3

Neural Coding of Pleasure: "Rose-tinted Glasses" of the Ventral Pallidum

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Pleasure is not a sensation. What is it then? Nico Frijda's answer in the "pleasure questions" section of this book (which he suggested a number of years ago) epitomizes an emerging consensus among many psychologists and neuroscientists (Frijda, Chapter 6, this book). He notes that pleasure "is a 'pleasantness gloss' added to whatever is pleasant."

Other chapter authors in this book describe pleasure similarly in their answers to "pleasure questions" as "the subsequent valuation of sensory stimuli" (Kringelbach, Chapter 12, this book); "integrated with sensation" (Dickinson and Balleine, Chapter 4, this book); or "arises from a weighted combination of the sensory signals" (Kringelbach, Chapter 12, this book; Leknes and Tracey, Chapter 19 this book). Pleasure as a hedonic "gloss" (Frijda, Chapter 6, this book; Smith et al., Chapter 1, this book) on sensations is a succinct way to describe how brain signals representing mere sensations (or applied to behavior-generating signals, actions) become glazed by coincident hedonic neural activity that imbues them with pleasure, transforming the signals into hedonic stimuli (or hedonic actions). Thus, viewed through the brain's metaphoric "rose-tinted glasses of pleasure," ordinary sensations become pleasurable sensations.

Here we ask: how is a "pleasure gloss" encoded in brain activity? Where in the brain is this glossing operation performed and how does it work? Is it possible for neuroscientists to recognize the signature patterns of neural activity that represent a pleasure gloss? These are difficult questions that are only beginning to be addressed. The "pleasure gloss" metaphor, applied to the transformation of neural signals for a stimulus, is like a varnish that is applied on top of a dull object to transform it into a shiny one. Adding hedonic tone to the signal passed on to downstream structures, the neural gloss effectively gives the entire brain a "rose-tinted" hedonic perception of the stimulus as pleasant.

In the context of neural firing signals, our idea is that a particular pattern of neuronal spikes or action potentials in crucial neurons may apply a glaze of pleasure on what might otherwise be an ordinary sensation or action signal. At the moment of such a signal, neural activity related to a potentially hedonic sensation will be comingled with signals that specifically implement the pleasure gloss. It is the pleasure-generating neural pattern we wish to identify. A pleasure transformation might excite, inhibit, or vary the pattern of firing activity within the target structure it modulates and as a result dynamically recruits changes in activity profiles throughout an entire circuit. The particular pattern we will describe is an excitation in a large population of neurons within a hedonic hotspot of the ventral pallidum.

This chapter will focus on neural activity profiles in the ventral pallidum because we believe this brain structure is particularly important to applying a hedonic gloss (Figure 3.1). This structure in the subcortical forebrain is a nexus of circuits that process emotion information. We will describe reasons as to why we think the ventral pallidum is especially

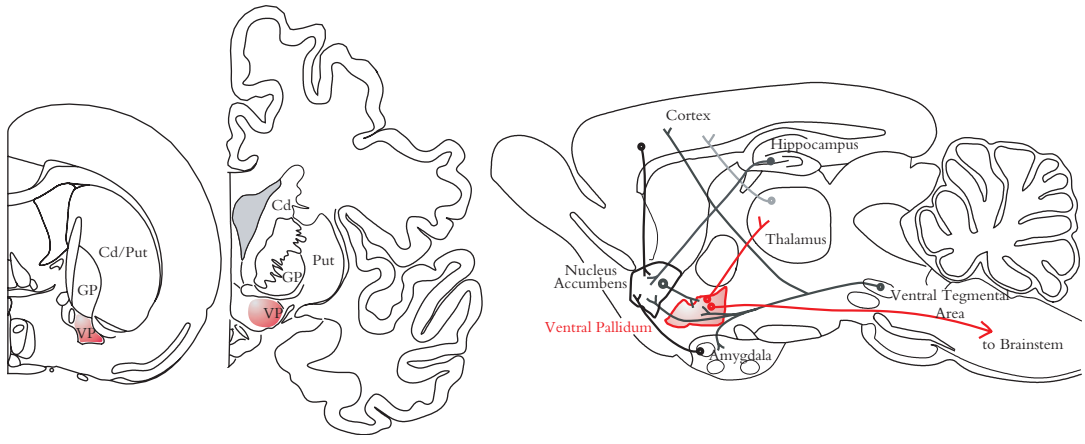

Figure 3.1 Ventral pallidum—sketches of rat and human coronal sections (left and middle panels). Schematic in right panel shows major input and output pathways of ventral pallidum.

likely to perform a hedonic transformation. It is worth noting that the ventral pallidum has only recently become appreciated as a distinct neuroanatomical entity, let alone one with special hedonic functions. Older literature did not usually discuss the ventral pallidum because it used to be considered as just the ventral part of the globus pallidus (a component of the basal ganglia, which are brain structures that include the neostriatum, globus pallidus, entopeduncular nucleus, subthalamic nucleus, and the substantia nigra in the midbrain ventral tegmentum). The basal ganglia were traditionally viewed as important to controlling movements, but now are also recognized as crucial for neural processing related to emotion, motivation, and reward too. Especially important to affective-motivational functions are particular components of basal ganglia such as ventral tegmentum and its mesolimbic dopamine projections, the nucleus accumbens (formerly known as the ventral portion of neostriatum), and the ventral pallidum.

We do not mean to exclude the importance of other brain structures. We focus on the ventral pallidum simply because it is a good place to start to understand pleasure. Besides the basal ganglia, of course, many other brain structures are also involved in assigning pleasure (Kringelbach, 2005) (many of the chapters, this book). Many of them might do so in cognitive and predictive ways that go beyond painting the basic pleasure gloss onto a sensation. Much of human pleasure has cognitive qualities that infuse uniquely human properties, and it is likely that abstract or higher pleasures depend on cortical brain areas for those qualities. For example, full pleasure derived by humans from tasty food, a humorous joke, or from listening to music requires learning and complex cognitive representations, such as in orbitofrontal cortex, insula cortex, and anterior cingulate cortex (Blood and Zatorre, 2001; Kringelbach, 2005; Watson et al., 2007). Thus, the particular pattern of coactivated cortical circuits would resolve the high level cognitive features of a pleasantness gloss on sensations or actions.

Ventral Pallidum: Applying a Pleasure Gloss to Sweetness?

Still, for seeing the basic glazing operation by which the pleasure gloss is actually generated and applied to sensations, the ventral pallidum has particular advantages. Here a special insight may be gained into why sugar tastes nice and how some other sensations can become as nice as sugar, at least when they get the same neuronal hedonic gloss.

Several reasons have led us to focus on the ventral pallidum, in particular, for adding a pleasure gloss to ongoing sensations via its neuronal firing patterns. First, the ventral pallidum contains a "hedonic hotspot" in its posterior half, a roughly cubic-millimeter brain site in which neuronal events can lead to amplifications of a sensory pleasure (Peciña and Berridge, 2005; Peciña et al., 2006; Smith and Berridge, 2005, 2007; Smith et al., Chapter 1, this book). In hedonic hotspots, microinjections of opioids and other neurochemicals are able to glaze an extra gloss of pleasure onto sweet sensations, enhancing 'liking' responses. Several hotspots have recently been mapped in the

medial shell of the nucleus accumbens (sometimes called ventral striatum) and the ventral pallidum. In the ventral pallidum particularly, Kyle Smith, in his doctoral dissertation work in our laboratories, identified a 0.8 mm^3 hedonic hotspot in the posterior end of ventral pallidum in rats (Smith et al., Chapter 1, this book). If hotspots are scaled to overall brain size, the volume of a corresponding hotspot in humans might be closer to a cubic centimeter. In the ventral pallidum hotspot, for example, opioid stimulation caused over a doubling in the level of 'liking' reactions elicited by sucrose taste (Smith and Berridge, 2005; Tindell et al., 2006).

Another reason to focus on ventral pallidum for sensory pleasures is that electrophysiological recordings of neurons in its same hotspot, by Amy Tindell in her own dissertation study in the Aldridge laboratory, revealed vigorous firing in response to the taste of sugar (Tindell et al., 2004). With learning, ventral pallidal neurons shifted their activation pattern gradually to fire in response to predictive cues that were associated with sweet reward. Still, neurons continued to fire vigorously when the rats received their sugar pellet reward, suggesting that the neurons may encode persisting hedonic pleasure too.

A third reason is that neurons in the ventral pallidum appear to be especially crucial to normal hedonic 'liking' perhaps more so than in almost any other brain structure. That conclusion was suggested by an earlier lesion study in our laboratories by Casey Cromwell, who showed that destruction of neurons within the ventral pallidum hotspot eliminated normal 'liking' reactions to sweet tastes and replaced them with 'disliking' reactions (Cromwell and Berridge, 1993). Cromwell found that damage to ventral pallidum was more important to the loss of core 'liking' reactions than other nearby brain structures that had traditionally been associated with lesion-induced aversion (e.g., lateral hypothalamus). Indeed ventral pallidum might be the only brain structure known where discrete lesions can convert pleasure 'liking' to 'disliking'.

A final reason to think that this brain structure participates in applying a core 'liking' gloss is that the ventral pallidum in people has now been shown also to increase activity in response to diverse human rewards from food to money, even when the reward stimulus is so subliminally brief that it is not consciously perceived (Beaver et al., 2006; Childress et al., 2008; Pessiglione et al., 2007; Small et al., 2008). These considerations suggest that the ventral pallidum is a promising candidate to find out how the pleasure gloss looks from the point of view of the neurons that might apply it.

In terms of its neuroanatomical connections, the ventral pallidum receives convergent signals from the nucleus accumbens, a brain structure that is implicated generally in rewards (see Figure 3.1) (Baldo and Kelley, 2007; Burke et al., Chapter 2, this book; Carelli and Wightman, 2004; Day and Carelli, 2007; Garris and Rebec, 2002; Knutson et al., 2001a; Kringelbach, Chapter 12, this book; Leknes and Tracey, Chapter 19, this book; Salamone et al., 2007; Schultz, 2006; Smith et al., Chapter 1, this book; Wan and Peoples, 2006). Ventral pallidum also receives signals from other key limbic structures in the forebrain such as amygdala, orbitofrontal cortex, and insular cortex, as well as inputs from reward-related structures in the brainstem such as ventral tegmentum and parabrachial nucleus (Groenewegen and Trimble, 2007; Heimer and Van Hoesen, 2006; Kalivas and Volkow, 2005; Zahm, 2006). In return, the ventral pallidum sends output signals back to limbic areas of prefrontal cortex via the dorsomedial thalamus (Figure 3.1), including orbitofrontal, anterior cingulate, and insular regions of cortex. Ventral pallidum projects as well to many other brain structures involved in reward and thus may serve as a common focal point for integrating and distributing pleasure-related signals. Our studies exploit the ventral pallidum's natural pleasure responses to tasty foods to probe neural coding mechanisms of its hedonic gloss. The pleasure of foods is primary and is evolutionarily programmed into brains so much so that food pleasure may be one driving force behind the obesity epidemic today (Finlayson et al., 2007; Mela, 2006; Pelchat et al., 2004; Zheng and Berthoud, 2007). By recording firing patterns of neurons in the ventral pallidum hotspot at moments when rats are given pleasant and unpleasant tastes, we are able to probe hedonic coding mechanisms directly.

Amy Tindell, Kyle Smith, and others in our laboratory have begun the task of dissecting the hedonic qualities of food tastes in the pattern of firing activation of ventral pallidal neurons (Tindell et al., 2006). In the experiment described below, 'liking' and 'disliking' reactions were elicited from rats by the taste of salt, sugar, or plain water solutions infused directly into their mouths (painlessly and without disturbing them via tubes attached to oral cannula that had been previously implanted when they were anesthetized) (Tindell et al., 2006).

Sensory pleasure or aversion evoked by the tastes was determined by measuring facial affective 'liking' or 'disliking' reactions on video recorded in temporal synchrony with neural recordings on a computer. The natural positive 'liking' reactions elicited by

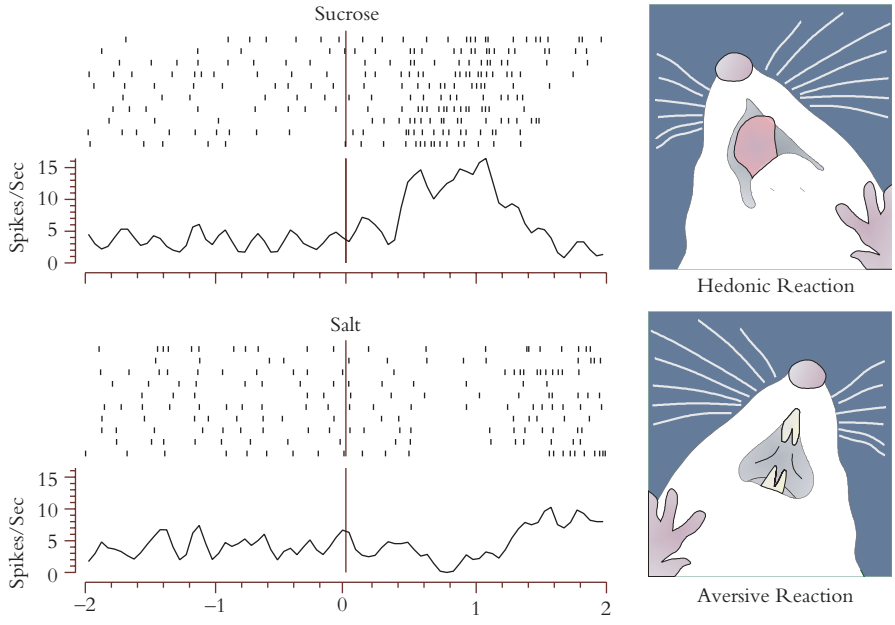

Figure 3.2 Neural responses in a single neuron to infused tastes of sucrose and salt. The perievent rasters on left consist of 10 trials aligned at time = 0 to the moment the infusion pump started. Each row represents a single trial and each dash represents a single spike. The histogram (line below each raster) shows the averaged response across all trials. Activity increased with the sucrose and decreased with concentrated salt tastes. The taste reactions are illustrated to the right. Sucrose evokes hedonic tongue protrusions while salt triggers gape movements.

pleasurable tastes, and 'disliking' reactions elicited by aversive tastes, reflect core pleasure/displeasure evaluations of taste in many different species, including infant humans, and nonhuman primates and rodents (Berridge, 2000). Positive hedonic taste reactions include anterior and lateral tongue protrusions (see Figure 3.2), and (in rats) paw licking movements. Aversive reactions, by contrast, include mouth gapes (see Figure 3.2) that spit out the taste solutions, along with headshaking, forelimb flailing, and (in rats) face washing and chin rubbing movements.

Isolating the Pleasure Code

We compared firing patterns in ventral pallidum during small infusions of pleasurable sugar (sucrose) solutions or aversively intense salt (NaCl) solutions. The crucial experimental strategy employed to dissociate sensory taste qualities (salty vs. sweet) from hedonic valence ('liked' vs. 'disliked') was to convert the unpleasant taste of a concentrated salt solution temporarily to one that was pleasant. The salt solution was three times more concentrated than seawater, or 10 times more concentrated than tears. Such an intense taste is normally too salty to most rats as well as to most people. The salty sensory stimulus itself did not change in our experiment; only the pleasurable affective quality of the taste changed dramatically and thus could be dissociated from sensation. That is, the *hedonic valence* was converted from *bad to good* by a physiological appetite, but the salt solution itself was the same on the tongue. (We note as slight caveat that salt appetite can produce minor sensory changes in brainstem gustatory nuclei, but those changes mostly make taste systems more sensitive to saltiness—which normally would make intense salt even worse. So those minor sensory changes could never explain why concentrated salt taste becomes pleasant.)

It is also important to note that this experimental strategy does not rely on learning in order to alter the hedonic value. Learning-based revaluations are themselves interesting and able to change hedonic valence, but they are complicated and introduce the possibility of alternative interpretations besides a change in core 'liking' reaction (for example, a change in reward

expectations instead). Here we wished to focus on the basic hedonic reaction to taste, free of any other complication that we could avoid, and so a purely physiological method was used to change hedonic impact.

Converting the taste of concentrated salt solutions from negative to positive valence was effected by inducing a temporary physiological state of sodium deficiency (via furosemide/DOCA injections, which cause the kidneys to excrete sodium and stimulate brain systems of salt appetite) (Cabanac, 1971). Sodium deficiency induces a psychological appetite to ingest salt, which involves a selective increase in the hedonic perception of salty tastes (Schulkin, 2003). This phenomenon of a change in the hedonic quality of a sensation is called taste "alliesthesia" (Cabanac, 1971, Chapter 7, this book). People display salt appetite and alliesthesia too (Beauchamp et al., 1990). In fact, one of the first scientific reports of salt appetite was a case study of a young boy with an adrenal gland dysfunction, who insisted on eating handfuls of salt each day, and seemed to think of it as candy, to the alarm of his parents (Wilkins and Richter, 1940). In a physiological salt appetite state, 'disliking' gapes and other aversive reactions of rats to intensely salty tastes are diminished and replaced by hedonic 'liking' reactions (Berridge et al., 1984; Schulkin, 1991). Salt appetite exerts powerful effects on brain limbic processing. For example, inducing a salt appetite alters the morphology of nucleus accumbens neurons and changes dopamine and enkephalin release into the nucleus accumbens (Lucas et al., 2003; Roitman et al., 2002). Even previous exposures to salt appetite can have longlasting consequences, such as increasing the behavioral response to amphetamine through alterations in D2 dopamine receptor function (Clark and Bernstein, 2006). The powerful reach of salt appetite into brain limbic operations makes it a useful tool to probe the pleasure code in ventral pallidum recording experiments.

When Tindell and her colleagues put rats into a state of increased salt appetite, the aversive taste reactions to salt fell nearly to zero (Tindell et al., 2006), approaching the extremely low levels seen with sucrose. Most importantly, salt tastes were now 'liked' by rats as evidenced by increased numbers of positive hedonic facial reactions, such as tongue protrusions, that rose from near-zero to counts equaling those seen with sucrose tastes.

The neural representation of tastes was assessed by recording firing patterns of neurons in the hedonic hotspot of the ventral pallidum during behavioral testing. With this method, Tindell and her coworkers were able to show that firing rates of ventral pallidal neurons were directly correlated to 'liking' (hedonically positive behavioral reactions). Firing rates in response to sugar tastes were high while firing rates to tastes of salt solutions were low in the normal homeostatic physiological state (see Figure 3.3). After inducing a

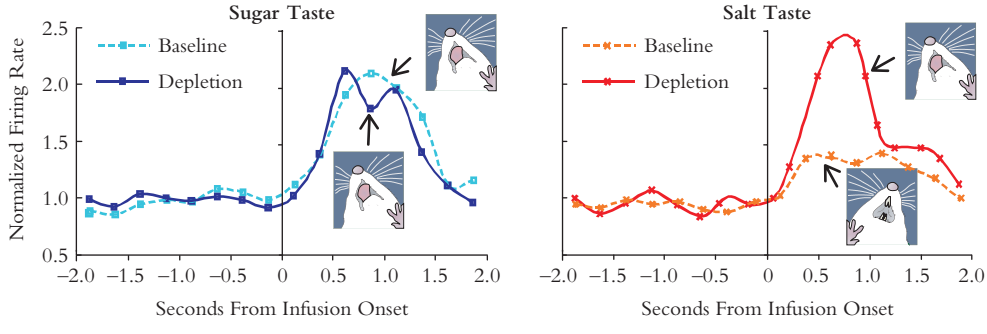

Figure 3.3 Average firing rates (normalized, relative to prestimulus baseline) of all neurons (n = 167 neurons) recorded in the ventral pallidum hotspot to sugar (left) or salt (right) taste infusions, which occurred at time = 0 on x-axis. Most neurons were excited by taste infusions and thus, on average the net change was an increase in firing. Neural responses to sugar did not change with salt depletion, but the response to salt increased dramatically during the salt appetite state, reaching peak amplitudes similar to sugar (solid line, right panel). In general, there were few inhibitory responses to salt tastes (6% before and 6% after depletion) and to sucrose tastes (1% before and 19% after depletion). Depletion (salt appetite) did not change the bias toward excitation significantly (Tindell et al., 2006). The insets indicate hedonic reactions to sucrose and aversive reactions to salt in baseline (dashed lines). After salt depletion (solid lines) the taste reactions to salt switched to hedonic.

physiological state of sodium deficiency, however, firing rates to infusions of salt tastes rose to equal or even exceed firing to sugar (Figure 3.3). In other words, ventral pallidal neurons fired faster when a taste was 'liked' and slower when a taste was 'disliked'. Thus the affective neural and facial responses to concentrated salt tastes were a function of the physiological state interacting with its sensation and not the sensory quality per se.

These findings suggested that firing rates of ventral pallidal neurons may be contributing to a neural code that implements the hotspot of hedonic value or sensory pleasure of taste. Neural firing changes in the ventral pallidum tracked the hedonic reversal of salt palatability specifically. Firing to sucrose tastes, which continued to evoke hedonic facial reactions in both physiological states, was relatively unchanged. Ventral pallidal neurons always fired at high rates to sucrose, and the rats always showed positive 'liking' reactions behaviorally, indicating the hedonic impact of sweetness remained constant. Since the sensory qualities of the stimuli did not change for either salt or sucrose, the changing activity of the ventral pallidum could be viewed as transforming the taste of salt with *a glaze of hedonic pleasure*. In this case, the pleasure gloss of neuronal firing was sufficient to convert a normally aversive sensation to one that is hedonically positive.

Separating the Code for Pleasure from Learning, Arousal, Movement…

Several features of our experiment were designed to help rule out alternative interpretations of the findings. For example, sucrose and salt stimuli were unchanged, and the physiologically induced salt deficient state had never been experienced by the rats before, which combine to rule out simple sensory or learning interpretations.

Other alternative explanations can be discounted in various ways. First, the experiment was designed to bypass all voluntary behavior or decisions by the rat that might have modulated its consumption of a taste and its resulting pleasure. All tastes were infused directly into the mouth in the same manner in every animal. Thus, rats could not "turn off" their experience of unpleasant salt, for example, by moving away from it. They could not change the amount of salt in their mouth to dilute it and so increase its pleasure. Further, acknowledging that behavioral electrophysiologists must always be alert to the possibility that movements might account for neural firing (as either neural commands to move or feedback from the movement), we took special steps to see whether movement coding could be ruled out.

We performed detailed analyses of movement reactions, and the results suggested that a simple motor explanation for the findings was unlikely. First, we found that the timing of neural firing to a taste differed substantially from the timing of motor reactions (assessed by a frame-by-frame video analysis of taste reactions). Ventral pallidal neurons fired nearly a second (800 ms) before taste reactions, which is much longer than one might expect in a neural circuit directly coupled to movement execution. Timing of this sort is much more likely to reflect a sensory-evoked psychological function, such as signaling hedonic impact. In addition, neuronal firing died away at the end of the taste stimulus, while the movements of 'liking' or 'disliking' reactions persisted for up to 10 s longer. These temporal dissociations suggest that neural firing was bound to sensory taste pleasure rather than to movements.

Finally, many movements of the mouth occurred when ventral pallidal neurons remained silent, especially when movements occurred spontaneously outside of a taste presentation. Still, we note in passing, for readers interested in the relation between affective and motor functions, that although hedonic activation patterns described above cannot be explained by simple movements, it does not completely exclude some role for the ventral pallidum in motor control, for example, perhaps a role in translating affect into movement.

The ventral pallidum is anatomically well-positioned to play an important role in higher levels of motor expression, consistent with the original Mogenson's proposal nearly 30 years ago that it may transform motivation to action (Mogenson et al., 1980). The basal ganglia have long been thought of as key structures in selecting appropriate movements from competing motor programs (Mink, 1996). Such ideas are entirely compatible with our view that ventral pallidum implements a pleasure gloss on stimuli and behavior. One idea we think worth considering is that the ventral pallidum could impart a motivational context function to movement selection, which is especially visible in the process of facilitating species-specific facilitatory consummatory actions that are often hedonically laden (eating, copulation, etc.) (Glickman and Schiff, 1967). It is axiomatic that pleasure mechanisms of the brain evolved to serve survival value (Frijda, Chapter 6, this book), and to

the degree that engaging in particular actions promote survival, it seems plausible that some pleasurable actions might tap rather directly into ventral pallidal hotspot mechanisms, resulting in neural activity that occurs in tandem with movement.

Pleasure Versus Displeasure

In addition to pleasure, the brain must represent aversion or negative hedonic value. Does the ventral pallidum have this role too? A definitive answer is not possible from our experiments, but the data so far do not strongly support such a role at least in the caudal part of the ventral pallidum studied. In normal sodium balance, highly concentrated salt solutions evoked aversive reactions and although the corresponding firing rates were low, they still differed from no taste at all in the baseline period (see Figure 3.3). Could these lower (but still above baseline) firing rates represent a negative hedonic value of nasty salt? A bivalent coding scheme structured in this fashion would mean that baseline rates would represent no taste input while aversive tastes were represented by low elevations and hedonic tastes represented by high elevations of neural firing rates (and presumably neutral tastes might be represented by intermediate elevations that occur during an oral infusion). Although such a scheme is theoretically possible, it has logical difficulties and seems a potentially fragile mechanism. One problem with this idea, at least as stated so simply earlier, is that it means that with every "nice" taste encountered the trajectory of neural firing would be such that for a moment in time as the firing rate first passed through an intermediate range the signal would represent a "bad" taste and then a "good" taste. That seems delicate, and additional mechanisms would be needed to make this coding scheme work.

A related question, then, is just how the firing pattern of ventral pallidal neurons represents pleasure? The question remains unanswered, but we suspect the eventual answer will be more complicated than the mere firing *rate* code we have described so far. Of course, caution is always needed in assigning psychological processes in a one-to-one fashion to particular neuronal firing patterns. We think that neural firing rates alone, without taking other factors into consideration, are unlikely to fully account for a psychological affective reaction, whether it be pleasure or aversion.

There are other sites connected to ventral pallidum that are also involved in the hedonic code. There are also other possible coding mechanisms besides mere rates, for example, more complex patterns of spike timing and interspike intervals, and temporal and spatial patterns of selective activation that extend across multiple neurons to form coordinated networks. Dynamic recruitment of neuronal assemblies that form coordinated circuits within the ventral pallidum, and larger assemblies that stretch to other brain structures, including nucleus accumbens, brainstem, and orbitofrontal cortex, is likely to be crucial in generating pleasure or displeasure.

Even our own work has already shown that there is a likely population coding mechanism involved as well as rate coding. For example, we observe that more neurons are recruited during the presentation of 'liked' tastes than 'disliked' tastes, and even during conditioned stimuli that predict those 'liked' tastes. Neurons in related circuits that extend through globus pallidus and subthalamic nucleus are thought to have complex and irregular patterns of activity that defy notions of simple rate coding (Terman et al., 2002) and similar rules may hold for ventral pallidum. Future investigations will need to consider these possibilities, along with the organizational features between structures, to uncover interconnected firing patterns that might participate in codes for pleasure. Still, the identification of firing patterns in neurons of the ventral pallidum hotspot that appear to code pleasure, as described earlier, is an important step forward in the search for neural assemblies that use coded signals to add a gloss of pleasure to ongoing sensations and behaviors.

Beyond Pleasure: Other Reward Features Coded by Ventral Pallidum

Although ventral pallidal activity correlates to hedonic impact or pleasure gloss as described above, ventral pallidal circuits also code other additional features of reward alone besides pleasure, and neurons in the ventral pallidum hotspot may possibly be able to track each feature separately (Smith et al., 2007; Tindell et al., 2005). Besides pleasure or 'liking', reward also involves 'wanting' (motivation or incentive salience) and learning features (associations between predictive cues and hedonic rewards) (Berridge, 2007; Berridge and Robinson, 2003). Ventral pallidum firing carries encoded signals for these other aspects of reward in overlapping neuronal populations. For example, learning: after rats have learned that a Pavlovian conditioned stimulus (CS; an auditory tone) predicts sugar pellet rewards, some neurons in the ventral pallidum fire to the predictive CS as well as to the sweet reward

itself, while other neurons respond to only predictive CS or to the sweet reward itself (i.e., unconditioned stimulus [UCS]) (Tindell et al., 2004, 2005, 2006). Neural activity in the ventral pallidum is associated with incentive 'wanting' properties of reward too (Lim et al., 2004; McFarland et al., 2004; Tindell et al., 2005). For instance, when incentive 'wanting' is amplified selectively and pulled apart from learning by sensitizing or pharmacologically activating mesolimbic dopamine systems that magnify incentive salience, ventral pallidal neurons fire higher bursts of action potentials to cues that carry the highest incentive salience (Tindell et al., 2005).

There is reason to think that the dopamine magnified 'wanting' signal instantiates a relatively pure code for incentive salience, because the Tindell experiment was arranged in way that separated the CS with the highest incentive salience from a different CS learned previously with the highest predictive value, and from the sweet reward (UCS) that gave the highest pleasure. The results of that experiment showed that dopamine magnification did not magnify either a predictive learning signal or a hedonic 'liking' signal, although both of those signals passed through ventral pallidal neurons too, but instead selectively magnified the incentive 'wanting' signal alone (Berridge and Aldridge, 2008; Tindell et al., 2005). Manipulations that alter the constellation of dopaminergic activity across limbic structures modulate the profiles of neural activity in ventral pallidum to separate 'wanting', 'liking'. and "predictive learning components" of reward (Tindell et al., 2005).

Thus, parsing the pleasure properties of food reward from 'wanting' and learning properties, as well as from sensation and movement properties, is an achievable experimental goal even if a challenging one. When it is done, results so far suggest that ventral pallidal neurons may keep track of each reward feature in a manner that allows tracking the features separately. It is an exciting task to try to understand the interactions among these various properties of rewards in coded signals as ventral pallidum processes pleasure information together with other sensory, motor, motivational, predictive, or cognitive aspects of reward.

Commingled 'Wanting' and 'Liking'

Neural codes for 'liking' pleasure are likely to commingle (i.e., be "multiplexed") with codes for 'wanting' and "learning" about those pleasures even on individual neurons. Multiplexed signals commingle in a manner akin to how wire and optical communications systems carry telephone or computer data signals from multiple telephone conversations, email communications, and internet web traffic over a single wire. Just as the different signals can be resolved at their destination by receivers that decode appropriately, we believe that multiple reward signals can be packed into the activity of single ventral pallidal neurons in much the same way, for potential unpacking downstream. The different signals represent different information about the reward at different moments, or perhaps multiple signals encoded in complex patterns of firing at the same moment. Decoding neural communication systems will involve parsing these multiple signals.

One reason we believe that multiple functional signals are carried by single neurons of the ventral pallidum is that we have observed a single neuron to encode all three signals, pleasure 'liking' motivation 'wanting', and "predictive learning" at various moments or in different ways (Smith et al., 2007; Tindell et al., 2005). The firing patterns produced in the same neuron by the three signals, however, are not necessarily identical even when the neuron is. For example, the same neuron may respond to the different signals with different temporal patterns of multispike activity. Individual neurons and the population as a whole often exhibit patterns of activity with highly complex *profiles* representing combinations of predictive information, reward value as well as incentive, in which different information signals can be discerned to be embedded in different aspects of the firing profile (Tindell et al., 2005). Further, these individual "information channels" can be manipulated experimentally such that the overall *profile* can change to selectively alter one signal more than others. For example, as mentioned above, mesolimbic activation by acute amphetamine injections or by sensitization results in a relative boost of the incentive component over reward value and predictive information in the overall activity profile of the same neurons (Tindell et al., 2005). Thus, it is conceivable that a pleasure gloss on behavior or sensations (i.e., 'liking') may also be represented by subtle and complex aspects of the firing profile that have yet to be uncovered.

Commingling together of 'liking' and 'wanting' signals in the same ventral pallidal neurons may be part of the reason why most rewards are both 'wanted' and 'liked' together. In normal circumstances, we like what we want and want what we like (see Question 4 in Pleasure Questions section

of this book). The integrative nature of neural profiles in the ventral pallidum and the fact that this structure lies at an output nexus in the reward circuit suggest that the ventral pallidum may subserve a role for glossing sensations with pleasure as well as imbuing incentive value. It is the combination of a pleasure gloss with sensations or behavior and the ability of neurons in the ventral pallidum to have comingling signals that may allow the ventral pallidum to subserve a pleasure-glossing mechanism, and perhaps also help translate hedonic 'liking' into motivational 'wanting' for the same reward.

Reward in Other Brain Structures

We have focused here on the ventral pallidum as a hedonic hotspot that has special roles in coding and generating core 'liking' reactions to pleasure, but, of course, as mentioned in the beginning, many other brain regions participate with ventral pallidum to play roles in reward (see many other chapters in this book). For example, Morten Kringelbach has summarized cogent evidence that the orbitofrontal region of prefrontal cortex is especially important for cortical representations of reward (Kringelbach, 2005; Kringelbach, Chapter 12, this book). Additional cortical areas such as rostral insula, frontal operculum, and anterior cingulate cortex also respond to pleasant tastes, odors, sights, and textures of foodstuffs, and other sensory rewards, and participate in positive emotional reactions to diverse learned cultural rewards, ranging from attractive photographs and winning money to humor, art, and music (Blood and Zatorre, 2001; Burke et al., Chapter 2, this book; Feldman Barrett and Wager, 2006; Knutson et al., 2001b; Kringelbach, Chapter 12, this book; Rolls, 2005; Skov, Chapter 16, this book; Small and Veldhuizen, Chapter 9, this book; Watson et al., 2007).

A number of subcortical brain structures also code reward and interact with ventral pallidum. They include the mesolimbic dopamine system and its chief targets in the nucleus accumbens as well as the amygdala and other limbic structures. Wolfram Schultz and colleagues showed that mesolimbic dopamine neurons themselves are activated by food rewards, especially when they are surprising, as well as by cues that predict those rewards (Schultz, 2006). Many studies have shown the nucleus accumbens to be implicated in almost every type of reward (Everitt and Robbins, 2005; Green et al., Chapter 18, this book; Leyton, Chapter 13, this book; Smith et al., Chapter 1, this book), and the amygdala is also activated by many rewards including food, drugs, pleasant photographs, and sex (Burke et al., Chapter 2, this book; Komisaruk et al., Chapter 10, this book; Phan et al., 2002).

Several studies have demonstrated that cortical brain regions are especially activated by food rewards when individuals are hungry, but activation declines to the same reward after the individuals eat to satiety (Burton et al., 1975; Kringelbach, 2004, in press; Kringelbach et al., 2003; O'Doherty et al., 2000). These studies used an experimental logic similar to the salt appetite experiments we described above to show specifically that reward was coded by the brain activations they measured. Other studies have used learning to devalue a reward, for instance, by pairing the reward with an aversive event such as visceral illness in a learned taste aversion paradigm to similarly implicate reward or value predictions as the function embodied in the neural activation (Burke et al., Chapter 2, this book; Dickinson and Balleine, Chapter 4, this book). All such studies provide important insights into how brain systems code and process reward-related information.

Conclusion

The ventral pallidum is just one brain structure among many that code reward, but it may be special in applying the pleasure gloss to stimuli that makes them rewarding. It contains a hedonic hotspot that is both needed to generate normal core 'liking' reactions to pleasant stimuli and able to amplify 'liking' reactions to double normal levels when neurochemically stimulated. Neural firing in the ventral pallidum hotspot encodes 'liking' for the positive hedonic impact of sweet and salty taste rewards in a specific fashion. These coded 'liking' signals may reflect pleasure gloss generation from the neurons' point of view. The same neurons code other reward components too using different signal patterns (e.g., motivation 'wanting' and predictive learning), and link to other brain sites that participate in generating those components as well as hedonic 'liking'.

It seems plausible that ventral pallidum firing patterns mediate 'liking' for other natural sensory pleasures besides food and drug and other pleasures too. And, although our studies have used rats instead of people, we think our finding of pleasure coding in neuronal firing patterns of the ventral pallidum has direct implications for understanding the generation of the pleasure gloss in humans and for the way people perceive pleasure. As a result, conceivably, dysfunction

in ventral pallidum firing and in its connections could be one reason why some people develop pathological problems that distort pleasure such as depression or that distort incentive salience and lead to pursuit or consumption of rewards, such as drug addiction, eating disorders, or compulsively excessive gambling. That is, if ventral pallidum signals code the normal hedonic impact of rewards, then pathological distortions of those hedonic signals might knock their pleasure response off balance, and contribute to hedonic dysfunction. Thus the ventral pallidum is an ideal focus for affective neuroscience studies to probe the causal brain mechanisms that gloss sensations with pleasure. It may be equally useful for understanding disorders of pleasure mechanisms and even perhaps eventually to develop more effective treatments.

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