

Parsing reward

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Advances in neurobiology permit neuroscientists to manipulate specific brain molecules, neurons and systems. This has led to major advances in the neuroscience of reward. Here, it is argued that further advances will require equal sophistication in parsing reward into its specific psychological components: (1) learning (including explicit and implicit knowledge produced by associative conditioning and cognitive processes); (2) affect or emotion (implicit 'liking' and conscious pleasure) and (3) motivation (implicit incentive salience 'wanting' and cognitive incentive goals). The challenge is to identify how different brain circuits mediate different psychological components of reward, and how these components interact.

Studies of the neurobiology of reward are important to advance affective neuroscience, and they provide insights into a variety of psychopathologies, including drug addiction, eating disorders, obsession and depression. Progress has been helped by the ability of neuroscientists to manipulate an ever-expanding number of brain components. Future studies will be most useful for elucidating the roles of brain components if they can similarly parse behavioral reward into its actual psychological components.

For example, imagine a new inducible knockout mouse that shows abnormally slow (or fast) acquisition of cocaine self-administration behavior. The gene manipulation apparently alters cocaine reward – but which part of reward? Reward contains multiple psychological components (Fig. 1). The mutation might have changed any of them, and their implications for function are very different. To say simply that a brain manipulation alters reward, without specification, is akin to saying it alters a 'neurotransmitter receptor' – without specifying which receptor or even which neurotransmitter. It is important to be more precise.

What are the psychological components of reward? First, it is necessary to learn about relationships among stimuli and about the consequences of actions. Second, reward consumption can produce hedonic consequences. Third, the individual has to be motivated to learn and act. Further, each of these three explanatory classes contains multiple component psychological processes, any of which could be affected by a neurobiological manipulation. Neuroscientists will find it useful to distinguish these psychological components of reward because understanding the role of brain molecules, neurons and circuits requires understanding what brains really do – which is to

mediate specific behavioral and psychological functions. The following summarizes some important psychological components of reward, many of which have been revealed by neurobiological manipulations.

Learning

Multiple forms of learning are mediated by different brain systems, and a change in any one of them might change rewarded responses [1–7]. Learned responses require knowledge – of some type – about the relationships between stimuli and actions. Knowledge is required for reward prediction, for making anticipatory responses, for guidance by cues, and for goal-directed action. Learning processes can be either associative or cognitive. The products of learning can be declarative (conscious memories) or procedural (habits). And the elements of learning can involve just stimuli [stimulus–stimulus (S–S) associations and predictive reward expectation] or involve responses too [stimulus–response (S–R) associations and act–outcome representations].

Associative learning usually refers to either Pavlovian conditioning (S–S and S–R associations) or instrumental conditioning (response–contingent reinforcement). In Pavlovian conditioning, which is a procedural form of reward prediction, conditioned stimuli (CSs) elicit conditioned responses (CRs). The CRs can be anticipatory responses, behavioral habits or even conditioned motivations and emotions appropriate to the unconditioned reward stimulus (UCS). In instrumental conditioning, specific instrumental responses are strengthened by response–contingent reinforcement. Neural substrates for Pavlovian and instrumental associations are distributed relatively widely across both subcortical and cortical brain structures [4,8–10].

Cognitive forms of knowing are more elaborate [11,12]. They encode multiple relationships among stimuli and actions, including declarative representations of temporal, spatial, predictive and causal relationships that guide goal-directed plans of action. Brain mechanisms of cognitive reward representation are more heavily cortical and include orbitofrontal, insular and other regions of cortex, plus particular subcortical structures that interact with cortical regions [2,11,13,14].

Thus, neural manipulations could influence rewarded behavior because they alter any one of many forms of learning. But their particular consequences will depend on precisely which form is altered.

Reward: more than learning

Alternatively, neural manipulations can alter an affective (emotional) or motivational process. Components of

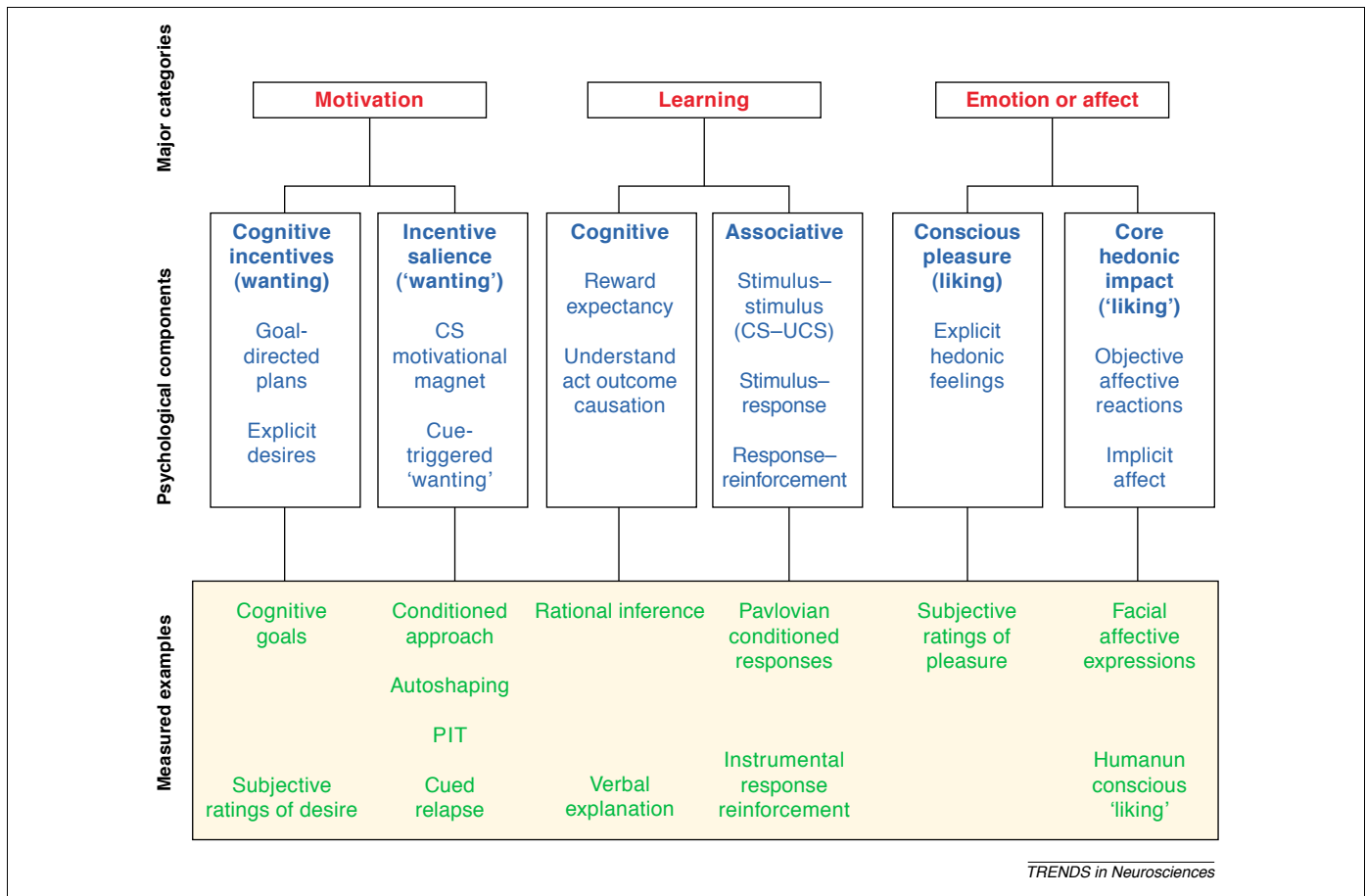


Fig. 1. Reward components and how to recognize them. The categories of learning, motivation, and emotion or affect categories (top, in red) each contain different psychological components as shown (middle boxes, in blue). Both explicit and implicit psychological component processes are contained in each top category. Explicit processes are consciously experienced (e.g. explicit desire, expectation or pleasure), whereas implicit psychological processes are unconscious in the sense that they can operate at a level not always directly accessible to conscious experience (implicit incentive salience, habits and 'liking' reactions). Additional psychological and neural processes of cognitive awareness can sometimes transform the products of implicit processes into explicit representation, but explicit awareness is not necessary for implicit processes to powerfully influence behavior [5,12,18,22]. Explicit versus implicit processes within a single category (e.g. motivation) also can operate by quite different psychological rules (e.g. conscious desires based on cognitive expectations versus cue-triggered incentive salience based on Pavlovian associations) and can have different neural mechanisms. At the bottom are listed some behavioral procedures or measures (in green) that are especially sensitive assays of the processes listed above them. For example, incentive salience ('wanting') is revealed especially through conditioned incentive approach and Pavlovian-to-instrumental transfer (PIT) experiments [5,23,45,47,50,54,55], whereas explicit desires and plans are revealed through subjective reports and experiments that study goal-directed behavior [5,12-14,50,55,58]. Although each psychological category is depicted in a separate column here for simplicity, it is stressed that categories of motivation, learning and emotion or affect constantly interact in reward. Even each measured behavioral example listed here involves a combination of motivation, learning and affective processes (although the behavioral examples are particularly sensitive to different processes). In fact, brain manipulations are needed to dissociate many of these processes to reveal their psychological and neural separation. For example, the dissociation of 'wanting' motivation versus 'liking' affect or emotion has been revealed chiefly by manipulations of mesolimbic dopamine systems that changed reward 'wanting' without changing reward 'liking' [21,23,26,27,48]. Abbreviations: CS, conditioned stimulus; UCS, unconditioned reward stimulus.

emotional and motivational processes have received less attention from neuroscientists than learning, but neurobiological studies have now illuminated several distinct components that need to be considered.

First, it is important to note that emotional and motivational components can exist objectively apart from conscious awareness of them. That is, they can occur implicitly. Why posit implicit components of reward? One reason is that people sometimes react to a rewarding stimulus without any apparent awareness of either the stimulus or their own hedonic reaction. For example, drug addicts in some circumstances will work for low doses of stimulants or morphine, doses that produce no subjective effects and even no autonomic responses, without being aware that they are doing so [15-17]. Implicit emotion can occur in people who are not addicts too. For example, a subliminally brief view of happy facial expressions produces no change in subjective feeling or mood ratings at

the moment it occurs. But it still causes thirsty people to consume more of a fruit drink moments later and to give higher subjective value ratings to the pleasantness, attractiveness and monetary value of the drink - all with no awareness that they either saw the subliminal stimulus or had an emotional reaction [18]. These and related findings have prompted suggestions that implicit affective reactions can exist objectively without necessarily being experienced subjectively [18-20].

The existence of both implicit and explicit reward processes poses a nuisance of complexity, although not more so than traditional distinctions between implicit and explicit memories. Yet there is a potential benefit for affective neuroscience if implicit reward is separable from its subjective feelings, because then core reward processes might be more amenable to objective measurement in experiments where brain systems are manipulated - even in animals. One fundamental distinction among core processes

of reward that has recently become apparent is between the affective consequences of rewards ('liking') and their motivational consequences ('wanting') [21–23].

Affect (core 'liking' and conscious pleasure)

If conscious pleasure is a subjective affective reaction, then what we have called 'liking' (in quotes) is an objective affective reaction (Box 1). 'Liking' for tastes involves activity in a distributed neural network that also has been implicated in drug reward. One neural component of 'liking' involves opioid neurotransmission onto GABAergic spiny neurons in the nucleus accumbens (especially in the shell region). Microinjection of opioid agonists into the

accumbens shell causes increased facial 'liking' reactions to sweetness [24,25]. Similarly, GABA-receptor feedback onto spiny neurons can either increase or decrease 'liking' depending on microinjection location in the shell [26]. Other components include mesolimbic outputs to the ventral pallidum, and related structures elsewhere in the brain [27–29] (Fig. 2).

Interestingly, the neurotransmitter that traditionally has been most touted for mediating sensory pleasure, dopamine, turns out to be neither necessary nor sufficient for generating 'liking' [21,22]. 'Liking' expressions for sweet tastes are not changed by either activation or suppression of mesolimbic dopamine systems [23,30–33]. Even massive 6-hydroxydopamine (OHDA) lesions that eliminate nearly all dopamine in the nucleus accumbens and striatum and produce profound aphagia fail to disrupt taste 'liking' [21]. And activation of accumbens dopamine activity by amphetamine microinjection in the shell of the nucleus fails to increase 'liking', despite increasing a different motivational component of reward [23]. Consistent with this, dopamine-receptor antagonists often do not suppress the subjective pleasure ratings of amphetamine or cigarettes in humans [34–36]. Finally, activation of the human accumbens–striatal dopaminergic systems by amphetamine has been reported to correlate better with subjective ratings of wanting for drug or food reward than with subjective ratings of pleasure [37,38]. Thus, despite the popular view, dopamine is not after all a pleasure neurotransmitter in the sense of mediating immediate hedonic impact. It does not mediate objective 'liking' for sweet rewards in animals, and accumulating evidence suggests that it does not mediate subjective pleasure of drug rewards in people. Naturally this forces consideration of alternative roles for dopamine in reward. Suggestions have included incentive salience, reward learning and other functions [21,39–44].

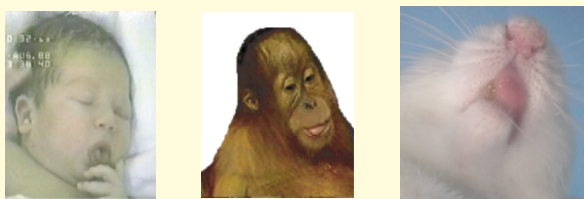
Box 1. 'Liking'

Examples of objective hedonic 'liking' reactions include affective facial expressions elicited by the hedonic impact of tastes in human infants and many animals (Fig. 1). The sweet taste of sucrose elicits positive facial 'liking' expressions (e.g. tongue protrusions), whereas bitter quinine elicits instead facial 'disliking' (e.g. gapes). These affective expressions are homologous in humans, orangutans, chimpanzees, monkeys and even rats and mice [60,61], and the degree of expression similarity mirrors the degree of phylogenetic relatedness. Homology of 'liking' reactions is also indicated by sharing of the same identical rule for generating certain aspects of expression microstructure, such as allometric timing [60,61]. For example, the duration of expression components observes the equation:

$$\text{expression duration (ms)} = 0.26 \times [\text{species weight (kg)}]^{0.32}.$$

This rule means a human or gorilla tongue protrusion or gape might appear languidly slow, whereas a rat or mouse reaction seems blinkingly fast, yet all have identical timing 'deep structure' scaled to their evolved size. 'Liking' timing rules for each species are actively programmed by brain circuits, not passively constrained by size – for example, infants and adults share the same species timing, despite their different sizes [60,61]. In upshot, the probable homology of 'liking' reactions indicates that studies of neural mechanisms in one species (rats) can provide general insights into brain hedonic circuits that will apply also to others (including humans).

'Liking' expression – sweet



'Disliking' expression – bitter



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Fig. 1. Objective 'liking' reactions. Homologous affective facial expressions by infant human [60], juvenile orangutan [60] and adult rat [61] to 'liked' sucrose (top) versus 'disliked' quinine (bottom). 'Liking' reactions are neurally modulated by a distributed brain network that includes the nucleus accumbens shell, ventral pallidum and brainstem parabrachial nucleus [24–28]. Reproduced, with permission, from Ref. [60].

Motivation [incentive salience ('wanting') and cognitive wanting]

If the word wanting generally refers to a conscious or subjective desire, then the term 'wanting' (in quotes) can be used as a short-hand phrase to refer to an underlying implicit and objective motivation process: incentive salience. Rewards that are 'liked' are usually also 'wanted'. Indeed, most traditional formulations of incentive motivation viewed 'wanting' and 'liking' to be so causally connected that they were considered effectively identical – two words for the same process. But 'wanting' and 'liking' are in fact dissociable and have different neural substrates [21–23,27,30,31]. Although usually activated together, they can be pulled apart by brain manipulations. The dissociation and isolation of 'wanting' has been especially useful in understanding the contribution of mesolimbic dopamine to reward (Box 2).

The concept of incentive salience was first proposed by Berridge and Robinson [21,22] because of the findings already mentioned here: that manipulation of dopamine systems powerfully changes motivated behavior (instrumental performance and consumption of rewards) but not taste 'liking' (affective facial expressions). So if 'wanting' is not 'liking', what is it?

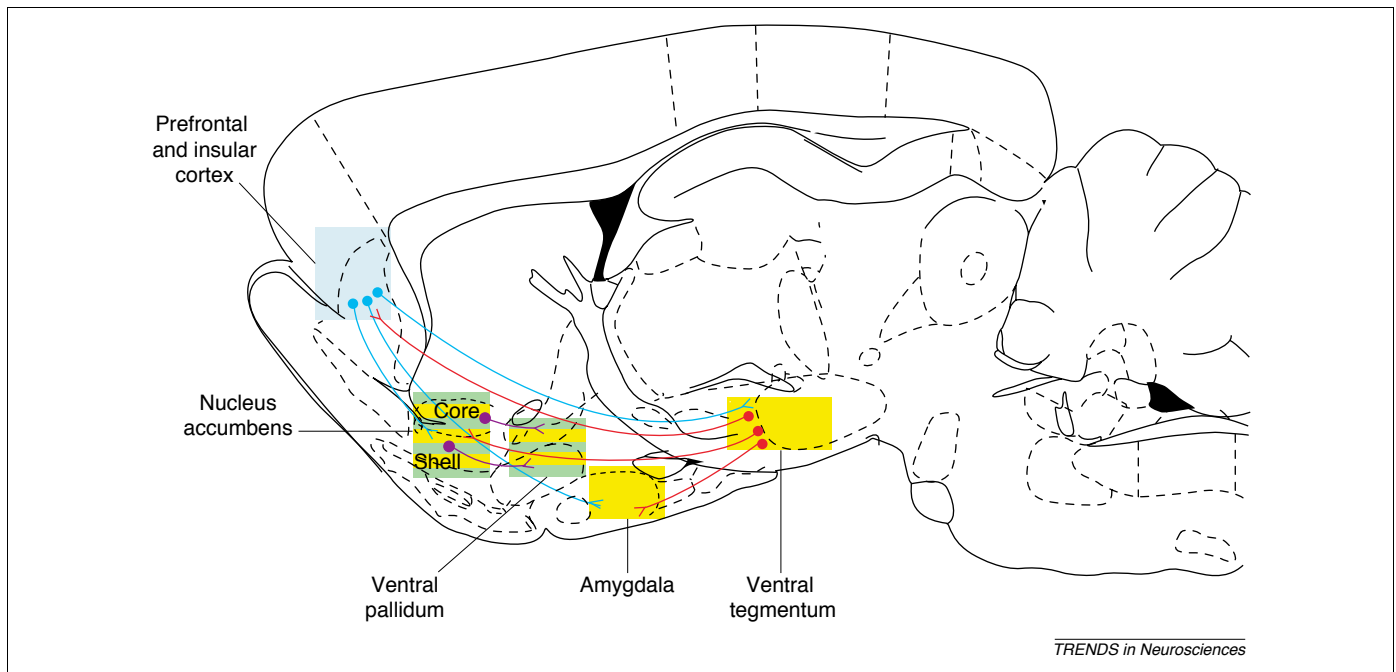


Fig. 2. Simplified schematic showing brain substrates of different components of reward. Brain regions linked to 'liking' (green) [27], 'wanting' (yellow) [21,22,50] and cognitive incentive processing (blue) [5,14,58] are shown. The box coloring indicates which reward components have been shown to be altered after manipulation of that brain structure. For example, the nucleus accumbens has both 'wanting' and 'liking' functions [3,5,21,22,27,42,53]. Dopamine manipulations [e.g. amphetamine microinjection or 6-hydroxydopamine (6-OHDA) lesions] in the accumbens change 'wanting' without changing 'liking', whereas opioid- or GABA-agonist microinjections in the accumbens can also change 'liking' reactions to sweet rewards [24–26]. The ventral pallidum is also tentatively depicted as mediating 'liking' in addition to 'wanting', because ventral pallidal lesions reduce behavioral 'liking' reactions and ventral pallidal neurons activate in response to sweet tastes [27,29] (and because the area has been implicated in traditional behavioral measures of reward in animals that tap 'wanting'). It should be noted that this diagram is only a heuristic, and in reality each brain structure has multiple functions not depicted here. For example, amygdala nuclei might also participate in associative learning, and the prefrontal and insular cortex might also participate in 'wanting' and 'liking' functions. Furthermore, as emphasized in the main text, all psychological components of reward are intertwined and normally operate together as part of coordinated network integrating motivational, learning and emotional processes in reward. It is often only after manipulation of specific brain circuits that reward dissociates into psychological components, revealing the identity of distinct components of reward. The core and shell are components of the nucleus accumbens. Selected dopaminergic (red), glutamatergic (blue) and GABAergic (purple) connecting projections are also shown [48].

Incentive salience is a motivational, rather than an affective, component of reward. Its attribution transforms mere sensory information about rewards and their cues (sights, sounds and smells) into attractive, desired, riveting incentives [21–23,27,30,31]. The sight of food, drugs or other incentives is merely a sensory configuration of shape and color that is not intrinsically motivating. Attribution of incentive salience to a percept or other representation is what is suggested here to make it a 'wanted' target of motivation. Incentive salience or 'wanting', unlike 'liking', is particularly influenced by dopamine neurotransmission [3,21–23,30,31,44,45]. However, incentive salience depends on other brain substrates too. Candidates include intrinsic spiny neurons of the accumbens, and connections to the amygdala, basal forebrain and cortex – all regions that interface 'wanting' with attention, learning and cognition [3,9,26,46–49].

Interactions among wanting, learning and liking

Distributed and interconnected brain circuits allow learning, 'wanting' and 'liking' to interact in particular ways. Here are highlighted a few important interactions among these components of reward, and details of how to recognize them.

Conditioned stimuli as motivational magnets

Stimuli attributed with incentive salience become motivational magnets, eliciting appetitive approach and even

consummatory behavior [5,8,22,44,50]. For example, Pavlovian CSs elicit approach CRs. In 'autoshaping' or 'sign tracking' experiments, laboratory animals even attempt to capture and eat or drink CS cues (if the stimulus is physically discrete enough to try to ingest). Autoshaped pigeons make eating pecks at light cues that predict edible rewards but make drinking pecks at cues for liquid reward, and rats or monkeys often bite their predictive lever CSs. Even humans can sometimes find CSs magnetic, as when a crack-cocaine addict compulsively searches the floor for small white crystals – despite knowing them more likely to be sugar than cocaine. These can be viewed as instances in which conditioned incentive salience is attributed to the Pavlovian cues themselves, making them into 'wanted' stimuli – motivational magnets that pull appropriate behavioral responses. This form of incentive salience depends heavily on mesolimbic dopamine systems, and its associative guidance seems to depend on the basolateral amygdala and nucleus accumbens core (although different types of CSs can recruit slightly different neural circuits) [4,9,51–53].

Cue-triggered 'wanting'

CSs also trigger motivation for their unconditioned rewards (just as UCS rewards prime incentive motivation for themselves). An example is when drug cues elicit craving or reinstate drug-taking behavior. This might happen because CSs cause mesolimbic systems

Box 2. 'Wanting'

Why evolve different brain systems for reward 'wanting' and 'liking'? Here, it is speculated that 'wanting' emerged early in evolution as an elementary form of stimulus-guided goal direction, to mediate pursuit of a few innate food or sex unconditioned stimuli. Subsequently extended to learned 'wants', incentive salience might have been preserved separately from 'liking' to facilitate comparison and choice among competing rewards that have incommensurate 'likes' (e.g. food, sex and shelter). A common neural currency is needed to compare the relative quantity of different qualitative rewards. By channeling even differently 'liked' rewards down a common path, the mesolimbic 'wanting' system creates a decision utility to choose among many targets [3,62–64].

'Wanting' is also separable from learning, although the two are linked in mammalian brain function. The link is so tight between mesolimbic dopamine activity and associative reward prediction that some have interpreted dopaminergic-cell firing to mediate reward learning or prediction itself [39,65,66]. But dopamine is probably not necessary for reward associations or representations *per se* – at least some new values for sweet rewards can be learned even after near-total lesions of dopamine systems [21]. Instead, it could be that anticipatory mesolimbic dopamine neurotransmission mediates learned 'wanting', as a motivational conditioned response of the brain [3,22,44,46,50,53,64,67–71]. Learned 'wanting' is distinct from the associative prediction that triggers it, which can be neurally generated elsewhere. Manipulations of mesolimbic dopamine might change rewarded behavior by changing learned 'wanting', rather than by changing learning or prediction *per se* [21–23,44,45].

Finally, independent evolution of 'wanting' also preserved freedom for brain circuits to use mesolimbic components as building blocks in counter-intuitive ways. These might include similar mesolimbic construction of both reward and aversive motivation. Dopaminergic systems are activated by alerting stimuli and even by aversive events, not just by rewards [41,42,46,72–74]. Beyond the dopamine synapse, spiny accumbens neurons might further separately channel signals for both appetitive and aversive salience functions [26,49]. For example, appetitive eating and aversive fearful behaviors are triggered by identical GABA and glutamate manipulations of local microcircuits in the accumbens shell, but at different rostrocaudal sites. The proximity and similarity of these neural signals suggests that brains parsimoniously might use related mesolimbic components to construct oppositely valenced motivations as different as feeding and fear [26,49].

additionally to attribute incentive salience to associated neural representations of their reward UCS (and associated responses), spurring cue-triggered 'wanting' for that reward.

In the laboratory, cue-triggered 'wanting' can be measured best in conditioned incentive experiments (sometimes called Pavlovian-to-instrumental transfer [PIT] experiments), which can screen out alternative explanations for cue effects, such as conditioned 'liking' and Pavlovian S–R habits [22,23,50]. Cue-triggered 'wanting' can be sudden, intense, reversible and repeatable [5,22,23,45,50]. Neurally, cue-triggered 'wanting' is particularly sensitive to manipulations of dopamine and related mesolimbic circuits [4,5,8,54,55]. For example, dopamine-receptor antagonists suppress cue-triggered 'wanting' even when they do not affect other aspects of behavior [55], and microinjections of amphetamine into the nucleus accumbens potently increase cue-triggered 'wanting' for sucrose reward [23,45]. Neural sensitization of mesolimbic systems by psychostimulant drugs also increases cue-triggered 'wanting' [22,45]. Cue-triggered 'wanting' might be mediated by brain systems slightly

differently from the Pavlovian conditioned approach [4,9,52], perhaps because the neural computations required to make a physically perceived stimulus into a motivational magnet are different from those required to attribute 'wanting' to an associated neural representation of a reward UCS (that is not actually present).

Finally, it seems possible that some vivid cognitive images of reward, which potently elicit motivation, might also activate mesolimbic 'wanting' circuits even in the absence of CSs, at least in humans [22,46,56,57]. If so, additional 'top-down' brain circuits involving corticolimbic projections are likely required to activate mesolimbic incentive salience via cognitive reward imagery.

Response reinforcement

Instrumental responses are strengthened by making delivery of reward UCSs contingent on them. Conditioned reinforcers (Pavlovian reward CSs) can similarly be used to strengthen new instrumental responses. In CR reinforcement, the response contingency makes the temporal order of events opposite from the Pavlovian conditioned incentive effects discussed in the preceding section. In conditioned reinforcement, the response happens first and the subsequent reward or cue reinforces it. In conditioned incentive effects, the cue or reward happens first and triggers the 'wanting' response that follows.

Primary response reinforcement and conditioned response reinforcement share similar processes but their neural circuits partly diverge [4,8,52]. Additional neural circuitry might be needed in conditioned reinforcement for CSs, to activate indirectly the neural affective and other circuits that are more directly activated by UCS reinforcers. Mesolimbic incentive salience might contribute to both types of response reinforcement by causing 'wanting' for CSs and their UCS representations. The effects of dopamine on response reinforcement might largely reflect this contribution of incentive salience [5,9,50,55].

However, incentive salience by itself cannot mediate the response contingency in response reinforcement. That requires additional psychological processes (and their brain systems), such as instrumental S–R habit learning [5–7,9,50] and instrumental cognitive representations of act–outcome ('cognitive incentives') [3,5,8,12–14,50,58].

Cognitive incentives

People often have an explicit cognitive expectation that they will like the things they want. In those cases (and unlike implicit Pavlovian incentives), a cognitive incentive is: (1) known or imagined (cognitive incentive representation); (2) expected to be pleasant (hedonic expectation); (3) subjectively desired and intended to be gained (explicit cognitive representation of wanting) and, perhaps, (4) known to be obtainable by actions that cause it to occur (understanding of act–outcome causality). Nonhuman animals have also evolved at least basic forms of cognitive incentives [5]. Clever experiments over the past decade have shown that even rats pass some relevant tests for cognitive expectation and act–outcome representation [5,12–14,58].

In these illuminating experiments, a rat must draw upon its memory of the hedonic value of a reward in the past and generate cognitive expectations of its hedonic value in the

future [5,12,58]. One essence of rational cognition is its inferential exploitation of lawful consistencies in the world and, typically, future value is best inferred from past value. In addition, the rat must use its understanding of which actions cause which outcomes to select from several possible actions the one that will produce the best reward. These studies paved the way for identification of brain substrates for cognitive incentives that differ from those of other motivational components [3,5,12,14,50,55,58,59].

The evolution of such cognitive incentives brings the obvious benefit of goal-directed strategies of action that could not be produced by mere associative responses. But cognitive interactions do not completely replace the more basic learning, 'liking' and 'wanting' components. This is not only because brains evolved associative, emotional and motivational interactions first but also because both 'wanting' and cognitive incentives serve unique functions. Cognitive incentive expectations and Pavlovian incentive salience ('wanting') appear to operate simultaneously at different levels and are exposed in different tests. Usually they act in concert to motivate behavior in the same direction, but under some conditions their directions diverge, such as when future value suddenly becomes different from past value owing to a sudden change in physiological drive state [3,5,50]. Cognitive incentive processes are relatively immune to manipulations of mesolimbic dopamine systems that change Pavlovian-guided 'wanting' [55]. Not surprisingly, cognitive incentive representations (even in rats) depend heavily on neocortical structures, including orbitofrontal and insular cortical regions [3,5,13,14,58].

Neuroscience of reward: which component?

In closing, consider again the knockout mouse with distorted cocaine reward. Clearly, it is not enough to say that reward has changed without also asking which specific component of reward. Is there a change in learning? If so, in which form of learning (e.g. Pavlovian associations or cognitive expectancies)? Is there a change in emotional, affective and hedonic reactions to reward? If so, in which form of affect (e.g. immediate 'liking' reaction or cognitive representations of hedonic outcome)? Is there a change in motivation? If so, in which form of motivation (e.g. Pavlovian incentive salience or cognitive representations of value)? A neurobiological manipulation might change any one or all of these, and a change in any will distort rewarded behavior. The role of specific brain molecules, cells or systems in reward can be understood only by parsing reward into specific psychological components and probing each component of reward in turn.

Acknowledgements

Our work has been supported by grants from NIDA, NIMH, and NSF. We thank Susana Peciña for assistance in preparation of the manuscript and Fig. 2.

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