

Complementary roles of the ventral striatopallidal pathway in motivation and affective judgment: Pathway manipulation and neuronal activity analyses in nonhuman primates during approach–avoidance decision-making

動機づけと情動的判断における腹側線条体–腹側淡蒼球路の相補的役割：非ヒト霊長類を対象とした接近–回避意思決定課題における神経路操作と神経活動解析

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Background

Motivation and affective judgment are fundamental processes that enable organisms to initiate and sustain goal-directed behavior. These processes involve weighing potential rewards against aversive costs such as punishment. Classical reinforcement learning theories emphasized the role of outcome valuation, whereby the subjective value of anticipated outcomes drives behavior. However, recent computational accounts suggest that behavioral initiation may be regulated independently of valuation, particularly under aversive conditions. This dissociation has strong clinical implications, as it could explain how motivational deficits such as avolition in depression and schizophrenia emerge despite relatively intact hedonic capacity.

The ventral striatum (VS) and ventral pallidum (VP) are critical nodes within the basal ganglia implicated in both appetitive and aversive processing. Anatomical studies reveal dense projections from the VS to the VP, forming the ventral striatopallidal pathway. Dysfunctions in this pathway have been linked to behavioral syndromes resembling apathy and compulsivity in primates. Yet, its causal role in regulating initiation of behavior under aversive contexts has not been firmly established. Moreover, although both VS and VP contribute to motivational regulation, little is known about how they differentially operate across distinct phases of decision-making, anticipation (cue-period) and experience of outcomes (outcome-period). Addressing these questions requires both pathway-level manipulations and temporally resolved electrophysiological analyses in nonhuman primates, whose striatopallidal circuitry closely resembles that of humans. Accordingly, this dissertation aimed (1) to determine whether the VS–VP pathway causally regulates initiation of goal-directed behavior under aversive contexts, and (2) to examine VS and VP neuronal activity across cue and outcome phases of decision-making with respect to motivation and affective processing.

Materials and methods

Two complementary experiments were conducted in Japanese macaques performing two decision-making tasks: the approach–approach (Ap–Ap) task, which involved only appetitive outcomes, and the approach–avoidance (Ap–Av) task, which included conflict cases where animals could face a choice between a larger reward paired with an aversive air-puff and a smaller safe reward. The Ap–Av task systematically induced motivational conflict, while the Ap–Ap task served as a control with matched sensory and motor demands.

In **Chapter 2**, a chemogenetic approach was used to test the causal role of the VS–VP pathway. Inhibitory DREADDs (hM4Di) were expressed in VS medium spiny neurons via viral vectors. Deschloroclozapine (DCZ), a highly specific DREADD ligand, was locally infused into the VP to selectively suppress VS outputs. Behavioral measures included fixation errors during the precue period (reflecting willingness to initiate trials), reaction times (reflecting vigor of task execution), and choice patterns (reflecting outcome valuation).

In **Chapter 3** for temporal-level neuronal recording, single-unit recordings were obtained from VS and VP neurons during alternating blocks of Ap–Ap and Ap–Av tasks. Cue-period activity (anticipation phase) and outcome-period activity (experience phase) were analyzed. Two behaviorally derived variables guided interpretation: chosen value (ChV), a model-based estimate of subjective affective value, and frequency of fixation errors (FoE), an index of motivational engagement. Task transitions were unsignaled, allowing quantification of neuronal adaptation latency in response to context switches. This combination of pathway-selective suppression and temporal-level neural activity analyses enabled direct tests of causality and temporal dynamics within the same VS–VP circuit.

Results

In **Chapter 2**, pathway-level findings revealed that chemogenetic suppression of the VS–VP pathway prevented the typical decline in motivation observed during the Ap–Av task. Under normal conditions, animals gradually exhibited increasing fixation errors during the precue period, reflecting reduced motivation to initiate trials when facing conflict. Local infusion of DCZ into the VP significantly attenuated this decline, thereby restoring the animals’ initiation capacity. In addition, reaction times were shortened following pathway suppression in Ap–Av sessions, consistent with enhanced vigor of task execution. Despite these improvements in initiation, choice patterns remained unchanged, indicating that outcome valuation was not significantly affected. Importantly, none of these effects were observed in the approach–approach (Ap–Ap) task.

In **Chapter 3**, electrophysiological recordings revealed complementary activity profiles in VS and VP neurons across different decision-making phases. During the cue period, VS neurons displayed significantly higher firing rates in Ap–Av trials and rapidly adapted between Ap–Av and Ap–Ap blocks, whereas VP neurons exhibited slower and unidirectional adjustments. During the outcome period, VS neurons maintained flexible bidirectional adaptation but without a strong overall bias. VP neurons, by

contrast, showed a stronger appetitive bias and included subpopulations that were immediately suppressed by aversive outcomes, reflecting outcome-locked responses. Furthermore, subsets of neurons in both regions encoded either frequency of fixation error (FoE, as an index of motivational engagement) or chosen value (ChV, as an estimate of subjective affective value). Despite this heterogeneity at the single-cell level, population-level activity consistently showed negative correlations with FoE and positive correlations with ChV, indicating stable ensemble representations of motivational and affective signals.

Discussion

This dissertation demonstrates a functional dissociation between initiation and valuation in motivational regulation, along with a temporal division of labor between the ventral striatum (VS) and ventral pallidum (VP). At the pathway level, chemogenetic suppression of the VS–VP projection selectively restored motivational initiation under aversive conditions without affecting outcome valuation. This supports the view that aversive contexts impose direct costs on behavioral initiation, independent of value computation. At the temporal level, VS neurons acted as rapid, flexible encoders of anticipatory signals, whereas VP neurons provided slower, stabilizing responses and outcome-locked activity to aversive events. Such complementary dynamics enable both flexible anticipation and stable affective control. Mechanistically, inhibitory VS input likely suppresses VP activity during aversive anticipation, elevating the threshold for initiation. Chemogenetic suppression could relieve this inhibition and facilitate initiation, possibly through downstream effects on dopaminergic and habenular circuits. Clinically, these findings offer insight into avolition, a motivational deficit seen in depression and schizophrenia. Dysfunction of the VS–VP pathway may underlie impaired initiation despite preserved valuation, highlighting this circuit as a potential therapeutic target.

Conclusion

This dissertation elucidates how the ventral striatum (VS) and ventral pallidum (VP) cooperatively regulate motivation and affective judgment through complementary circuit and temporal mechanisms. Chemogenetic and electrophysiological evidence revealed that the VS–VP pathway specifically regulates motivational initiation under aversive contexts, while valuation processes remain largely intact. VS neurons provide rapid anticipatory signals, whereas VP neurons generate slower, outcome-related activity that may help to stabilize motivational states. Together, these findings delineate a mechanistic framework in which inhibitory interactions between the VS and VP regulate the initiation of goal-directed behavior under conflict while preserving stable representations of outcome value. Dysfunction of this pathway may lead to selective initiation deficits such as avolition, suggesting a potential circuit-level target for treating motivational impairments in psychiatric disorders.