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Review

Pleasure Systems in the Brain

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Pleasure is mediated by well-developed mesocorticolimbic circuitry and serves adaptive functions. In affective disorders, *anhedonia* (lack of pleasure) or *dysphoria* (negative affect) can result from breakdowns of that hedonic system. Human neuroimaging studies indicate that surprisingly similar circuitry is activated by quite diverse pleasures, suggesting a common neural currency shared by all. Wanting for reward is generated by a large and distributed brain system. Liking, or pleasure itself, is generated by a smaller set of hedonic hot spots within limbic circuitry. Those hot spots also can be embedded in broader anatomical patterns of valence organization, such as in a keyboard pattern of nucleus accumbens generators for desire versus dread. In contrast, some of the best known textbook candidates for pleasure generators, including classic pleasure electrodes and the mesolimbic dopamine system, may not generate pleasure after all. These emerging insights into brain pleasure mechanisms may eventually facilitate better treatments for affective disorders.

The English word "hedonic" comes originally from the ancient Greek for pleasure (ἡδονή; in Latin script: hédoné), in turn derived from the word for "sweet" (ἡδύς or *hēdús*). Today hedonic refers to sensory pleasures as well as many higher types of pleasure (e.g., cognitive, social, aesthetic, and moral).

Some goals of affective neuroscience are to understand how brain mechanisms generate pleasures, and also displeasures, and eventually find more effective treatments for affective disorders (Anderson and Adolphs, 2014; Damasio and Carvalho, 2013; Haber and Knutson, 2010; Heller et al., 2013; Kringelbach and Berridge, 2010; Panksepp, 2011). Capacity for normal pleasure is essential to healthy psychological function or well-being. Conversely, affective disorders can induce either the pathological absence of pleasure reactions (as in clinical anhedonia) or the presence of excessive displeasure (dysphoric emotions such as pain, disgust, depression, anxiety, or fear).

But is a neuroscience of pleasure feasible? Doubts that pleasure might be scientifically understood have been expressed for over a century. Early doubts stemmed from behaviorist convictions that only objective behavioral-neural reactions were eligible for scientific study and never subjective experiences (including the experience of pleasure). However, progress in the past 50 years proves that many complex psychological processes involving subjective experience can be successfully studied and related to underlying brain mechanisms. Still, some objections persist today. For example, LeDoux's recent recommendation that affective neuroscientists should focus only on behavioral affective reactions, rather than on subjective emotions, shares those earlier concerns (LeDoux, 2014).

In our view, a neuroscience of pleasure can be pursued as successfully as the neuroscience of perception, learning, cognition, or other well-studied psychological functions. The crucial test of this proposition is: can affective neuroscience produce important new conclusions into how brain systems mediate hedonic impact? Evidence in support of this, we think, now exists in the form of recent findings. In this article we discuss some of these new findings, including (1) separation of reward liking, wanting, and learning mechanisms in mesocorticolimbic circuitry; (2) identification of overlap in neural circuitry underlying sensory pleasures and higher pleasures; (3) identification of particular sites in prefrontal limbic cortex that encode pleasure impact; (4) mapping of surprisingly localized causal hedonic hot spots that generate amplifications of pleasure reactions; (5) discovery that nucleus accumbens (NAc) hot spot and cold spot mechanisms are embedded in an anatomically tuned keyboard organization of generators in NAc that extends beyond reward liking and wanting to negative emotions of fear and disgust; and (6) identification of multiple neurochemical modes within NAc mechanisms that can retune keyboard generators into flipping between oppositely valenced motivations of desire and dread.

A Neuroscience of Pleasure

In a sense, pleasure can be thought of as evolution's boldest trick, serving to motivate an individual to pursue rewards necessary for fitness, yet in modern environments of abundance, also inducing maladaptive pursuits such as addictions. An important starting point for understanding the underlying circuitry is to recognize that reward involves a composite of several psychological components: liking (core reactions to hedonic impact), wanting (motivation process of incentive salience), and learning (Pavlovian or instrumental associations and cognitive representations) (Berridge and Robinson, 2003). These component processes also have discriminable neural mechanisms. The three processes can occur together at any time during the reward-behavior cycle, though wanting processes tend to dominate the initial appetitive phase, while liking processes dominate the subsequent consummatory phase that

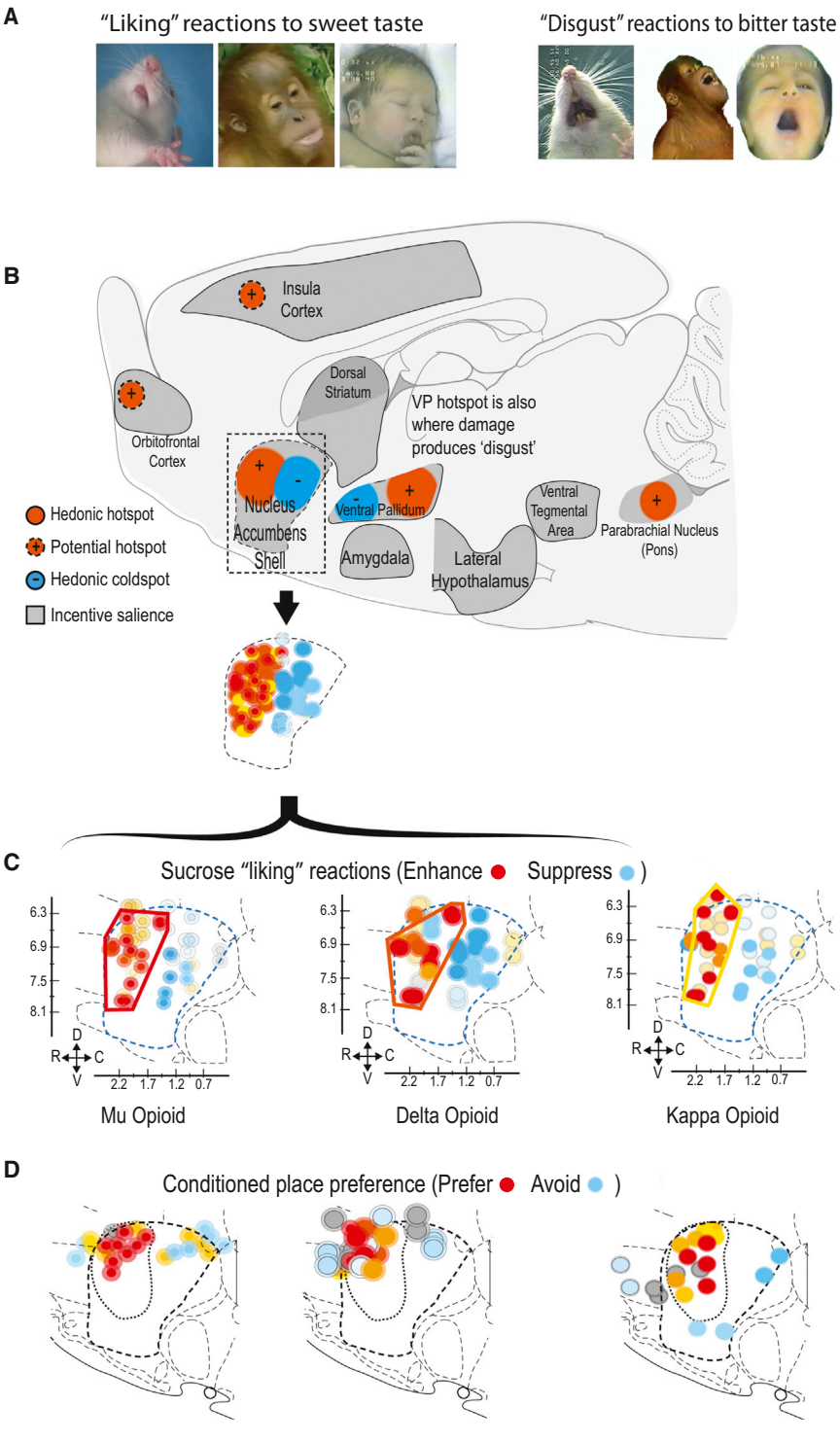

Figure 1. Causal Hedonic Hot Spots and Cold Spots in the Brain

(A) Top shows positive hedonic orofacial expressions ("liking") elicited by sucrose taste in rat, orangutan, and newborn human infant. Negative aversive ("disgust") reactions are elicited by bitter taste.

(B) Middle shows sagittal view of hedonic hot spots in rat brain containing the NAc, VP, and prefrontal cortex. Hot spots (red) depict sites where opioid stimulation enhances "liking" reactions elicited by sucrose taste. Cold spots (blue) show sites where the same opioid stimulation oppositely suppresses "liking" reactions to sucrose.

(C) NAc blow-up of the medial shell shows effects of opioid microinjections in the NAc hot spot and cold spot (red/orange dots in hot spot = > 200% increases in "liking" reactions and blue dots in cold spot = 50% reductions in "liking" reactions to sucrose). Panels show separate hedonic effects of mu opioid, delta opioid, and kappa opioid stimulation via microinjections in the NAc shell on sweetness "liking" reactions. Bottom row shows effects of mu, delta, or kappa agonist microinjections on establishment of a learned place preference (i.e., red/orange dots in hot spot) or place avoidance (blue dots). Surprisingly similar patterns of anterior hedonic hot spots and posterior suppressive cold spots are seen for all three major types of opioid receptor stimulation. Modified from Castro and Berridge (2014).

(D) Bottom row shows effects of mu, delta, or kappa agonist microinjections in NAc medial shell on establishment of a learned place preference (i.e., red/orange dots in hot spot) or place avoidance (blue dots). Surprisingly similar patterns of anterior hedonic hot spots and posterior suppressive cold spots are seen for all three major types of opioid receptor stimulation. Modified from Castro and Berridge (2014).

may lead to satiety. Learning, on the other hand, happens throughout the cycle. A neuroscience of reward seeks to map these components onto necessary and sufficient brain networks (see Figure 1).

To study pleasure comprehensively, good human neuroimaging studies are needed to explore correlative encoding of pleasant experiences and good animal studies are needed to explore causation of underlying hedonic reactions. This two-pronged approach exploits a fundamental duality in hedonic processes, related to the objective versus subjective faces of pleasure (Damasio and Carvalho, 2013; Kringelbach and Berridge, 2010; Schooler and Mauss, 2010; Winkielman et al., 2005). Pleasure is sometimes assumed to be a purely subjective feeling. But pleasure also has objective features in the form of measurable hedonic reactions, both neural and behavioral, to valenced events. In this review, we denote objective hedonic reactions as "liking" reactions (with quotes) to distinguish them from the subjective experience of liking (in the ordinary sense, without quotes). Objective hedonic reactions can be measured in both human and animal neuroscience studies, which together allow some comparisons across species and can lead to a more complete causal picture of how brain systems mediate hedonic impact.