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The role of the ventral pallidum in psychiatric disorders

Largely garnered from studies in laboratory animals, the ventral pallidum (VP) is recognized as an integrator of sensory, emotional, and cognitive information with appropriate motoric responses. These functional complexities are reflected in behaviors associated with pain experiences, reward-motivated function, stress, social interaction and affiliation. With the increased resolution of modern-day human brain imaging technology, preclinical studies are being substantiated, and the role of the VP in the human emotional repertoire and psychiatric disorders is being clarified.

Several clinical reports point to VP involvement in disorders of motivation. For example, single-photon emission computed tomography of Parkinson's Disease (PD) patients with pathological gambling show enhanced resting state activity (regional cerebral blood flow) in the VP of these individuals compared with non-gambling PD patients (Cilia *et al*, 2008).

Functional magnetic resonance imaging can assess rapid responses of the brain to 'unseen' reward cues or cues that are recognized outside our awareness. Presentation of unseen cues for natural and drug-related rewards (Childress *et al*, 2008), or monetary rewards (Pessiglione *et al*, 2007), results in rapid activation of the VP before conscious recognition. These rapid responses also predict the positive affect responses to the same stimuli when presented in a visible manner, suggesting that the affective/motivational processes within and outside awareness are continuous and regulated by the VP (Childress *et al*, 2008).

Another behavior with high emotional valence is social affiliation, for example, pair bonding. Both the formation and the maintenance of pair bonding are associated with VP activation (assessed with structural magnetic resonance imaging and positron emission tomography) in non-human primates (Bales *et al*, 2007). It follows that a dysregulation of the VP and its limbic circuit may contribute to disorders of social bonding such as autism.

Positron emission tomography with receptor-selective radiotracers adds neurochemical assessments to studies on neuroanatomical substrates regulating emotional states. For example, increases in negative affect ratings by healthy human volunteers who are associated with sustained sadness (Zubieta *et al*, 2003) or sustained muscle pain (Zubieta *et al*, 2002) correlate with deactivation of μ-opioid receptors in the VP. By inference, these findings indicate that positive affect is regulated by activated μ-opioid receptors in the VP.

The imaging literature converges to indicate that VP transmission is involved in the emotional overlays of motivated behaviors. This interpretation is substantiated by preclinical studies on μ-opioid receptors in the VP, wherein these receptors are capable of inducing a profound and enduring plasticity (Mickiewicz *et al*, 2009). Future laboratory and clinical studies will aid in fully appreciating the role of the VP in emotional processing and motivated behaviors, and the psychiatric consequence of its dysregulation.

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DISCLOSURE

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Exploring the molecular basis of addiction: drug-induced neuroadaptations

Abuse of a number of psychoactive substances can eventually control an individual's behavior by producing dependence and/or addiction. Recent surveys estimate that there are about 200 million users of illegal drugs worldwide, which represent 3.4% of the world population. An ever-increasing number of neuroscientists are searching for clues regarding the molecular determinants of addictive behavior. The low-hanging fruit would be to study dopamine receptors and transporters in the nucleus accumbens (NAc); however, scientists are now exploring mechanisms far beyond dopaminergic targets.

For example, some scientists have chosen to target molecular mechanisms within the hippocampus because of its role in encoding and retrieving