that act on the mesotelencephalic

dopamine system: 6-hydroxydopamine lesions; electrical stimulation of the hypothalamus; and administration of dopaminergic agonists and antagonists.*

Mesotelencephalic Dopamine Systems and Food Reward

The importance of mesotelencephalic dopamine function to reward has been demonstrated by hundreds of studies, and perhaps captured most vividly in Wise's famous anhedonia hypothesis. In an important series of papers, Wise elegantly mustered several lines of evidence to argue that moderate suppression of dopaminergic function reduced the hedonic value of brain stimulation, psychoactive drugs, and preferred foods quite separately from motor, coordination, or general arousal effects (151,152,157). For example, dopaminergic antagonists suppress preference and consumption of sweet rewards in a manner strikingly similar to the manner produced by dilution of the reward itself (55,115). For a recent and compelling update of the evidence that dopamine systems mediate food reward, see Smith (126).

The anhedonia hypothesis implies a reduction in liking after suppression of dopamine function. It is important to realize, however, that virtually all the evidence which supports the hypothesis has come from experiments that demonstrate a reduction in wanting measures of reward. All such measures require the animal to "reach out" in some way and to actively engage its world in order to obtain its next bit of reward. Even the act of voluntary intake, which might be viewed as consummatory rather than appetitive, involves an appetitive aspect so long as it requires biting or licking directed toward an external target reward. In studies of the effect of dopamine antagonists on consumption, for example, the drugs appear to specifically target this appetitive aspect of consummatory behavior (126).

The most compelling evidence that mesotelencephalic dopamine systems do not mediate a liking component of food reward, despite their importance to wanting measures of reward, comes from taste reactivity studies which show that affective patterns of reactions are unchanged (or even changed in the opposite direction from that predicted by the hedonia hypothesis) by manipulations that dramatically appear to alter appetite, such as 6-OHDA lesion-induced aphagia or ESLH-induced feeding.

Aphagia After 6-OHDA Lesions

Extensive destruction of mesotelencephalic dopamine projections produces profound aphagia that can persist for at least several weeks. These lesions reduce general sensorimotor arousal in the sense that animals ignore many stimuli that would ordinarily elicit examination and goal-directed behavior (136,137). However, sensorimotor capacity to respond behaviorally to a number of stimuli remains unimpaired after 6-OHDA lesions; the animals are not unable to move in any straightforward sense (e.g., 103,125). While the nature of the sensorimotor deficit needs to be better understood, it is clear that dopaminergic neural systems also play a role that is specific to motivation (e.g., 126). Although aphagic dopamine-depleted rats remain capable of performing the movements needed for eating, they seem not to want food or any other incentive object. At least, they ignore these incentives when they are readily available, even though they can manifestly perform the movements they would need to obtain them. A question is—do dopamine-depleted aphagic rats fail to like food as the anhedonia hypothesis would suggest? If so, they would be similar to rats with lesions of the trigeminal sensory projection system, which show reduced hedonic reactions to food, or of the ventral pallidum/substantia innominata (8), which show enhanced aversive reactions (38). Or is their deficit more specifically one of wanting alone?

To answer this question, Professor Terry Robinson and I have examined the impact of dopamine depletion on appetite and affective reactions to taste. In an initial study, the cell bodies of dopaminergic neurons in the midbrain substantia nigra were targeted for destruction by microinjections of the neurotoxin, 6-hydroxydopamine (16). Eleven rats were rendered aphagic for periods ranging from 1 week to 1 month. The dopamine content of the neostriatum was later determined to be depleted in these rats on average by 85%. While the rats were still aphagic, their hedonic and aversive reaction to sweet and bitter solutions was examined using taste reactivity measures. Hedonic reactions to sucrose were not suppressed relative to control levels, even while the rats were aphagic. Conversely, aversive reactions were not enhanced. We concluded that taste palatability was unaltered by the dopamine lesions—the liking component of food reward was unchanged, regardless of how wanting had changed.

But our original study had several limitations that constrained the strength of its conclusions. The 85% level of striatal depletion, although sufficient to produce a period of aphagia, still left up to 15% of normal dopamine levels remaining, perhaps enough to sustain hedonic function. Further, we had measured depletion only in the neostriatum. The level of depletion in the nucleus accumbens, possibly more crucial to motivational aspects of dopaminergic systems, was unknown and was likely to be less severe. In order to address these shortcomings, we repeated the study with a second group of eight aphagic rats that received bilateral 6-OHDA injections into the ascending dopaminergic bundle, at a point in the lateral hypothalamus where fibers join together from both midbrain A9 and A10 sites, traveling to both neostriatum and nucleus accumbens. Dopamine depletion was later assessed in both the neostriatum and the nucleus accumbens, and found to be depleted by 95–99% in both. As in the first study, the hedonic reactions of aphagic dopamine-

*In discussing the role of dopamine systems in "wanting" vs. "liking," I take it for granted that these systems also have many other functions in movement control, etc. My aim here is specifically to identify the "motivational" role of these systems, above and beyond their role in basic sensorimotor function.

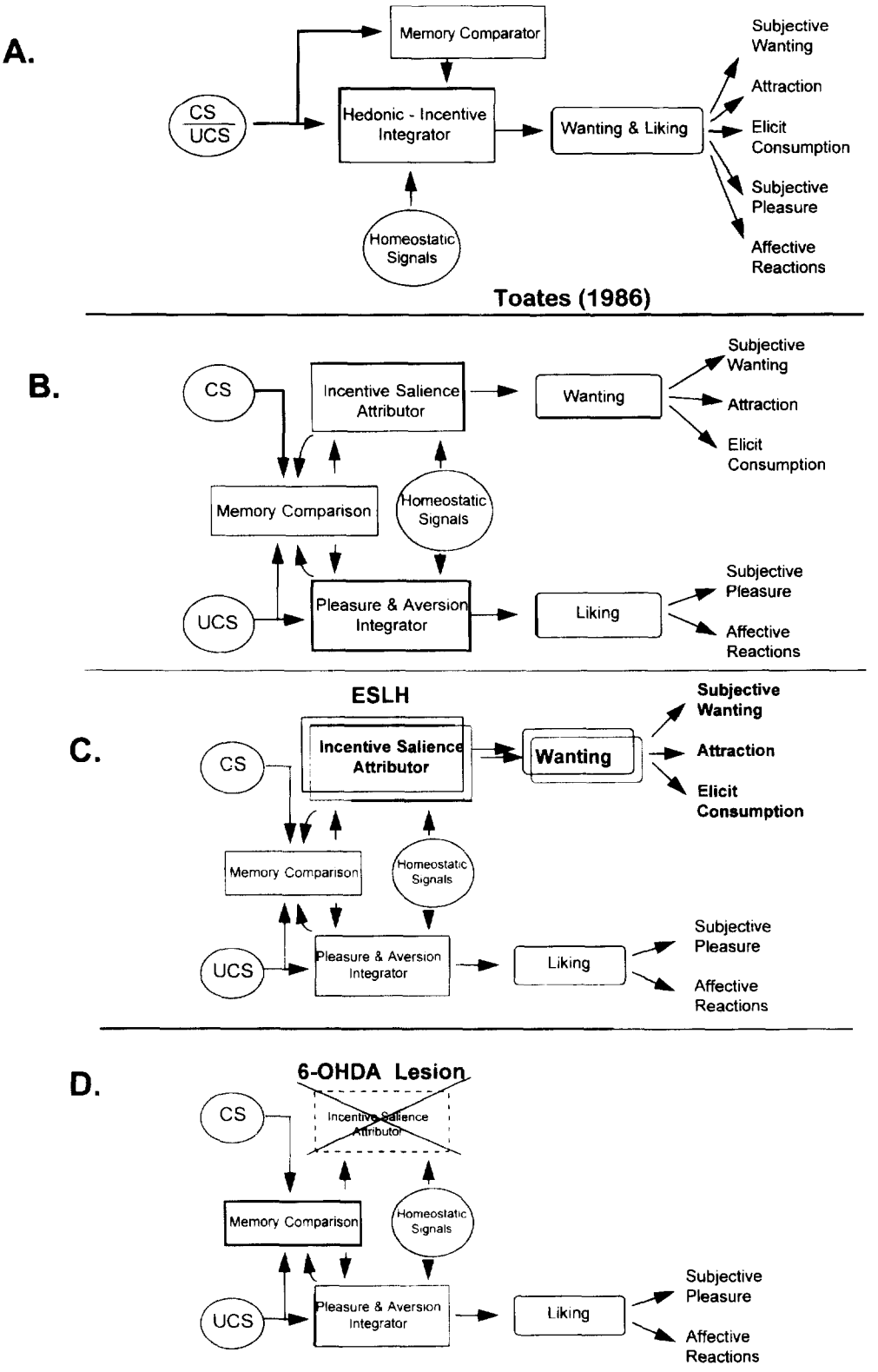

FIG. 5. Models of incentive motivation: (A) contemporary Bindra/Toates model in which wanting and liking are identical [modified from Toates (141)]. (B) Incentive salience model in which liking and wanting are processed separately [modified from (106)]. Neural substrates of the pleasure integrator include all those whose manipulation produces changes in palatability shown in Fig. 3, responsible for liking aspects of food reward. Neural substrates of the incentive salience integrator include mesotelencephalic dopamine projections, responsible for wanting aspects of food reward. (C) Hypothesized food reward during selective activation of wanting without liking by electrical stimulation of the lateral hypothalamus. Food becomes an attractive incentive and elicits consumption, but liking is not enhanced [see (106) for a similar account of addictive drug craving induced by sensitized hyperactivity of incentive salience systems]. (D) Hypothesized food reward after selective loss of incentive salience produced by high doses of neuroleptics or by 6-OHDA lesions of mesotelencephalic dopamine systems. All wanting aspects are eliminated, but liking remains intact. Low neuroleptic doses that produce extinction mimicry, without initially suppressing wanting, remove only the feedback depicted from incentive salience to associative learning involved in reboosting familiar incentives.

depleted rats to sweet tastes were no lower than control levels (Berridge and Robinson, unpublished observations). Aversive reactions were also once again unchanged.

A failure to change affective reactions after aphagia-inducing dopamine lesions is striking, and suggests that mesotelencephalic dopamine systems are not a neural substrate for taste liking. But an alternative interpretation is still possible. Perhaps 6-OHDA lesions render affective reactions invalid as measures of affect by decoupling behavioral reactions from forebrain affective systems. Could a 6-OHDA lesion possibly remove descending influences from the forebrain on brainstem reactivity circuits, thus creating in a sense what would amount to a functional decerebrate?* If dopamine lesions decoupled forebrain taste processing from behavioral taste reactivity, then the forebrain might indeed be anhedonic after a 6-OHDA lesion, but unable to express this altered taste affect through affective reactivity patterns.

If forebrain systems of taste affect were prevented from exerting descending control on behavioral taste reactivity patterns, then manipulations which ordinarily change palatability via forebrain control should become ineffective after 6-OHDA lesions. Associative taste aversion conditioning, which switches the pattern of affective reactions from hedonic to aversive for an illness-paired taste, is such a manipulation. Taste aversion conditioning is a form of associative learning that appears to require the forebrain for behavioral expression. For example, taste–illness pairings cannot switch the behavioral reactions of decerebrate rats, in sharp contrast to their effect in normal rats (62). In order to ascertain whether the hedonic reactions remain under descending forebrain control after mesotelencephalic dopamine depletion, Terry Robinson and I investigated whether dopamine depletion rendered rats incapable of learning and expressing a conditioned aversion by replacing hedonic reactions with aversive ones. We tested whether the +95% dopamine depleted rats described above were capable of altering their affective reactions to a sweet taste (a mixture that was 0.2% saccharin and 32% polycose) after three associative pairings of the taste with LiCl-induced illness. All 6-OHDA rats showed fully hedonic reaction patterns to this sweet taste on their first encounter, just as normal rats did. Both dopamine-depleted and control rats also showed marked and equivalent aversive reaction patterns to the same taste after it had been associatively paired with illness (Fig. 6; Berridge and Robinson, previously unpublished observations). The aversive shift in affective reactions after conditioning implies that the forebrain retains its descending control over brainstem generation of taste reactivity patterns after 6-OHDA lesions. It also implies that affective reaction patterns remain faithful indicators of forebrain-based affective taste evaluations. The difference between a normal rat

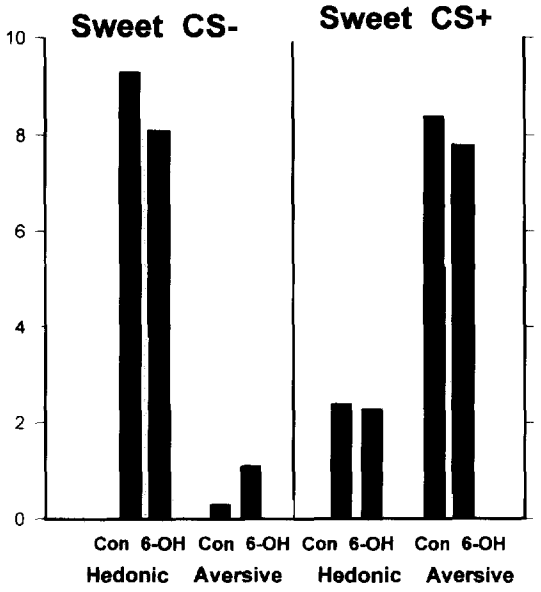

FIG. 6. Normal taste palatability and normal conditioned aversion after 95–99% depletion of dopamine from nucleus accumbens and neostriatum. Left panel shows hedonic/aversive reactions by control rats and 6-OHDA lesion rats to a novel sweet taste—both groups responded with strongly hedonic reactions. Right panel shows the reactions of the same rats to a sweet taste that was associatively paired with LiCl-induced illness—both groups responded with pronounced aversion. Thus rats that lack mesotelencephalic dopamine projections retain both normal taste liking and the capacity to modify liking via forebrain systems of associative learning and affect. Data are from previously unpublished observations by Berridge and Robinson.

that seeks a sweet food and a 6-OHDA rat that does not appears to be solely a difference in food wanting, not liking (Fig. 5D). Both rats like the taste, but only one wants it. In the same vein, the difference between an aphagic 6-OHDA rat that fails to consume a safe sweet reward and an equally aphagic 6-OHDA rat that rejects an illness-paired sweet is more specifically a difference in liking, not of wanting. Neither of the 6-OHDA rats wants the sweet reward, but only one of them does not like it. Apparently, the dopamine-depleted rat is quite capable of suppressing hedonic affective reactions to a sweet taste, and is not a functional decerebrate. The truth is just that dopamine depletion by itself is not sufficient to shift hedonic reactions, in contrast to what would be expected according to the anhedonia hypothesis.

Appetite Elicited by ESLH

Electrical stimulation of the lateral hypothalamus is well known to be a potent stimulus for feeding in animals. ESLH elicited feeding, like ESLH self-stimulation reward, depends crucially upon the integrity of mesotelencephalic dopamine systems (82,102). In order to find out whether ESLH potentiates feeding by enhancing hedonic properties of food reward, Professor Elliot Valenstein and I have examined affective patterns of taste reactivity emitted by rats that were avid ESLH-induced feeders (15).

*We owe the "functional decebrate" hypothesis to Dr Jane Stewart, who suggested it to us over dinner at the 1991 Society for Neuroscience meeting.

The question of whether ESLH enhances food liking is of interest only if the electrode enhances food wanting. For this reason, rats were prescreened by a rigorous criterion for ESLH stimulus-bound feeding. The affective taste reactivity patterns of rats that demonstrated robust stimulation-bound feeding were then compared when ESLH was administered vs. when it was not. In spite of the hedonia prediction that dopamine-dependent ESLH would enhance food palatability, ESLH consistently failed to potentiate hedonic reactions to any sweet or bitter taste. On the contrary, for sweet and sour tastes, ESLH actually increased aversive reactions. In other words, stimulation-bound feeders did not appear to eat because ESLH made food taste better. Rather they ate in spite of its failure to enhance taste liking, and even perhaps in spite of its ability to make taste more disliked (Fig. 5C).

Suppression of Food Reward by Dopamine Antagonists.

At high doses, drugs that suppress dopamine systems should produce effects similar to dopamine depleting lesions (and perhaps additional ones due to the abruptness of acute blockade). At low doses, behavioral effects are much more subtle. It is chiefly the study of low doses of antagonists, which do not produce complete aphagia or akinesia, that has produced the most interesting data for hypotheses of the role of dopamine in food reward. Chief among these effects are the ability of dopamine antagonists, including specific D1 and D2 antagonists, to produce changes in intake patterns that mimic natural dilution of reward value (55,115,151,152,154,156). Such observations, consistent with changes of either wanting or liking, have provided support for the hypothesis that dopamine mediates food reward (126), and typically have been interpreted in terms of the anhedonia hypothesis—that dopamine antagonists suppress food liking.

Actually, dopamine antagonists seem to be relatively ineffective at changing taste reactivity measures of food liking. In a taste reactivity comparison of dopamine agents and other drugs, Treit and Berridge (143) failed to find any suppression of hedonic reactions, or any increase in aversive reactions, to 1 min infusions of sweet or bitter tastes after systemic administration of haloperidol. Conversely, the dopamine agonists, apomorphine and amphetamine, did not alter affective patterns of responding. A similar failure to find a decrement in hedonic reactions to a 5 min sucrose infusion after pimozide administration was reported by Parker and Lopez (92).*

However, Professor Linda Parker and her colleagues have found evidence that dopamine agents may exert effects on taste reactivity patterns under certain limited conditions, especially involving long exposures to a taste stimulus. For example, Parker and Lopez (92) found an increase in aversive reactions to a 5 min oral infusion of highly concentrated quinine solution, after pimozide administration (0.5 mg/kg), though aversion was not increased to a low or moderate concentration of quinine, nor to a saccharin solution made aversive by prior associative pairing with LiCl. In this study, hedonic reactions emitted to sucrose were not altered by pimozide. Leeb, Parker, and Eikelboom (78) also reported that pimozide (0.5 mg/kg) had no effect on hedonic reactions to a 10 min sucrose infusion in naive rats, but that if the infusion was repeated on subsequent days a mixed effect on hedonic tongue protrusions was seen. During the first minute of the 10 min infusion, hedonic reactions were either unchanged (Day 2) or actually increased (Day 3) by pimozide, whereas during the second half of the test pimozide suppressed hedonic reactions; the effect of pimozide on aversive reactions to quinine was not examined in that study (78). Leeb, Parker and Eikelboom suggest that pimozide suppressed the hedonic palatability of sucrose with repetition and over a prolonged exposure, but not immediately. Taken together, the results of Parker and colleagues indicate that pimozide may have complex effects on affective reaction patterns at least under certain conditions. Regarding the anhedonia hypothesis, they suggest that palatability suppression may require repeated sustained interaction with the reward.

Does a delayed suppression of palatability account for the discrepancy between our taste reactivity results and "anhedonia" studies concerning whether dopamine mediates food liking? This is an interesting possibility that deserves further investigation. However, there are several lines of evidence that argue against it as a sufficient explanation of the role of dopamine in food reward. The first line of evidence comes from early suppressions of wanting aspects of behavioral reward. Pimozide and other neuroleptics have been reported to reduce licking and instrumental responding for sucrose within the first minute of a trial (57,58). This is similar to the early suppression of response rate seen when sucrose concentration is decreased (e.g., 39). Pimozide is also known to reduce responding to conditioned incentive stimuli, prior to encounter with the hedonic reward (e.g., 59). If a common mechanism is responsible for the reduced motivational value of both primary and secondary rewards in such situations, then a delayed hedonic suppression cannot be the cause since it would not yet have been experienced when the effect was observed. The wanting hypothesis of dopamine function, however, can account for both kinds of suppression in the same way by interference with the attribution of incentive salience to both primary and secondary reward stimuli (Fig. 5D).

*Another result with similiar implications maybe the observation by Smith and colleagues that although dopamine antagonists suppress the free voluntary intake of sucrose, actively lapped up from a sucrose-soaked substrate by young rat pups (1–3 weeks after birth), they are much less effective at suppressing intake in the same pups if the sucrose is infused intraorally (126,145,146). The difference supports the hypothesis that dopamine mediates a process specifically required for the individual to reach out to an external incentive, such as incentive salience, rather than a process involved in assessing or ingesting a palatable stimulus already in the mouth.

A second line of evidence against a delayed hedonic suppression effect as explanation for the effects of pimozide on instrumental behavior comes from studies of reinforcement schedules. Mimicry of extinction by certain doses of antagonists has provided evidence for the anhedonia hypothesis. However, the anhedonia hypothesis explains the extinction-like suppression of instrumental behavior as due to an immediate suppression of hedonic "liking." The extinction-like reduction of instrumental performance is viewed by the anhedonia hypothesis as due to gradual learning by the animal that the response is no longer rewarded. If pimozide produced a delayed hedonic suppression, then we should not predict a simple extinction of instrumental behavior. Since a delayed hedonic suppression would actually result in the animal experiencing sequential "on–off" pattern of early hedonic reward followed by late anhedonia during a meal, an animal would receive a mixture of intermittent rewarded and non-rewarded trials. We might then expect neuroleptics to produce partial reinforcement (rather than extinction) effects: for example, sustained responding and resistance to later extinction. Although neuroleptics are capable of producing partial reinforcement mimicry, this happens only if they are given in a schedule that explicitly duplicates intermittent reinforcement. For example, if haloperidol is given in a pattern that explicitly mimics a partial reinforcement schedule, on only 10 of 30 rewarded discrete, daily instrumental trials, thus mixing normal rewards with drug conditions, a partial reinforcement resistance to later extinction is observed (46). That pattern of results should always be observed if neuroleptics produced alternation between hedonic and anhedonic experience, but it is not.

Still, the demonstrations by Parker and colleagues that pimozide can alter subtle aspects of affective reaction patterns, at least in response to prolonged infusions, must be explained. Since the argument for a separation of wanting and liking depends heavily on the conclusion that dopamine manipulations fail to alter liking, it is crucial to understand how dopamine drugs might change taste reactivity patterns under any circumstances. In several recent unpublished studies of pimozide in my laboratory, carried out partly in collaboration with Professor Linda Parker's laboratory, we have confirmed the findings of Parker and colleagues that pimozide produces a change in taste reactivity that grows during a prolonged 10 min infusion. But our results indicate that the nature of the change is due to a sensorimotor suppression or fatigue effect, which impairs the capacity to emit high rates of any physically demanding response over prolonged periods, and not to an affective shift in palatability.

In a study of the effect of pimozide (0.5 mg/kg, IP) on hedonic reactions, eight rats received pimozide or control vehicle injections, 4 h prior to a 10 min oral infusion of 17% sucrose (Peciña and Berridge, unpublished observations). The next day, the procedure was repeated but in the opposite drug condition for each rat. This was continued daily until each rat had received three 10 min infusions under pimozide and three 10 min infusions under the control condition (a total of six trials). In a separate series of trials, the rats received oral quinine infusions (0.1%) under the same conditions. We replicated the delayed suppression of hedonic reactions to sucrose reported by Leeb, Parker and Eikelboom (78). However, we also observed a delayed suppression of aversive reactions to concentrated quinine. In other words, in these experiments, pimozide produced a general suppression of all taste reactivity components in a fashion that appeared to reflect a sensorimotor inability to sustain high rates of responses over a prolonged period. This seems similar to the role for dopamine in maintaining high levels of sustained responses that has been suggested by Salamone and colleagues (e.g., 112). Such a response maintenance role could exist in addition to dopamine's role in incentive salience; both are distinct from sensory pleasure. In our hands, dopamine blockade does not produce an anhedonia-compatible change in hedonic or aversive reactions. For further discussion of how taste reactivity changes may be interpreted in terms of sensorimotor vs. affective causes see (12). Although more work remains to be done on pimozide's effects, especially on the role of procedural variables on the outcome of taste reactivity studies, the majority of evidence available to date indicates that dopamine antagonists do not produce a shift in taste liking, in contrast to what would be expected by the hedonia hypothesis of dopamine function. Instead, these drugs appear to produce a mixture of wanting—specific motivational effects (seen in instrumental behavior) and subtle sensorimotor effects (seen in taste reactivity).*

Amygdala Mediation of Wanting in Salt Appetite

Neural manipulations other than dopaminergic may also dissociate wanting and liking under some conditions. One example of this may be provided by a study conducted by Galaverna et al. of the effects of lesions of the central nucleus of the amygdala on the expression of salt appetite (54). Galaverna et al. compared wanting and liking consequences of amygdala lesions for salt appetite triggered by sodium depletion. Unlike 6-OHDA lesions of mesotelencephalic dopamine

* The effects of dopamine agonists on taste reactivity may be subject to a similar sensorimotor interpretation. For example, Parker and Leeb found *d*-amphetamine (1 mg/kg) suppressed aversive reactions to concentrated quinine solutions, and also suppressed hedonic reactions to sucrose in an unfamiliar (but not familiar) environment compared to a separate group of rats that received vehicle injections (90). They concluded that amphetamine attenuated quinine aversiveness but had attention-related effects on sucrose reactions. Using a similar procedure, but again testing the same rats with both drug and vehicle, we have replicated the finding of suppressed aversive reactions to concentrated quinine, but found no effect of amphetamine on aversion to weak to moderate quinine solutions. However, we also found that amphetamine produced a delayed suppression of hedonic reactions to concentrated sucrose, even though the rats were familiar with the environment (Peciña and Berridge, personal observations). Thus doses of amphetamine that alter taste reactivity appear like pimozide to impose sensorimotor ceiling effects. These preclude high rates of reactions elicited by long infusions of concentrated tastes. Pronounced disruption of dopaminergic function, either up or down, by drugs thus impairs the capacity to generate intense sustained sensorimotor coordination, but as yet appears to have no clear or immediate effect on palatability.

projections, electrolytic lesions of the central amygdala do not produce aphagia. Amygdala damage instead is associated with more subtle changes in feeding: loss of neophobia; deficits in associative preference or aversions; etc. (76). In the case of salt appetite, the amygdala lesions completely blocked the ordinary specific increase in voluntary intake of hypertonic (3%) NaCl that typically follows drug-induced sodium depletion. Even after sodium depletion, the rats with amygdala lesions treated the concentrated salt solution as though they were physiologically normal, in terms of their voluntary intake—they ignored it, apparently not "wanting" it. But when hedonic liking for the concentrated salt solution was examined, in a study of affective taste reactivity patterns, rats with amygdala lesions showed a clear hedonic shift in affective patterns. Ordinarily the hypertonic salt elicited a primarily aversive reaction pattern. After sodium depletion, the same salt elicited hedonic reactions primarily in both intact and amygdala-lesion rats. The alliesthesia shift in taste reactivity, induced by the shift in physiological state, was comparable in magnitude to intact rats, even though the rats that had amygdala lesions failed to act voluntarily upon their shift in salt liking, unlike intact rats. This deficit in voluntary drinking cannot be attributed to a general inability to attribute incentive salience—the amygdala-lesion rats ate and drank normally otherwise. But they failed to adjust the specific incentive salience of the spout and other conditioned stimuli that indicated the presence of salt based upon their physiological state—a specifically targeted modulation of incentive salience based upon an integration of associative cues and internal state. Perhaps the central nucleus of the amygdala contributes to incentive salience primarily by associatively directing its attribution to particular targets, based upon associative information, whereas the dopaminergic projections by contrast participate in the attribution of incentive salience itself. This interpretation is also consistent with the results of many studies of amygdala lesions on learned responses to motivational stimuli other than food (1,77). Finally, I should note that other divisions of the amygdala, beyond the central nucleus, might well play a role in liking as well as in wanting. For example, a taste reactivity study by Simbayi, Boakes and Burton indicated that damage to "basolateral" divisions of the amygdala may block associatively-induced changes in taste palatability (124)

Incentive Salience Attribution: A Closer Analysis of Wanting

The sight of food has no intrinsic motivational value. It is merely an aggregation of visual shapes and colors, like the sight of any object. It is not an incentive until value becomes attached to it by experience. Similarly, the associative or cognitive representation that a food reward is to be found at a particular place, or is to be gained by performing a particular instrumental response, is merely information about contingencies within the environment, and not motivating by itself. The question is—what must be done by the brain to a perception or representation to transform mere information into an attractive, riveting, and desired incentive? What must be done to make it capable of capturing the attention and of instigating approach and strategies of capture?

Contemporary incentive theories provide one answer (17,141). To transform such events into wanted incentives, according to these theories, it is necessary and sufficient to enhance their hedonic/incentive value, via alliesthesia or associative manipulations (Fig. 5A). But if wanting and liking are separable psychological processes with separable neural substrates, as my colleagues and I have argued, then transformation of liking by itself is not sufficient to create wanting. Instead, transformation by a separable system of wanting is also required in addition to achieve full reward (Fig. 5B).

"Wanting" is at best a vague word that denotes a class of psychological processes. To move beyond colloquial words to concepts that more adequately capture the contribution of mesotelencephalic dopamine and related neural systems to behavior, we can now proceed to build more precisely defined concepts. My colleagues and I have suggested that the primary motivational role of such systems is to attribute incentive salience to selected percepts and representations (13,15,16,106). We view the attribution of incentive salience largely as a transformation of a perceptual/representational event, which causes it to become attractive and wanted.* The active attribution of incentive salience by the brain confers upon a representation the ability to capture attention, to directly elicit orientation and approach, to instigate instrumental and cognitive strategies directed towards it as the goal, and potentially to become manifest in subjective awareness as an object of desire. Each of these manifestations has its own appropriate executive systems: sensorimotor systems for orientation and approach, instrumental learning and goal-directed cognitive procedures for instrumental behavior, and cognitive generating systems for translating elemental sensory processes into conscious awareness for subjective desire. But each output shares in common that its input is an incentive representation made salient at least in part by dopaminergic activation. An important corollary of the incentive salience hypothesis is that the generation and attribution of incentive salience is not directly experienced in consciousness (see below). Only the product of the process, the transformed percept, can be subjectively perceived in its new status and consciously experienced as a desired incentive (13,106). As others have suggested concerning mesotelencephalic dopamine function, this process combines motivational and

*The role of mesotelencephalic dopamine systems in aversive motivation, such as fear or stress, is an open issue. There is evidence to implicate dopaminergic activation to frightening events as well as to incentives (113), and some properties of incentive salience attribution may extend beyond positive incentives. At present, our incentive slience hypothesis does not make claims regarding aversive events, because several different roles are possible [see note 9 in (106) for more discussion of aversive events].

sensory processing together (49,153). Incentive salience builds upon prior suggestions merely by specifying the nature of the modulation and its relation to liking and associative learning (Fig. 3B).

Dopamine Systems are Activated by Wanted Incentive Stimuli

Mesotelencephalic dopamine systems are not sensory neural systems in the traditional meaning of that term. They convey no primary sensory modality, and they are unnecessary for the sensation of visual, auditory, etc. stimuli. But the larger striatal/accumbens neural systems in which mesotelencephalic projections are embedded receive extensive sensory projections from most sensory modalities in the neocortex (e.g., 78,84). This massive projection of sensory information from the cortex into cortico-striatal–mesotelencephalic loops offers ample opportunity to influence the activity of ascending dopamine projections, and allows sensory processing to be influenced in turn by dopaminergic activation. The anatomical intertwining of sensory projections with the targets of mesotelencephalic dopamine systems sets the necessary stage for perception/motivation interaction posited by the incentive salience hypothesis.

Both the neural activation patterns of mesotelencephalic dopamine systems and the motivational consequences of dopamine activation appear to be linked to aspects of sensory processing. Dopaminergic activity is increased by presentations of a broad range of natural rewards and by their conditioned stimuli (18,100,101,117,119,123). In an illustrative example, Schultz and his colleagues have reported studies of the pattern of electrophysiological activity of dopamine systems in monkeys receiving food rewards (116–119). Initially, for naive monkeys that had not yet experienced rewards in the testing context, mesotelencephalic dopamine neurons were activated only when the reward was actually received and tasted. But with repeated experience, as monkeys grew able to anticipate the reward through conditioned stimuli provided by the procedure and experimenters' behavior, dopaminergic activity which began to precede the reward—maximal activity was elicited by the conditioned stimuli that predicted the impending reward, and actually declined during the reward itself (116,117,119). Similar patterns of anticipatory activity, triggered by predictive conditioned stimuli for food rewards, have been reported by other laboratories using other techniques. Simansky, Bourbonais and Smith (123) reported DOPAC to dopamine ratios in the hypothalamus to be increased by presentation of conditioned stimuli for food as much as by the actual ingestion of a meal of 1 h duration. In the nucleus accumbens, Blackburn et al. (18) found DOPAC/DA ratios to be more elevated after presentation of a light/tone conditioned stimulus for food, even if food itself was not presented, than by an actual meal that was unexpected by the rat. In recent in vivo voltammetry studies, Phillips and his colleagues have tracked the rise and fall of mesotelencephalic dopaminergic activity associated with the various stages of feeding (e.g., 100,101). They have found dopamine to be increased in both the nucleus accumbens and neostriatum by a conditioned stimulus for food. The elevation in dopamine triggered by the CS+ persisted until and throughout the meal, finally decaying to baseline 10–30 min after the meal (100). In an instrumental setting, Kiyatkin and Gratton recently used chronoamperometry to study dopamine-related activation as rats worked for food pellets. They found that the highest level of activation occurred in an anticipatory fashion as the rat approached and pressed the bar, and that activation actually declined as the rat received and ate the food reward (72). Such anticipatory activation of dopamine systems is clearly consistent with the incentive salience view of dopamine function. The question of whether dopamine-related systems remain activated or decline once the reward is received is an open one, but is especially interesting from the incentive salience hypothesis. To the degree that activation is sustained, either in mesotelencephalic neurons themselves or in later stages of the system, it is conceivable that "late stage" dopaminergic activity, elicited directly by the reward itself, plays a role in the reboosting of incentive salience to the representation of the CS that preceded it.

Wanting Involves Perceptual Modulation

Just as neural activation patterns are linked to sensory stimulation, so also are the motivational consequences of dopaminergic activation intertwined with sensory processing. Perhaps the most powerful single demonstration of this principle for food reward comes from a remarkable study by Beagley and Holley (3). In that study, feeding was elicited from rats by electrical stimulation of the lateral hypothalamus, and the rats were trained that bar-pressing would be reinforced by food only when two signal lights were on. The lights were arranged so that each could be seen by only one eye. In the final test phase of the experiment, only one light was illuminated and only one side of the hypothalamus was stimulated. Of all the possible light–electrode combinations, it was found that rats pressed for food only when the signal light was illuminated contralateral to a stimulating hypothalamic electrode. A given electrode, in other words, was effective in eliciting bar pressing for food only if a visual conditioned stimulus for food was delivered to its side of the brain from the contralateral eye. From an incentive salience perspective, the electrode transformed the perception of the signal light from a mere informative cue into an attractive food incentive. Only when signal and neural activation was conjoined were the conditions met for creating a salient food incentive, and only then did the rats press for food.

Extinction Mimicry and Incentive Salience Reboosting

There is one well-documented aspect of the effects of neuroleptics on instrumental behavior that poses an obstacle to at least the simplest form of the incentive salience hypothesis. This is the ability of dopamine antagonists to produce mimicry of extinction—a

gradual reduction in instrumental responding as the drugged animal is allowed to experience the reward. The phenomenon of delayed wanting decay is beautifully consistent with the anhedonia hypothesis, which posits dopamine antagonists to reduce liking primarily and immediately [despite the fact that "extinction mimicry" does not truly mimic all aspects of real extinction, it still mimics the most important aspects of the phenomenon; e.g., (126)]. By the anhedonia hypothesis, on the first rewards, the dopamine antagonist has directly reduced hedonic liking. But the effect on instrumental behavior itself should be delayed, as it is in real extinction, because the animal would require several "anhedonic" trials in order to learn that the response was no longer hedonically rewarded (151,152). A wanting hypothesis of dopamine function, on the other hand, needs a more complicated explanation to account for why any dose of neuroleptic might suppress instrumental behavior only gradually, rather than immediately. But it is possible to explain extinction mimicry by an incentive salience model, if we add one additional postulate to the model: low doses of neuroleptics interfere with the incremental reboosting of conditioned incentive salience more readily than they disrupt the existing incentive salience of pre-established incentive stimuli. As mentioned above, incentive salience is ordinarily "reboosted" every time a familiar reward produces its expected hedonic consequences—the targeting of salience specifically on the associatively-paired event is strengthened by feedback (the arrow to associative learning from the incentive salience attributor in Fig. 5B). This feedback may be disrupted by very low doses of dopamine antagonists that are insufficient to disrupt the process of assigning incentive salience to well-established, previously learned incentive events (the outflow arrows from memory to the incentive salience attributor, and from the incentive salience attributor to the manifestations of wanting). If this incremental reboosting is prevented, then the first time the incentive was obtained under the drug it would be both wanted and liked! But the failure of the expected associative reboost to follow would lead to a mismatch between the expected consequences and the actual registering of the event. The liking would not lead to the expected strengthening of wanting. From the point of view of associative targeting mechanisms, this would be very like extinction itself, but in this case due to a decoupling between reward and its registration by the incentive salience system rather than to an elimination of the reward itself. This explanation applies only to low levels of neuroleptics that are near threshold for effects on incentive salience attribution. Higher doses should disrupt all aspects of incentive salience function as depicted in Fig. 5D, and effectively suppress wanting immediately rather than in a delayed fashion.

Specific Food Cravings Due to Hyperactive Incentive Salience?

What implication does the incentive salience hypothesis have for the phenomenon of specific craving? A common assumption is that food cravings are due to intense likings for a specific food. For some cravings, such as salt appetite, this appears to be true (4,9). But it may not be true for all cravings. If hyperactivation of the dopamine-related system of wanting were induced selectively, the result would be a focused, intense craving for a specific target. Such craving could exist even in the absence of a special liking for the food. This result is essentially the same as that produced by electrical stimulation of the lateral hypothalamus depicted in Fig. 3 (15). To understand why such a hypothetical craving would be directed toward one food in particular, it is important to note that the incentive salience attributed by an activated dopaminergic system is not simply projected indiscriminately toward every stimulus in sight. Attributions of incentive salience are always guided by systems of associative learning (13,106). Stimuli that are already salient incentives become more salient. New stimuli that are associatively paired with activation of the system become future incentives themselves. If hyperactivation of the incentive salience system were induced, we would expect intense craving to be focused on particular foods. Such cravings would be specifically directed just as is feeding elicited by stimulation of the lateral hypothalamus (147). Terry Robinson and I have offered a similar explanation for the development of addiction, and for the focus of addictive craving on the act of taking drugs (13,106). The chief difference between addiction and food cravings is that psychostimulant drugs produce neural sensitization in dopamine-related systems, which greatly amplifies craving (106). This gives drug craving in addiction a degree of intensity that is unlikely to be matched by most food cravings, although the process may otherwise be quite similar.

Hedonic and Aversive Subcomponents: Further Divisions Within Liking

Human subjective experience of affective palatability corresponds to a continuum that stretches from very good to very bad (e.g., 159,162). Particular tastes fall along this continuum as points. People have no difficulty in categorizing the palatability of foods along a continuum bipolar scale. Even shifts in palatability, such as those caused by physiological alliesthesia or associative experience, are easily portrayed by human subjects using the continuum (26,27,73).

But although the subjective perception of taste pleasure/displeasure is unidimensional, it is another question as to whether the underlying mechanisms of palatability are also unidimensional. Is there a single affective system for taste, which can be driven to any degree in either of two directions (pleasant or unpleasant)? If so, then our unidimensional experience reflects accurately the underlying reality. Or are taste pleasantness and unpleasantness not merely opposite ends of the same spectrum, but actually orthogonal processes, corresponding to distinct neural substrates? If so, then our unidimensional experience simply blurs the complexity of the underlying real processes, by

averaging them together [for a historical precursor of this orthogonal hypothesis, e.g., (111)].

If palatability truly reflects a single continuum, then positive and negative qualities are mutually exclusive, and shifts in the palatability of a taste should change pleasure and displeasure reciprocally. But if subjective palatability actually reflects the averaged output of two orthogonal processes, then pleasure and displeasure are not mutually exclusive, even for a single taste. Some manipulations, at least, that shift the palatability of a taste might alter one process without changing the strength of the other. It is a difficult proposition to investigate in any species. Most tests of animal behavior, like most hedonic questionnaires for humans, are one-dimensional in their measurement outcomes. Preference, intake and instrumental measures, for example, produce a result that necessarily varies along a single continuum because of the nature of the measure.

Affective patterns of taste reactivity are different in this regard because they are not necessarily unidimensional in output, even though most manipulations of palatability may indeed produce reciprocal changes in hedonic and aversive reaction patterns. One early observation that suggested hedonic and aversive reactions may be made to vary orthogonally, at least under limited circumstances, was that certain tastes (which to humans produce salty/metallic or bitter/sweet compound sensations) evoked robust affective reactions from both hedonic and aversive categories, elicited in alternation (10). Although alternation by itself is not compelling evidence for parallel processing of hedonic and aversive palatability, it is consistent with the hypothesis from classical ethology that alternation between two categories of behavior can indicate the presence of two simultaneous and opposite response tendencies (68).

Stronger evidence for an orthogonal process model came from observations that hedonic and aversive reaction patterns could be changed independently, at least within limits. For example, in one study aversive reactions were increased without a decrease in hedonic reactions, and in another case both were increased together, by manipulating the bitter and sweet component intensities of bittersweet tastes (11). Neural and pharmacological manipulations also have produced independent, rather than reciprocal, changes in hedonic reaction or aversive patterns of affective reactions. The aphagia induced by trigeminal deafferentation is accompanied by a reduction in hedonic reactions to palatable tastes but not an increase in aversive reactions to any taste (8) (Fig. 3). Conversely, hedonic enhancement by benzodiazepine agonists was found to occur without reducing aversive reaction patterns (14), and this observation has been replicated by several studies (91,143,144).

The most striking example of independent shifts so far in our laboratory has been produced by ordinary postprandial satiety. In a study of alliesthesia induced by caloric hunger, caloric satiety, and sensory-specific satiety, I found that only hedonic patterns of affective reactions were altered (7). Aversive reaction patterns were never changed, even by a "super-satiety" condition, in which rats were induced over 30 min to ingest a volume of milk or sucrose solution equal to 10% of their body weight. This super-satiety produced only a (large) decrement in hedonic reactions—without inducing any active aversion. The unidimensional "hedonic-only" implication of these data for alliesthesia concurs with the conclusion of Le Magnen [(75); p. 135]: "The unpalatability of a food that develops towards the end of a meal is not a true aversion."*

Unfortunately, it is usually not possible to tell unambiguously for many experiments on taste reactivity whether the results are produced by a one-dimensional vs. two-dimensional mechanism. That is because even a two-dimensional mechanism will produce a one-dimensional change in output if a manipulation acts simultaneously on both mechanisms, to increase pleasure and decrease aversion, or if it indirectly changes one system by directly changing the other. Many manipulations that change palatability appear to act on both affective dimensions, either directly or through reciprocal inhibition between the systems (Fig. 7). For example, Breslin, Davidson and Grill (24) traced such a reciprocal palatability shift during the development of a learned taste aversion. As associative pairing proceeded, hedonic reactions declined and aversive reactions simultaneously grew. As Breslin, Davidson and Grill concluded, this reciprocal change in hedonic/aversive reactivity can legitimately "be projected onto a single unidimensional scale of palatability." Similar reciprocal shifts are produced by many other manipulations [e.g., "thalamic" transection below the telencephalon (64); neuron death in the substantia innominata/ventral pallidum (38); sodium appetite (9,52,54); etc.].

What does it mean if most dramatic changes in palatability are expressed by reciprocal changes in hedonic and aversive patterns of affective reactions? It means that if there are orthogonal underlying mechanisms, then clearly in operation they tend usually to be coupled together in their outputs (Fig. 7). Mutual inhibition between the systems is one possible explanation for why this might be so. The "disinhibition of aversion" phenomenon produced by ventral forebrain lesions, which may disinhibit an aversive system in the remaining forebrain tissue, provides some support for this hypothesis. Only rarely can a manipulation alter just hedonic reaction patterns or aversive reaction patterns. The list of such dimension-specific manipulations is relatively short (caloric hunger, satiety, benzodiazepine administration, certain taste manipulations) and the magnitude of the shift in reaction pattern they produce is relatively small by comparison to those

*By contrast, enhanced "aversion" after caloric allisthesia has been described by Cabanac and Lafrane (29–31). However, this apparent contradiction of my claim that satiety alters only hedonic palatability, not aversion, maybe accounted for by two factors. First, they counted passive dripping of the solution from the mouth as an aversive reaction. But passive dripping is the mere failure to ingest, the default consequence of a lack of action, and so is not equivalent to active aversive reactions such as gapes, headshakes, etc. (7). Also, their caloric loads were infused intragastrically rather than ingested voluntarily. Conceivably, gastric intubation could have aversive consequences that might influence palatability. As far as I know, there is as yet no report of an increase in active aversion due soley to the caloric satiety of a voluntary meal.

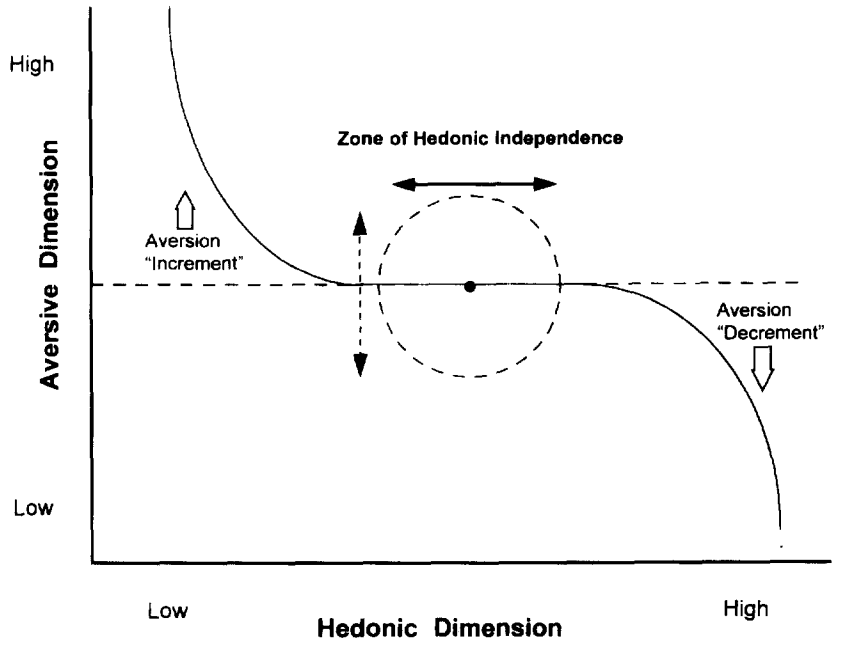

FIG. 7. Hypothesized interrelation of hedonic and aversive subcomponents of taste liking. Mutual inhibition allows interaction between separate hedonic and aversive dimensions of palatability. Manipulation of the hedonic evaluation of a particular taste (represented by center dot in two-dimensional plane) by itself will be expressed as a selective change in hedonic affective reaction patterns only if the shift is small enough to fit within the zone of hedonic independence (dotted circle and double arrow). Larger shifts along the horizontal hedonic dimension will produce indirect changes in aversive reaction patterns via changes in the strength of reciprocal inhibition. Very large hedonic enhancements will produce the appearance of decrements in aversion. Very large hedonic reductions will produce the appearance of increments in aversion. Although not depicted here, the same logic would apply to selective shifts along the vertical dimension of aversion. Small shifts within the zone of independence would be detectable as affecting only aversion. Larger shifts would produce indirect consequences on hedonic reaction patterns.

produced by a learned taste aversion or by damage to the ventral forebrain. This may mean that independent shifts in hedonic or aversive palatability can be observed only if the shift is mild to moderate in amplitude, again consistent with a hypothesis that the two systems interact by reciprocal inhibition. The test of whether two orthogonal systems indeed exist will rest on whether the dimension-specific shifts found so far can be replicated, and eventually upon whether separable neural substrates can be found to correspond to specific hedonic vs. aversive affective dimensions.

Human Consciousness of Food Reward

In principle, the question of the relation between pleasure and displeasure, between wanting and liking, and between palatability and appetite might be thought to be answerable by recourse to human subjective introspection. Why not simply ask people whether such phenomena are separate or not? The reason why not is that in practice human subjective reports may not be able to provide accurate answers. The strategy of asking people to report on their underlying state is useful only if subjective introspection has accurate access to underlying motivational processes. But there is a growing body of evidence that indicates humans are not directly aware of many aspects of the underlying psychological processes, motivational and otherwise, that control their behavior [e.g., (85), for a review].

This brings us to the heart of the argument concerning why reward should not be defined solely in terms of subjective experience. Many would assert that pleasure, by definition, is something of which we are aware. Certainly our awareness of pleasure is chiefly what we mean when we speak of our own rewards. But our awareness may be dissociable, at least under some conditions, from the underlying process that has given rise to that conscious pleasure. There is reason to believe that the conscious perception of pleasure, like the conscious perception of other events, is not a direct and faithful reproduction of an underlying core affective process. Instead, subjective perception is the product of an active reconstruction by cognitive mechanisms of sensory, affective, memory, etc. processes. The evidence discussed below shows that active reconstruction can introduce distortion. Our awareness may be blind to distinctions among processes that exist at lower levels, and may create new distinctions or distortions in consciousness that do not exist at those fundamental levels.

The results of a number of studies of human subjective reports related to reward combine to argue that our conscious experience of taste pleasure can be: (1) confused and indistinct; (2) stripped of affective details that exist distinctly in core affective evaluations, which are revealed by other measures; and (3) distorted by "cognitive contamination" from a variety of cognitive sources regarding food and culture that impose transformations upon affective evaluations of taste.

People are Unaware of Moderate Affective Shifts

Mook and Votaw (83) tested what they called the "strong hedonic hypothesis" of the relation between alliesthesia and appetite. By that they meant the joint hypotheses that the chief psychological consequence of ingesting a meal is to reduce the perceived palatability of the food, and that this hedonic decrement in food perception is the chief cause for the end of the meal. The strong hedonic hypothesis, in other words, posits that wanting is equivalent and due solely to liking, and that a reduction of liking induced by alliesthesia effectively terminates wanting. They asked college students to describe their subjective reasons for why they typically stopped eating at the end of a meal. A change in food palatability was not ranked highly among the list of reasons given. Students ranked reasons such as "the food tastes less good" toward the bottom of the list. Much more popular were feelings of "fullness" or other reasons such as "the food is all gone." As Mook and Votaw concluded, "the data suggest that hedonic changes are of little salience as factors in meal termination." They noted that although hedonic changes in human perception of palatability have been well documented in studies of alliesthesia, they appear not to be noticed unless attention is drawn to them specifically, or at least they are not remembered as very noticeable. Whatever the true reason for meal termination—and Mook and Votaw point out that the reasons seized upon and volunteered by subjects need not necessarily be the true reasons (e.g., 85)—people do not perceive changes in food liking to be striking features of a meal.

Convergence of Appetite Indices in Awareness

As interesting as the failure of people to report awareness of changes in palatability is the relationship among changes that they do report. Unquestionably, people usually have conscious access of some sort to states that exert causal force on behavior. The subjective report of hunger, for example, was found to be a better predictor of subsequent meal size than measures of the pre-meal gastric contents in a study conducted by de Castro and Elmore (40). As the authors concluded, "subjective hunger represents an intermediary (funnel) step in the cause effect cessation of meal ingestion." But the subjective hunger that people experience and report may be accurate precisely because it is a funnel, a merging together of multiple sources, and not because it reflects any single distinct deficit cue. This argument was made forcefully by Booth (21). In a study of the correlation among answers that people give, before and after a meal, subjects were asked questions about seemingly different psychological aspects of appetite such as: how hungry are you now? How strong are your sensations of hunger? How strong is your desire to eat? How pleasant is this food? Booth found extremely high correlation among the answers to these questions—average loadings on the main hunger factor for all of the answers of between 0.82 and 0.92. This extraordinary degree of correlation suggests that the answers to these questions are not as independent as their topics (desire, body sensations, food pleasure) would suggest. Booth raised the alternative hypothesis that instead all of the answers to these questions may be influenced by a similar set of underlying processes related to caloric hunger, appetite, etc. These are not directly experienced themselves, but rather interpreted as a general variable, and then elaborated into distinct desire–sensation–pleasure categories by the mediation of cognitive mechanisms. Since the cognitive mechanisms that produce the disparate categories are acting on the same set of input factors, they produce outputs that are highly correlated [though there are limits to this argument, e.g., (67)].

Distortion of Affective Perception by Cognitive Processes

Subjective reports of underlying processes carry "false positives" as well as "false negatives". The above examples suggest that people are not subjectively aware of all aspects of the motivational processes within them: they fail to notice some processes; and they merge others together. Such examples are false negatives, since they show failure to accurately report underlying processes. But could we at least maintain that subjective reports are accurate as far as they go? The answer even to this question may often be no. An example is provided by Wilson and Schooler (150), who asked two groups of college students to rate how much they liked the taste of five commercially prepared strawberry jams. The two groups of students differed in whether they were requested simply to give a numerical score vs. whether they were asked to think about why they gave particular rankings, and to list their reasons for liking or disliking a particular jam. The liking ratings given by the students were compared to rankings of the same jams previously obtained by consumer reports from an expert panel of trained sensory evaluators. Students who were asked simply to rate "liking" on a 9-point scale ranked the jams quite similarly to the expert panel, diverging by at most one step in rank from the experts. By contrast, students who were asked to justify their rankings with explicit reasons diverged more sharply from the judgment of experts and from their spontaneous peers, giving ranks that differed as much as two steps from the expert panel's. Wilson and Schooler (150) suggested that students who were asked to justify their rankings,constructed criteria and reasons that differed from the criteria of experts, and then altered their ratings to correspond to the reasons they had chosen. If hedonic processes were simply "read off" by

consciousness, we might expect introspective attention to improve accuracy and reduce the variation among hedonic ratings. But if subjective ratings are constructed by active cognitive processes from underlying events (85), then excessive cognitive processing may distort the underlying process to a greater degree than usual. From the results of Schooler and Wilson, we do not know whether excessive introspection led simply to the misreading of underlying hedonic judgments or whether cognitive justification actually altered the underlying hedonic processes. But in either case, it is clear that subjective ratings of taste pleasure do not provide a direct and faithful translation of stable underlying hedonic evaluations. Of course this does not mean that human subjective reports are inaccurate about what is experienced, if the report is given in good faith. But it means that what is experienced may diverge from the underlying process that is the object of experience.

Manifestation of Unconscious Reward

The most powerful demonstrations of a separation between reward processes and human conscious access to those reward processes have come from studies of drug reward. In a study that perhaps most dramatically illustrates this principle, Lamb et al. (74) gave recovered heroin addicts the opportunity to work for a morphine injection in a controlled hospital setting. In classic instrumental fashion, the addicts were required to press a bar many times in a given period if they wished to receive a dose of morphine that they had previously received several times earlier that week. At the same time, after each injection, the addicts were asked to rate how much they liked the morphine, how high they felt, how much drug they thought the injection contained and how much it would be worth on the street. Each week the dose of morphine changed, and ranged over weeks from zero to moderately high. For high doses of morphine, the subjects worked at high rates to obtain the injection. Not surprisingly, they rated these doses as very much liked, valuable, of high amount, etc. Conversely, when the injection contained no drug at all (vehicle control), they did not work for the injection once they had experienced it several times. Accordingly, they rated this injection as not liked, worthless, empty, etc. The result of special interest, however, comes from the week when injections contained a relatively low dose of morphine. For this dose, the addicts continued to work. They pressed instrumentally in order to obtain it at response rates as high as they had shown for any other morphine dose. However, when they actually received this injection they rated it as subjectively equal to the vehicle control: not liked, worthless, empty etc. Clearly this low dose of morphine activated processes sufficient to motivate their behavior, but insufficient to produce any degree of subjective reward. Similar observations of what appears to be an unconscious yet behaviorally evident reward have been made in studies of cocaine (50). Such results drive home the conclusion that fundamental reward processes are not essentially phenomena of conscious awareness, but rather processes that can exist either with or without conscious awareness.

Regarding human subjective ratings of food reward, it may still be possible to dissociate "wanting" and "liking," "liking" and "disliking," etc., in studies constructed to examine these aspects independently (e.g., 19,48,67,107,161). My argument here is simply that introspective subjects often may not be directly aware of these dissociations, even when the subjects themselves generate data that demonstrate them.

CONCLUSIONS

Where in the Brain is Food Reward?

Taste sensory quality and palatability may not be strictly segregated from each other into thalamocortical vs. limbic brain pathways. Aspects of palatability processing begin at the earliest stages of neural processing, within the hindbrain nucleus of the solitary tract and parabrachial nucleus, and continue in both the limbic and cortical gustatory pathways. Food reward is embedded in the brain as a distributed neural system, stretching from end to end. Damage to any single neural structure can distort, but cannot obliterate, this system.

Psychological and Neural Components of Reward

Reward contains separable psychological components, corresponding roughly to "wanting" (incentive salience attribution) and "liking" (hedonic/aversive evaluation). These wanting and liking processes are mediated by separable neural substrates. In particular, opioid and benzodiazepine/GABA neurotransmitter systems, and substantia innominata/ventral pallidal circuits that mediate feeding appear to be most directly related to liking. By contrast, mesotelencephalic dopamine neurotransmitter systems and the central nucleus of the amygdala appear to participate more directly in wanting than in liking. Manipulations that apparently change appetite in similar ways may thus have very different and distinct effects on food liking. Conversely, under some circumstances, liking can be manipulated without apparent consequences to food wanting.

Subcomponents Within Liking

Even further subdivisions may exist. The liking component of food reward may contain orthogonal subcomponents: taste pleasure (true liking); and taste displeasure or aversion (disliking). As yet, the neural basis for this subdivision between hedonic and aversive dimensions is not clear, though some manipulations offer promising possibilities for investigation (caloric hunger, benzodiazepine/GABA induced feeding and ventral pallidum/innominata lesion-induced aphagia).

Reward and Subjective Awareness

Subjective awareness is as much a component of food reward as it is of sensory perception or memory, but no more. Reward is not essentially a conscious

phenomenon any more than are other psychological processes of perception, memory, etc. Fundamental processes of reward may occur with or without consciousness of them, and consciousness of reward may at times distort the true state of underlying processes. The phenomenon we experience as reward is a complex integration of a collection of functions, not a direct readout of a single function.

Prospects for Future Research

What implications follow if liking is not equal to wanting, and if the basic processes of reward are experienced only indirectly in human consciousness?

First, for the study of ingestion, it is crucial to recognize that a given change in intake can be achieved by multiple psychological routes. Some involve changes in liking; others involve changes in wanting alone. Different psychological routes to a given level of intake are mediated by different neural substrates. Although it may be possible in some laboratory settings to predict and control intake without bothering about psychological or neural causation, it will never be possible to understand how and why a manipulation has changed intake unless we recognize these factors. And for clinical feeding disorders in particular, even successful control of intake is likely to depend upon a correct understanding of the original causes of the distortion of intake patterns.

Second, for the neuroscience of reward, the question is not merely whether a brain substrate is involved but rather how a particular substrate mediates reward. For a neural manipulation known to change reward value, has the manipulation changed liking, wanting, or still another aspect of the reward process? Answers to this question will help build a more complete understanding of the way in which pleasure and motivation are instantiated by the interplay among neural systems. To distinguish among so many psychological subcomponents of food reward may seem to make the behavioral neuroscientist's situation uncomfortably complex. But it would be wrong to reject such distinctions merely because of their psychological complexity. We are accustomed in behavioral neuroscience to accommodate an ever increasing complexity of neural systems. We should not be surprised that the psychological functions and behavioral output of this neural complexity are complex too.

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REFERENCES

1. Aggleton, J. P.; Mishkin, M. The amygdala: Densory gateway to the emotions. In: Plutchik, R.; Kellerman H., eds. Emotion: Theory, research and experience. Orlando, FL: Academic Press; 1986:281–299.
2. Bakshi, V. P.; Kelley, A. E. Feeding induced by opioid stimulation of the ventral striatum: Role of opiate receptor subtypes. J. Pharmacol. Exp. Ther. 265:1253–1260; 1993.
3. Beagley, W. K.; Holley, T. L. Hypothalamic stimulation facilitates contralateral visual control of a learned response. Science 196:321–323; 1977.
4. Beauchamp, G. K.; Bertino, M.; Burke, D.; Engelman, K. Experimental sodium depletion and salt taste in normal human volunteers. Am. J. Clin. Nutr. 51:881–889; 1990.
5. Berridge, K.; Grill, H. J.; Norgren, R. Relation of consummatory responses and preabsorptive insulin release to palatability and learned taste aversions. J. Comp. Physiol. Psychol. 95:363–382; 1981.
6. Berridge, K. C. Brainstem systems mediate the enhancement of palatability by chlordiazepoxide. Brain Res. 447:262–268; 1988.
7. Berridge, K. C. Modulation of taste affect by hunger, caloric satiety, and sensory-specific satiety in the rat. Appetite 16:103–120; 1991.
8. Berridge, K. C.; Fentress, J. C. Trigeminal-taste interaction in palatability processing. Science 228:747–750; 1985.
9. Berridge, K. C.; Flynn, F. W.; Schulkin, J.; Grill. H. J. Sodium depletion enhances salt palatability in rats. Behav. Neurosci. 98:652–660; 1984.
10. Berridge, K. C.; Grill, H. J. Alternating ingestive and aversive consummatory responses suggest a two-dimensional analysis of palatability in rats. Behav. Neurosci. 97:563–573; 1983.
11. Berridge, K. C.; Grill, H. J. Isohedonic tastes support a two-dimensional hypothesis of palatability. Appetite 5:221–231; 1984.
12. Berridge, K. C.; Peciña. S. Benzodiazepines, appetite, and taste palatability. Neurosci. Biobehav. Rev. 19:121–131; 1995.
13. Berridge, K. C.; Robinson, T. E. The mind of an addicted brain: Sensitization of wanting versus liking. Curr. Dir. Psychol. Sci. 4:71–76; 1995.
14. Berridge, K. C.; Treit, D. Chlordiazepoxide directly enhances positive ingestive reactions in rats. Pharmac. Biochem. Behav. 24:217–221; 1986.
15. Berridge, K. C.; Valenstein, E. S. What psychological process mediates feeding evoked by electrical stimulation of the lateral hypothalamus? Behav. Neurosci. 105:3–14; 1991.
16. Berridge, K. C.; Venier, I. L.; Robinson, T. E. Taste reactivity analysis of 6-hydroxydopamine-induced aphagia: implications for arousal and anhedonia hypotheses of dopamine function. Behav. Neurosci. 103:36–45; 1989.
17. Bindra, D. How adaptive behavior is produced: a perceptual-motivation alternative to response reinforcement. Behav. Brain Sci. 1:41–91; 1978.
18. Blackurn, J. R.; Phillips, A. G.; Jakubovic, A.; Fibiger, H. C. Dopamine and preparatory behavior: II. A neurochemical analysis. Behav. Neurosci. 103:15–23; 1989.
19. Blundell, J. E.; Hill, A. J. On the mechanism of action of dexfenfluramine: Effect on alliesthesia and appetite motivation in lean and obese subjects. Clin. Neuropharmac. 11:S121–134; 1988.
20. Blundell, J. E.; Rogers, P. J. Hunger, hedonics, and the control of satiation and satiety. In: Friedman, M.; Kare, M.; Tordoff, M., eds. Chemical senses. New York: Marcal Dekker, 1991:127–148.
21. Booth, D. A. Cognitive experimental psychology of appetite. In: Boakes, R. A.; Popplewell, D. A.; Burton M. J., eds. Eating habits. Chichester: Wiley; 1987:175-209.
22. Booth, D. A. How not to think about immediate dietary and postingestional influences on appetites and satieties [comment]. Appetite 14:171–179; 1990. [Discussion, 180.]
23. Breslin, P. A.; Davidson, T. L.; Grill, H. J. Conditioned reversal of reactions to normally avoided tastes. Physiol. Behav. 47:535–538; 1990.
24. Breslin, P. A.; Spector, A. C.; Grill, H. J. A quantitative comparison of taste reactivity behaviors to sucrose before and after

lithium chloride pairings: a unidimensional account of palatability. Behav. Neurosci. 106:820–836; 1992.
25. Burton, M. J.; Mora, F.; Rolls, E. T. Proceedings: Visual and taste neurones in the lateral hypothalamus and substantia innominata: Modulation of responsiveness by hunger. J. Physiol. 252:50P–51P; 1975.
26. Cabanac, M. Physiological role of pleasure. Science 173:1103–1107; 1971.
27. Cabanac, M. Sensory pleasure. Q. Rev. Biol. 54:1–29; 1979.
28. Cabanac, M. Pleasure: The common currency. J. Theor. Biol. 155:173–200; 1992.
29. Cabanac, M.; Lafrance, L. Postingestive alliesthesia: The rat tells the same story. Physiol. Behav. 47:539–543; 1990.
30. Cabanac, M.; Lafrance, L. Facial consummatory responses in rats support the ponderostat hypothesis. Physiol. Behav. 50:179–183; 1991.
31. Cabanac, M.; Lafrance, L. Ingestive/aversive response of rats to sweet stimuli. Influence of glucose, oil, and casein hydrolyzate gastric loads. Physiol. Behav. 51:139–143; 1992.
32. Chang, F. C.; Scott, T. R. Conditioned taste aversions modify neural responses in the rat nucleus tractus solitarius. J. Neurosci. 4:1850–1862; 1984.
33. Conover, K. L.; Shizgal, P. Competition and summation between rewarding effects of sucrose and lateral hypothalamic stimulation in the rat. Behav. Neurosci. 108:537–548; 1994.
34. Cooper, S. J. Benzodiazepines as appetite-enhancing compounds. Appetite 1:7–19; 1980.
35. Cooper, S. J. Ingestional responses following benzodiazepine receptor ligands, selective 5-HT-1A agonists and selective 5-HT-3 receptor antagonists. In: Rogers, R. J.; Cooper, S. J., eds. 5-HT-1A agonist, 5-HT-3 antagonists and benzodiazepines. Their comparative behavioral pharmacology. Chichester: Wiley; 1991:233–266.
36. Cooper, S. J.; Estall, L. B. Behavioural pharmacology of food, water and salt intake in relation to drug actions at benzodiazepine receptors. Neurosci. Biobehav. Rev. 9:5–19; 1985.
37. Cooper, S. J.; Moores, W. R. Benzodiazepine-induced hyperphagia in the non-deprived rat: comparisons with CL 218,872, zopiclone, tracazolate and phenobarbital. Pharmac. Biochem. Behav. 23:169–174; 1985.
38. Cromwell, H. C.; Berridge, K. C. Where does damage lead to enhanced food aversion: The ventral pallidum/substantia innominata or lateral hypothalamus? [published erratum appears in Brain Res. Apr 11; 642(1-2):355; 1994]. Brain Res. 624:1–10; 1993.
39. Davis, J. D.; Smith, G. P. Analysis of the microstructure of the rhythmic tongue movements of rats ingesting maltose and sucrose solutions. Behav. Neurosci. 106:217–228; 1992.
40. de Castro, J. M.; Elmore, D. K. Subjective hunger relationships with meal patterns in the spontaneous feeding behavior of humans: evidence for a causal connection. Physiol. Behav. 43:159–165; 1988.
41. Delamater, A. R.; LoLordo, V. M.; Berridge, K. C. Control of fluid palatability by exteroceptive Pavlovian signals. J. Exp. Psychol. [Anim. Behav.] 12:143–152; 1986.
42. Doyle, T. G.; Berridge, K. C.; Gosnell, B. A. Morphine enhances hedonic taste palatability in rats. Pharmac. Biochem. Behav. 46:745–749; 1993.
43. Drewnowski, A.; Krahn, D. D.; Demitrack, M. A.; Nairn, K.; Gosnell, B. A. Taste responses and preferences for sweet high-fat foods: Evidence for opioid involvement. Physiol. Behav. 51:371–379; 1992.
44. Edmonds, D. E.; Gallistel, C. R. Parametric analysis of brain stimulation reward in the rat: III. Effect of performance variables on the reward summation function. J. Comp. Physiol. Psychol. 87:876–883; 1974.
45. Epstein, A. N. Instinct and motivation as explanations for complex behavior. In: Pfaff, D. W. ed. The physiology of motivation. New York: Springer; 1982:25–58.
46. Ettenberg, A.; Camp, C. H. Haloperidol induces a partial reinforcement extinction effect in rats: implications for a dopamine involvement in food reward. Pharmacol. Biochem. Behav. 15:813–821; 1986.
47. Fantino, M., Hosotte, J.; Apfelbaum, M. An opioid antagonist, naltrexone, reduces preference for sucrose in humans. Am. J. Physiol. 251:R91–96; 1986.
48. Fantino, M., Hosotte, J.; Apfelbaum, M. An opioid antagonist, naltrexone, reduces preference for sucrose in humans. Am. J. Physiol. 251:R91–96; 1986.
49. Fibiger, H. C.; Phillips, A. G. Reward, motivation, cognition: Psychobiology of mesotelencephalic systems. Handbook of physiology—the nervous system, 4:647–675; 1986.
50. Fischman, M. W.; Foltin, R. W. Self-administration of cocaine by humans: a laboratory perspective. In: Bock, G. R.; Whelan, J., eds. Cocaine: scientific and social dimensions. Chichester: Wiley; 1992:165–180.
51. Fluharty, S. J.; Grill, H. J. Taste reactivity of lateral hypothalamic lesioned rats: effects of deprivation and tube feeding. Soc. Neurosci. Abstr. 7:29; 1981.
52. Flynn, F. W.; Grill, H. J.; Schulkin, J.; Norgren, R. Central gustatory lesions: II. Effects on sodium appetite, taste aversion learning, and feeding behaviors. Behav. Neurosci. 105:944–954; 1991.
53. Flynn, F. W.; Grill, H. J.; Schwartz, G. J.; Norgren, R. Central gustatory lesion: I. Preference and taste reactivity tests. Behav. Neurosci. 105:933–943; 1991.
54. Galaverna, O.; Seeley, R. J.; Berridge, K. C.; Grill, H. J.; Schulkin, J.; Epstein, A. N. Lesions of the central nucleus of the amygdala: I. Effects on taste reactivity, taste aversion learning, and sodium appetite. Behav. Brain Res. 59:11–17; 1993.
55. Geary, N.; Smith, G. P. Pimozide decreases the positive reinforcing effect of sham fed sucrose in the rat. Pharmacol. Biochem. Behav. 22:787–790; 1985.
56. Gosnell, B. A. Central structures involved in opioid-induced feeding. Fed. Proc. 46:163–167; 1987.
57. Gramling, S. E., Fowler, S. C.; Collins, K. R. Some effects of pimozide on nondeprived rats licking sucrose solutions in an anhedonia paradigm. Pharmacol. Biochem. Behav. 21:617–624; 1984.
58. Gramling, S. E., Fowler, S. C.; Tizzano, J. P. Some effects of pimozide on nondeprived rats' lever pressing maintained by a sucrose reward in an anhedonia paradigm. Pharmacol. Biochem. Behav. 27:67–72; 1987.
59. Gray, T.; Wise, R. A. Effects of pimozide on lever pressing behavior maintained on an intermittent reinforcement schedule. Pharmacol. Biochem. Behav. 12:931–935; 1980.
60. Grill, H. J.; Berridge, K. C. Taste reactivity as a measure of the neural control of palatability. In: Sprague, J. M.; Epstein, A. N., eds. Progress in psychobiology and physiological psychology. Orlando, FL: Academic Press; 1985:1–615.
61. Grill, H. J.; Kaplan, J. M. Caudal brainstem participates in the distributed neural control of feeding. In: Neurobiology of food and fluid intake, Stricker, E. M., eds. New York: Plenum Press; 1990:125–149.
62. Grill, H. J.; Norgren, R. Chronically decerebrate rats demonstrate satiation but not bait shyness. Science 201:267–269; 1978.
63. Grill, H. J.; Norgren, R. The taste reactivity test. I. Mimetic responses to gustatory stimuli in neurologically normal rats. Brain. Res. 143:263–279; 1978.
64. Grill, H. J.; Norgren, R. The taste reactivity test. II. Mimetic responses to gustatory stimuli in chronic thalamic and chronic decerebrate rats. Brain Res. 143:281–297; 1978.
65. Gundersen, H. J.; Bagger, P.; Bendtsen, T. F.; Evans, S. M.; Korbo, L.; Marcussen, N.; Moller, A.; Nielsen, K.; Nyengaard, J. R.; Pakkenberg, B. et al. The new stereological tools: disector, fractionator, nucleator and point sampled intercepts and their use in pathological research and diagnosis. Apmis 96:857–881; 1988.
66. Hetherington, M. M.; Vervaet, N.; Blass, E.; Rolls, B. J. Failure of naltrexone to affect the pleasantness or intake of food. Pharmacol. Biochem. Behav. 40:185–190; 1991.
67. Hill, A. J.; Magson, L. D.; Blundell, J. E. Hunger and palatability: Tracking ratings of subjective experience before, during, and after the consumption of preferred and less preferred food. Appetite 5:361–371; 1984.
68. Hinde, R. A. Animal behaviour: a synthesis of ethology and comparative psychology. London: McGraw-Hill; 1970.
69. Hoebel, B. G. Neuroscience and motivation: Pathways and peptides that define motivational systems. In: Atkinson, R. C.; Herrnstein, R. J., Lindzey, G.; Luce, R. D., eds. Stevens' handbook of experimental psychology. New York: Wiley; 1988:547–626.
70. Hughlings Jackson, J., ed. (1958). Selected writings of John Hughlings Jackson. London: Staples Press.
71. Kissileff, H. R. Some suggestions on dealing with palatability—

response to Ramirez [comment]. Appetite 14:162–166; 1990. [Discussion 180.]
72. Kiyatkin, E. A.; Gratton, A. Electrochemical monitoring of extracellular dopamine in nucleus accumbens of rats lever-pressing for food. Brain Res. 652:225–234; 1994.
73. Laeng, B.; Berridge, K. C; Butter, C. M. Pleasantness of a sweet taste during hunger and satiety: effects of gender and "sweet tooth." Appetite 21:247–254; 1993.
74. Lamb, R. J.; Preston, K. L.; Schindler, C. W.; Meisch, R. A.; Davis, F.; Katz, J. L.; Henningfield, J. E.; Goldberg, S. R. The reinforcing and subjective effects of morphine in post-addicts: a dose-response study. J. Pharmacol. Exp. Ther. 259:1165–1173; 1991.
75. Le Magnen, J. Palatability: concept, terminology, and mechanisms. In: Boakes, R. A.; Popplewell, D. A., Burton, M. J., eds. Eating habits. Chichester: Wiley; 1987:131–1557.
76. Le Magnen, J. Neurobiology of feeding and nutrition. San Diego, CA: Academic Press, 1992.
77. LeDoux, J. E. Emotion and the amygdala. In: The amygdala: neurobiological aspects of emotion, memory, and mental dysfunction, Aggleton, J. P. ed. New-York: Wiley-Liss; 1992:339–351.
78. Leeb, K.; Parker, L.; Eikelboom, R. Effects of pimozide on the hedonic properties of sucrose: analysis by the taste reactivity test. Pharmac. Biochem. Behav. 39:895–901; 1991.
79. Lidsky, T. I.; Manetto, C.; Schneider, J. S. A consideration of sensory factors involved in motor functions of the basal ganglia. Brain Res. 356:133–146; 1985.
80. Looy, H.; Callaghan, S.; Weingarten, H. P. Hedonic response of sucrose likers and dislikers to other gustatory stimuli. Physiol. Behav. 52:219–225; 1992.
81. Mark, G. P.; Scott, T. R.; Chang, F. C.; Grill, H. J. Taste responses in the nucleus tractus solitarius of the chronic decerebrate rat. Brain Res. 443:137–148; 1988.
82. Mittleman, G.; Castaneda, E.; Robinson, T. E.; Valenstein, E. S. The propensity for nonregulatory ingestive behavior is related to differences in dopamine systems: behavioral and biochemical evidence. Behav. Neurosci. 100:213–220; 1986.
83. Mook, D. G.; Votaw, M. C. How important is hedonism? Reasons given by college students for ending a meal. Appetite 18:69–75; 1992.
84. Nauta, W. J.; Domesick, V. B. Afferent and efferent relationships of the basal ganglia. Ciba Found Symp. 107:3–29; 1984.
85. Nisbett, R. W.; Wilson, T.D. Telling more than we can know: verbal reports on mental processes. Psychol. Rev. 84:231–259; 1978.
86. Norgren, R. Central neural mechanisms of taste. In: Darien-Smith, I., ed. Handbook of physiology: the nervous system III-sensory processes. American Physiological Society; 1984:1087–1128.
87. Norgren, R. Gustatory system. The rat nervous system. New York: Academic Press; 1995:751–771.
88. Norgren, R.; Nishijo, H.; Travers, S. P. Taste responses from the entire gustatory apparatus. Ann. N. Y. Acad. Sci. 575:246–263; 1989. [Discussion 263–264.]
89. Norgren, R.; Pfaffmann, C. The pontine taste area in the rat. Brain Res. 91:99–117; 1975.
90. Parker, L.; Leeb, K. Amphetamine-induced modification of quinine palatability: analysis by the taste reactivity test. Pharmac. Biochem. Behav. 47:413–420; 1994.
91. Parker, L. A. Chlordiazepoxide nonspecifically enhances consumption of saccharin solution. Pharmacol. Biochem. Behav. 38:375–377; 1991.
92. Parker, L. A.; Lopez, Jr., N. Pimozide enhances the aversiveness of quinine solution. Pharmacol. Biochem. Behav. 36:653–659; 1990.
93. Parker, L. A.; Maier, S.; Rennie, M.; Crebolder, J. Morphine- and naltrexone-induced modification of palatability: analysis by the taste reactivity test. Behav. Neurosci. 106:999–1010; 1992.
94. Peciña, S.; Berridge, K. C. Fourth ventricle microinjections of diazepam enhance hedonic reactions to taste. Soc. Neurosci. Abstr. 18:1231; 1992.
95. Peciña, S.; Berridge, K. C. Comparison of systemic and intracranial administration of morphine: Effects on hedonic taste reactivity (in rats). Soc. Neurosci. Abstr. 129:1820; 1993.
96. Pelchat, M. L.; Grill, H. J.; Rozin, P.; Jacobs, J. Quality of acquired responses to tastes by Rattus norvegicus depends on type of associated discomfort. J. Comp. Psychol. 97:140–153; 1983.
97. Pfaffmann, C. The pleasures of sensation. Psychol. Rev. 67:253–268; 1960.
98. Pfaffmann, C. Taste: a model of incentive motivation. In: Pfaff, D. W., ed. The physiology of motivation. New York: Springer; 1982:59–97.
99. Pfaffmann, C.; Norgren, R.; Grill, H. J. Sensory affect and motivation. Ann N. Y. Acad. Sci. 290:18–34; 1977.
100. Phillips, A. G.; Pfaus, J. G.; Blaha, C. D. Dopamine and motivated behavior: Insights provided by in vivo analyses. In: Willner, P. J.; Scheel-Kruger, J., eds. The mesolimbic dopamine system: from motivation to action. Chichester: Wiley; 1991:199–224.
101. Phillips, A. G. Neural basis of food reward. Neurosci. Biobehav. Rev., in press.
102. Phillips, A. G.; Nikaido, R. S. Disruption of brain stimulation-induced feeding by dopamine receptor blockade. Nature 258:750–751; 1975.
103. Price, M. T.; Fibiger, H. C. Discriminated escape learning and response to electric shock after 6-hydroxydopamine lesions of the nigro-neostriatal dopaminergic projection. Pharmacol. Biochem. Behav. 3:285–290; 1975.
104. Ramirez, I. What do we mean when we say "palatable food"? [see comments]. Appetite 14:159–161; 1990.
105. Reilly, S., Grigson, P. S.; Norgren, R. Parabrachial nucleus lesions and conditioned taste aversion: Evidence supporting an associative deficit. Behav. Neurosci. 107:1005–1017; 1993.
106. Robinson, T. E.; Berridge, K. C. The neural basis of drug craving: an incentive-sensitization theory of addiction. Brain Res. Brain. Res. Rev. 18:247–291; 1993.
107. Rogers, P. J. Why a palatability construct is needed [comment]. Appetite 14:167–170; 1990. [Discussion 180.]
108. Rolls, B. J. Sensory-specific satiety. Nutr. Rev. 44:93–101; 1986.
109. Rolls, E. T. Information processing in the taste system of primates. J. Exp. Biol. 146:141–164; 1989.
110. Rozin, P. N.; Schulkin. J. Food selection. In: Stricker, E. M., ed. Neurobiology of food and fluid intake. New York: Plenum; 1990:297–328.
111. Ruckmick, C. A. The psychology of pleasantness. Psychol. Rev. 32:362–383; 1925.
112. Salamone, J. D. Complex motor and sensorimotor functions of striatal and accumbens dopamine: involvement in instrumental behavior processes. Psychopharmacology 107:160–174; 1992.
113. Salamone, J. D. The involvement of nucleus accumbens dopamine in appetitive and aversive motivation. Behav. Brain Res. 61:117–133; 1994.
114. Schallert, T.; Whishaw, I. Q. Two types of aphagia and two types of sensorimotor impairment after lateral hypothalamic lesions: Observations in normal weight, dieted, and fattened rats. J. Comp. Physiol. Psychol. 92:720–741; 1978.
115. Schneider, L. H.; Davis, J. D.; Watson, C. A.; Smith, G. P. Similar effect of raclopride and reduced sucrose concentration on the microstructure of sucrose sham feeding. Eur. J. Pharmacol. 186:61–70; 1990.
116. Schultz, W. Responses of midbrain dopamine neurons to behavioral trigger stimuli in the monkey. J. Neurophysiol. 56:1439–1461; 1986.
117. Schultz, W.; Apicella, P.; Ljungberg, T. Responses of monkey dopamine neurons to reward and conditioned stimuli during successive steps of learning a delayed response task. J. Neurosci. 13:900–913; 1993.
118. Schultz, W.; Apicella, P.; Ljungberg, T.; Romo, R.; Scarnati, E. Reward-related activity in the monkey striatum and substantia nigra. Prog. Brain Res. 99:227–235; 1993.
119. Schultz, W.; Romo. R. Dopamine neurons of the monkey midbrain: Contingencies of responses to stimuli eliciting immediate behavioral reactions. J. Neurophysiol. 63:607–624; 1990.
120. Schwartzbaum, J. S. Electrophysiology of taste, feeding and reward in lateral hypothalamus of rabbit. Physiol. Behav. 44:507–526; 1988.
121. Scott, T. R. The effect of physiological need on taste. In: Taste, experience, and feeding, edited by Capaldi, E. D.; Powley, T. L. eds. Washington, DC: American Psychological Association; 1990:45–61.
122. Seeley, R. J.; Galaverna, O.; Schulkin, J.; Epstein, A. N.; Grill, H. J. Lesions of the central nucleus of the amygdala II: Effects

on intraoral NaCl intake. Behav. Brain Res. 59:19–25; 1993.
123. Simansky, K. J.; Bourbonais, K.A.; Smith, G. P. Food-related stimuli increase the ratio of 3,4-dihydroxyphenylacetic acid to dopamine in the hypothalamus. Pharmacol. Biochem. Behav. 23:253–258; 1985.
124. Simbayi, L. C.; Boakes, R. A.; Burton, M. J. Effects of basolateral amygdala lesions on taste aversions produced by lactose and lithium chloride in the rat. Behav. Neurosci. 100:455–465; 1986.
125. Smith, G. P. The arousal function of central catecholamine neurons. Ann. N. Y. Acad. Sci. 170:45–56; 1976.
126. Smith, G. P. Dopamine and food reward. In: Morrison, A.; Fluharty, S., eds. Progress in psychobiology and physiological psychology. New York: Academic Press, in press.
127. Spector, A. C., Norgren, R.; Grill, H. J. Parabrachial gustatory lesions impair taste aversion learning in rats. Behav. Neurosci. 106:147–161; 1992.
128. Stanley, B. G.; Lanthier, D.; Leibowitz, S. F. Multiple brain sites sensitive to feeding stimulation by opioid agonists: a cannula-mapping study. Pharmac. Biochem. Behav. 31:825–832; 1988.
129. Steiner, J. Gustofacial reactions to taste of various species of monkeys and apes. Unpublished videotape.
130. Steiner, J. E. The gustofacial response: observation on normal and anencephalic newborn infants. Symp. Oral. Sens. Percept. 4:254–278; 1973.
131. Steiner, J. E. Human facial expressions in response to taste and smell stimulation. Adv. Child Dev. Behav. 13:257–295; 1979.
132. Stellar, E. Brain mechanisms in hedonic processes. In: Pfaff, D. W., ed. The physiological mechanisms of motivation. New York: Springer; 1982:377–408.
133. Stellar, E. Brain and behavior. In: Stricker, E. M. ed. Neurobiology of food and fluid intake. New York: Plenum Press; 1990:3–22.
134. Stellar, J. R.; Brooks, F. H.; Mills, L. E. Approach and withdrawal analysis of the effects of hypothalamic stimulation and lesions in rats. J. Comp. Physiol. Psychol. 93:446–466; 1979.
135. Stellar, J. R.; Stellar, E. The neurobiology of motivation and reward. New York: Springer; 1985.
136. Stricker, E. M.; Zigmond, M. J. Brain catecholamines and the lateral hypothalamic syndrome. In: Novin, D.; Wyrwicka, W.; Bray, G., eds. Hunger: Basic mechanisms and clinical implications. New York: Raven Press; 1973:19–32.
137. Stricker, E. M.; Zigmond, M. J. Brain monoamines, homeostasis, and adaptive behavior. In: Bethesda, M. D., ed. Handbook of physiology: Intrinsic regulatory systems of the brain. American Physiological Society; 1986:677–696.
138. Teitelbaum, P. The use of operant methods in the assessment and control of motivational states. In: Honig, W. K. ed. Operant behavior: areas of research and application. New York: Appleton-Century-Crofts; 1966:565–608.
139. Teitelbaum, P. Levels of integration of the operant. In: Honig, W. K.; Staddon, J. E. R. eds. Handbook of operant behavior. Englewood Cliffs, NJ: Prentice-Hall; 1977:7–27.
140. Teitelbaum, P.; Epstein, A. N. The lateral hypothalamic syndrome: Recovery of feeding and drinking after lateral hypothalamic lesions. Psychol. Rev. 69:74–90; 1962.
141. Toates, F. Motivational systems. Cambridge: Cambridge University Press; 1986.
142. Toates, F. Cognition and evolution—an organization of action perspective. Behav. Proc., in press.
143. Treit, D.; Berridge, K. C. A comparison of benzodiazepine, serotonin, and dopamine agents in the taste-reactivity paradigm. Pharmacol. Biochem. Behav. 37:451–456; 1990.
144. Treit, D.; Berridge, K. C.; Schultz, C. E. The direct enhancement of positive palatability by chlordiazepoxide is antagonized by Ro 15-1788 and CGS 8216. Pharmacol. Biochem. Behav. 26:709–714; 1987.
145. Tyrka, A.; Smith, G. P. Potency of SCH 23390 for decreasing sucrose intake in rat pups depends on mode of ingestion. Pharmacol. Biochem. Behav. 39:955–961; 1991.
146. Tyrka, A.; Smith, G. P. SCH23390, but not raclopride, decreases intake of intraorally infused 10% sucrose in adult rats. Pharmacol. Biochem. Behav. 45:243–246; 1993.
147. Valenstein, E. S. The interpretation of behavior evoked by brain stimulation. In: Wauquier A.; Rolls E.T. eds. Brain-stimulation reward. New York: Elsevier; 1975: 557–575.
148. Weingarten, H. P.; Duong, A.; Elston, D. Interpretation of sham feeding data: Curve shift studies. Am. J. Physiol., in press.
149. Weingarten, H. P.; Watson, S. D. Sham feeding is a procedure for assessing the influence of diet palatability on food intake. Physiol. Behav. 28:401–407; 1982.
150. Wilson, T. D.; Schooler, J. W. Thinking too much: introspection can reduce the quality of preferences and decisions. J. Pers. Soc. Psychol. 60:181–192; 1991.
151. Wise, R. A. Neuroleptics and operant behavior: the anhedonia hypothesis. Behav. Brain Sci. 5:39–87; 1982.
152. Wise, R. A. The anhedonia hypothesis: Mark III. Behav. Brain Sci. 8:178–186; 1985.
153. Wise, R. A.; Bozarth, M. A. A psychomotor stimulant theory of addiction. Psychol. Rev. 94:469–492; 1987.
154. Wise, R. A.; Colle, L. M. Pimozide attenuates free feeding: Best scores analysis reveals a motivational deficit. Psychopharmacology 84:446–451; 1984.
155. Wise, R. A.; Dawson, V. Diazepam-induced eating and lever pressing for food in sated rats. J. Comp. Physiol. Psychol. 86:930–941; 1974.
156. Wise, R. A.; Raptis, L. Effects of naloxone and pimozide on initiation and maintenance measures of free feeding. Brain Res. 368:62–68; 1986.
157. Wise, R. A.; Spindler, J.; deWit, H.; Gerberg, G. J. Neuroleptic-induced "anhedonia" in rats: pimozide blocks reward quality of food. Science 201:262–264; 1978.
158. Woods, J. S.; Leibowitz, S. F. Hypothalamic sites sensitive to morphine and naloxone: effects on feeding behavior. Pharmacol. Biochem. Behav. 23:431–438; 1985.
159. Wundt, W. Principles of physiological psychology. New York: MacMillen, 1904.
160. Yaxley, S.; Rolls, E. T.; Sienkiewicz, Z. J.; Scott.; T. R. Satiety does not affect gustatory activity in the nucleus of the solitary tract of the alert monkey. Brain Res. 347:85–93; 1985.
161. Yeomans, M. R.; Wright, P.; Macleod, H. A.; Critchley, J. A. Effects of nalmefene on feeding in humans. Dissociation of hunger and palatability. Psychopharmacology 100:426–432; 1990.
162. Young, P. T. The role of affective processes in learning and motivation. Psychol. Rev. 66:1104–1125; 1959.