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The dark side of emotion: The addiction perspective

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ABSTRACT

Emotions are "feeling" states and classic physiological emotive responses that are interpreted based on the history of the organism and the context. Motivation is a persistent state that leads to organized activity. Both are intervening variables and intimately related and have neural representations in the brain. The present thesis is that drugs of abuse elicit powerful emotions that can be interwoven conceptually into this framework. Such emotions range from pronounced euphoria to a devastating negative emotional state that in the extreme can create a break with homeostasis and thus an allostatic hedonic state that has been considered key to the etiology and maintenance of the pathophysiology of addiction. Drug addiction can be defined as a three-stage cycle—*binge/intoxication*, *withdrawal/negative affect*, and *preoccupation/anticipation*—that involves allostatic changes in the brain reward and stress systems. Two primary sources of reinforcement, positive and negative reinforcement, have been hypothesized to play a role in this allostatic process. The negative emotional state that drives negative reinforcement is hypothesized to derive from dysregulation of key neurochemical elements involved in the brain incentive salience and stress systems. Specific neurochemical elements in these structures include not only decreases in incentive salience system function in the ventral striatum (within-system opponent processes) but also recruitment of the brain stress systems mediated by corticotropin-releasing factor (CRF), dynorphin-κ opioid systems, and norepinephrine, vasopressin, hypocretin, and substance P in the extended amygdala (between-system opponent processes). Neuropeptide Y, a powerful anti-stress neurotransmitter, has a profile of action on compulsive-like responding for drugs similar to a CRF_1 receptor antagonist. Other stress buffers include nociceptin and endocannabinoids, which may also work through interactions with the extended amygdala. The thesis argued here is that the brain has specific neurochemical neurocircuitry coded by the hedonic extremes of pleasant and unpleasant emotions that have been identified through the study of opponent processes in the domain of addiction. These neurochemical systems need to be considered in the context of the framework that emotions involve the specific brain regions now identified to differentially interpreting emotive physiological expression.

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1. What is emotion?

Emotion can be defined as "a psychic and physical reaction (as anger or fear) subjectively experienced as strong feeling and physiologically involving changes that prepare the body for immediate vigorous action" (Webster's Ninth New Collegiate Dictionary, 1984). The introspective emphasis on the "feeling" aspect of emotions had a prominent role in the development of many theories of emotion. Darwin argued as early as 1872 that both observable expressions of emotions as well as underlying brain processes (direct action of the excited nervous system on the body) are not unique to humans (Darwin, 1872). Indeed, key emotional expressions were considered innate, instinctive responses but subject to the evolutionary process.

1.1. Emotional behavior vs. feelings of emotion

Emotional behavior, or the measurement of bodily changes associated with emotional behavior, focused on peripheral response mechanisms largely related to the autonomic and endocrine systems. Peripheral measures of emotion ranged from galvanic skin responses to heart rate to salivary secretion to levels of autonomic hormones. Such peripheral responses have long been difficult to separate from the feelings of emotion. Indeed, William James in his famous theory of emotion argued, "Bodily changes follow directly the *perception* of the exciting fact, and that our feeling of the same changes as they occur in *is* the emotion" (James, 1884, pp. 189–190).

The brain became a key mediator of emotion by parallel advances in conceptual framework and neuroanatomical studies. Ferrier (1875) showed that orbitofrontal ablations in monkeys had

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no major effect on an organism's sensory abilities but produced a definite change in the disposition of the animal. Broca (1878) described the "grand lobe limbique" ("limbic" indicates that this lobe surrounds the brain stem) which included the olfactory tubercle, prepyriform cortex, diagonal band of Broca, septal region, hippocampus, and cingulate as a common emotional circuit in all mammals. The demonstration of decorticate "sham rage" in the 1920s led to the hypothesis that emotional expression involved specific subcortical structures. Later stimulation studies pointed to subcortical structures, such as the hypothalamus, soon to be labeled "limbic" structures in the neural circuitry of the expression of emotional responses (Masserman, 1941).

From a conceptual perspective, Cannon argued against the James–Lange Theory, largely on the basis of the observation that animals continued to express emotional behavior in the absence of information from the periphery. Later, he hypothesized that emotional experience and emotional behavior were a release from cortical inhibition of neural impulses originating in the thalamus (Cannon, 1927). Bard removed the neocortex of cats, leaving the rhinencephalon intact, which produced placidity (Bard and Mountcastle, 1948). This placidity could be changed to ferocity by removing the amygdaloid complex (Bard and Match, 1951). Bard's extensive work made modifying Cannon's theory possible so that it could better define the neurocircuitry of emotional behavior and led Papez to argue that the hypothalamus was critical for the expression of emotional behavior.

The Papez circuit was proposed in 1937 as a circuit for emotion and evolved into the terminology and conceptual framework of the limbic system which remains today (Papez, 1937, 1939). The Papez circuit included the cortex, cingulate gyrus, mammillary bodies, anterior thalamus, subthalamic areas, and hypothalamus. Thus, the limbic system came to represent not only Broca's 1878 grand lobe limbique but also most allocortical regions of the brain from the Papez circuit for the subjective experience of emotion and the hypothalamus for emotional expression. MacLean later added the hippocampus and its association with the amygdala as a key part of the experience of emotion (MacLean, 1949). To some extent, the term "limbic system" has been abrogated to include any brain structure involved in emotional function, leading to a somewhat circular argument of what constitutes the limbic system.

1.2. Recent perspectives on the neurobiological bases of emotion

Important to our conceptual understanding of the neuroscience of emotion was the suggestion of Schachter and Singer (1962) that cognitive factors may be major determinants of emotional states. More specifically, these authors argued that cognition arising from the immediate emotional experience, as interpreted by past experience, provides the framework for labeling one's feelings, and thus cognition determines whether a state of physiological arousal will be labeled as a given emotion (Schachter, 1975).

Later, a universality of six emotions was proposed based on extensive cross-cultural work on facial expressions—happiness, surprise, fear, sadness, anger, and disgust combined with contempt—with distinctive patterns of central nervous system activity (Ekman and Friesen, 1988). Similar emotional states were hypothesized even for rodents, including distress, anger, social bonding, play, and laughter (Panksepp, 1998). Yet others, such as Russell (2003), avoided a specific categorization of emotion and argued that any emotionally charged event is a state experienced as simply feeling good or bad, energized or enervated—in other words, a free-floating mood or core affect that is subject to interpretation by the perception of affective quality.

In an integration of modern thinking with some aspects of the original James–Lange Theory, the somatic marker hypothesis of Damasio (1996) argued that decision-making is a process that is influenced by somatic (of the body, not just the muscles) marker signals that arise in bioregulatory processes, including those that express themselves in emotions and feelings. A key part of the theory is that the ventromedial cortex provides the substrate for "learning an association between certain classes of complex situation, on the one hand, and the type of bioregulatory state (including emotional state) usually associated with that class of situation in past individual experience" (Bechara et al., 2000, p. 296). From this perspective, the amygdala has been shown to be a structure that is necessary for emotions to improve memory (Cahill et al., 1995) and the creation of biases and decision making (Bechara et al., 1999).

Modern brain imaging studies have consolidated such integrative views of emotions. Morris et al. (1996) showed that the amygdala in humans responds differentially in subjects shown facial expressions of fear and happiness, with the neuronal response in the left amygdala significantly greater in response to fearful vs. happy faces. Damasio (2002), in a series of studies, argued that the term "emotion" should be defined as specific and consistent collections of physiological responses triggered by certain brain regions when the organism is presented with a specific situation. The substrates for the representation of emotions include homeostatic circuitry in the brainstem, hypothalamus, basal forebrain, amygdala, ventromedial prefrontal cortex, and cingulate cortex. In contrast, Damasio defined "feelings" as the mental states that arise from the neural representation of the collection of responses that constitute an emotion and as such should be reserved for the private, mental experience of an emotion. Key structures involved in feelings, he argued, include the brainstem, hypothalamus, thalamus, cingulate, somatosensory cortices of the insula, and somatosensory I and II. He hypothesized that to monitor cognitive processing, the prefrontal cortex is engaged. This approach led to arguments in which specific brain systems, including the posteromedial cortices (precuneus, posterior cingulate cortex, and retrosplenial region) and anterior insula, are recruited in addition to the basic homeostatic circuitry for specific types of emotions, such as social emotions (e.g., admiration and compassion; Moll et al., 2005) and for engagement of the salience system (Seeley et al., 2007; Immordino-Yang et al., 2009).

2. Interface between emotion and motivation

2.1. Motivation

Motivation, similar to emotion, is a concept that has many definitions, but even early definitions reflected internal elements that drive behavior. Motivation was defined as "an inner psychological process or function, a driving force to be found chiefly within the organism itself and a plan, purpose or ideal with the definite implication of an ideational element" that may not be consciously or overtly recognized (Perrin, 1923). Richter argued that "spontaneous activity arises from certain underlying physiological origins and such 'internal' drives are reflected in the amount of general activity" (Richter, 1927). Hebb stated that motivation is "stimulation that arouses activity of a particular kind" (Hebb, 1949). Bindra defined motivation as a "rough label for the relatively persisting states that make an animal initiate and maintain actions leading to particular outcomes or goals" (Bindra, 1976). A more behavioristic view is that motivation is "the property of energizing behavior that is proportional to the amount and quality of the reinforcer" (Kling and Riggs, 1971). Finally, a more neurobehavioral view is that motivation is a "set of neural processes that promote actions in relation to a particular class of environmental objects" (Bindra, 1976).

An early and influential theory of motivation by Hull (1943), termed the "drive-reduction theory," was predicated on the hypothesis of homeostatic mechanisms of motivation, in which behavior