



The ventral pallidum: Subregion-specific functional anatomy and roles in motivated behaviors



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ABSTRACT

The ventral pallidum (VP) plays a critical role in the processing and execution of motivated behaviors. Yet this brain region is often overlooked in published discussions of the neurobiology of mental health (e.g., addiction, depression). This contributes to a gap in understanding the neurobiological mechanisms of psychiatric disorders. This review is presented to help bridge the gap by providing a resource for current knowledge of VP anatomy, projection patterns and subregional circuits, and how this organization relates to the function of VP neurons and ultimately behavior. For example, ventromedial (VPvm) and dorsolateral (VPdl) VP subregions receive projections from nucleus accumbens shell and core, respectively. Inhibitory GABAergic neurons of the VPvm project to mediodorsal thalamus, lateral hypothalamus, and ventral tegmental area, and this VP subregion helps discriminate the appropriate conditions to acquire natural rewards or drugs of abuse, consume preferred foods, and perform working memory tasks. GABAergic neurons of the VPdl project to subthalamic nucleus and substantia nigra pars reticulata, and this VP subregion is modulated by, and is necessary for, drug-seeking behavior. Additional circuits arise from nonGABAergic neuronal phenotypes that are likely to excite rather than inhibit their targets. These subregional and neuronal phenotypic circuits place the VP in a unique position to process motivationally relevant stimuli and coherent adaptive behaviors.

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Abbreviations: BLA, basolateral amygdala; BM, basal nucleus of Meynert; BNST, bed nucleus of the stria terminalis; ChAT, choline acetyltransferase; DLS, dorsolateral striatum; dHipp, dorsal hippocampus; dPFC, dorsal prefrontal cortex; DR, dorsal raphe; EPN, entopeduncular nucleus; GABA, γ -amino butyric acid; GAD, glutamic acid decarboxylase; GP, globus pallidus; GPi, internal globus pallidus/entopeduncular nucleus; HDB, horizontal diagonal band; Lat, lateral; LH, lateral hypothalamus; LHb, lateral habenula; LHbM, medial part of lateral habenula; LHbL, lateral part of lateral habenula; LPO, lateral preoptic area; IPAC, interstitial nucleus of the anterior commissure; IR, immunoreactivity; Med, medial; MD, mediodorsal thalamus; mPFC, medial prefrontal cortex; MPO, medial preoptic nucleus; Acb, nucleus accumbens; AcbSh, nucleus accumbens shell; AcbC, nucleus accumbens core; NTS, nucleus tractus solitarius; OT, olfactory tubercle; PPTg, pedunculopontine tegmental nucleus; PPTg-MEA, pedunculopontine tegmental nucleus-mesencephalic extrapyramidal area; RMTg, mesopontine rostromedial tegmental nucleus; RRF, retrorubral field; RTN, reticular thalamic nucleus; SLEAR, rostral sublentiform extended amygdala; SIB, basal part of substantia innominata; SN, substantia nigra; SNc, substantia nigra pars compacta; SNr, substantia nigra pars reticulata; STN, subthalamic nucleus; TH, tyrosine hydroxylase; VGluT, vesicular glutamate transporter; vHipp, ventral hippocampus; VP, ventral pallidum; VPdl, dorsolateral ventral pallidum; VPvm, ventromedial ventral pallidum; VPr, rostral VP; VPvl, ventrolateral VP; vPFC, ventral prefrontal cortex; VL/VMT, ventrolateral/ventromedial thalamus; VTA, ventral tegmental area.

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1. Introduction

More than four decades ago, the ventral pallidum (VP) was delineated from the subcommissural part of the substantia innominata by Heimer and colleagues (Heimer, 1972; Heimer and Wilson, 1975; Switzer et al., 1982; Heimer et al., 1982). In early discussions, Mogenson et al. (1980) proposed that the VP integrated limbic/emotionally salient signals from the nucleus accumbens (Acb) to brain motor systems. Swerdlow and Koob (1987) furthered this hypothesis with studies showing how the Acb to VP projection links the mesoaccumbal dopamine system to motor circuitry. At the time, dopamine was already well-known to be involved in reward-motivated behavior (Wise, 1980). Soon after, it was revealed that the VP is innervated by dopamine inputs from the midbrain and that dopamine directly alters VP neuronal firing (Napier and Potter, 1989). As early as 1991, Napier and colleagues (1991a) put forth the concept that in addition to

integrating various inputs from Acb, the VP incorporates reward-related signals carried by midbrain dopaminergic neurons. This concept was quickly expanded to encompass the idea that dopamine transmission within the VP regulates a collection of behaviors, including locomotion and cognition (Napier, 1992c). Building on the role of VP dopamine, and Mogenson's original concepts involving the VP in brain circuits that direct "motivation to action" (Mogenson et al., 1980), it was subsequently proposed that the VP forms part of a "final common pathway" for drug-seeking behavior (Kalivas and Volkow, 2005) and for reward processing in general (Smith et al., 2009). These concepts served as modern-day assessments of the ventral striatopallidal system. As our understanding of this system has grown, the importance of subregional circuits involving the ventromedial VP (VPvm) and dorsolateral VP (VPdl) with the Acb shell (AcbSh) and Acb core (AcbC) has become apparent. Furthermore, although considered a largely inhibitory structure, a substantial proportion of neurons

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