

olfactory bulb, could be canceled out if they were mirrored by increases in 5-HT input to the bulb. However, increases resulting from active sniffing (odor sampling), if they were accompanied by suppression of 5-HT input to the bulb, would be allowed to pass through or even amplified. Although such a role for 5-HT remains speculative, the experiments of Petzold *et al.*¹ make it clear that an understanding of the long-mysterious function of 5-HT in olfaction is now closer at hand.

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The rhythms of learning

Brian Lau & C Daniel Salzman

Projections from the amygdala to the ventral striatum are important for learning. A study finds that fleeting epochs of coherent gamma oscillations between these brain areas may be important for reinforcement learning.

When learning a dance with a partner, both of you must be in sync, following the musical rhythm to create a synergistic artistic piece. In many ways, the brain faces a similar challenge; different brain structures must seamlessly interact so that we can learn, feel and even move. Although this idea, one of cooperation and communication between brain structures, seems simple enough, we understand surprisingly little about the precise mechanism by which two brain structures interact during cognitive operations such as learning. Popescu *et al.*¹ make substantial progress toward this cause by using multi-electrode recordings to identify physiological correlates of communication between the amygdala and ventral striatum while animals learn that a sensory cue predicts reward. Their results suggest that the amygdala and striatum dance in step with each other during appetitive reinforcement learning.

A wealth of anatomical, behavioral and electrophysiological data indicates that the ventral striatum, consisting of the nucleus accumbens, the olfactory tubercle and ventral/medial portions of the caudate and putamen,

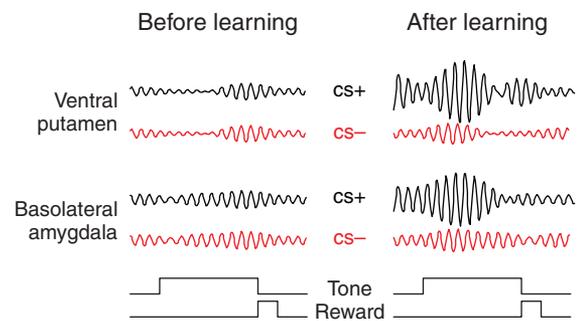
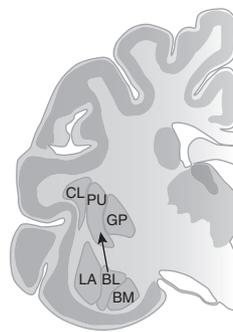


Figure 1 Gamma coherence increases during appetitive learning. Repeated presentations of a tone predicting reward increase the amplitude of phase-locked local field potentials (35–45 Hz) in the BLA of the amygdala and the ventral putamen, part of the ventral striatum. This increase is specific to the tone associated with the reward (CS+, black), changing little for a tone predicting no reward (CS-, red). BL, basolateral nucleus of the amygdala; BM, basomedial nucleus of the amygdala; CL, claustrum; LA, lateral nucleus of the amygdala; PU, putamen.

is critically important for reward prediction and certain types of appetitive learning². The ventral striatum receives inputs from a number of areas, including the hippocampus and rhinal cortices and the frontal and associative cortical areas. It also receives a substantial excitatory input from the amygdala, which, although clearly important for learning about aversive stimuli, is increasingly recognized as also being important for a broad range of appetitive behaviors^{3,4}. The ventral striatum can influence motor behavior via projections to the globus pallidus, substantia nigra and ventral pallidum, suggesting that it may be ideally situated to mediate motivational and affective influences on behavior.

Amygdalar inputs to the ventral striatum originate from the basolateral nucleus (BLA), which is necessary for updating outcome expectations, the ability of a cue to evoke

a representation of the current value of a reinforcer³. Such representations can be inferred using a behavioral assay known as reinforcer devaluation, which tests for the use of expectations by measuring whether behavior changes appropriately when outcome values are manipulated (such as by selectively satiating a subject to a reward). Animals with excitotoxic BLA lesions do not show reinforcer devaluation³ and fail to use changed outcome values to guide behavior. Similar to BLA lesions, inactivating the core of the nucleus accumbens also abolishes reinforcer devaluation⁵, consistent with the idea that the BLA projection to the ventral striatum is an important route for emotionally significant stimuli to influence behavior.

These results suggest that communication between the amygdala and ventral striatum should be observable when animals learn or

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update outcome expectancies. Popescu *et al.*¹ searched for evidence of this communication by correlating simultaneously recorded local field potentials (LFPs) from the BLA and ventral putamen in cats performing an appetitive learning task. Fast oscillations in LFPs are ubiquitous throughout the brain and evidence from recordings in laminated cortical structures indicates that LFPs largely reflect the spatial and temporal summation of subthreshold currents in local neuronal populations. Although our understanding of the neural basis of LFPs in nuclear structures such as the amygdala and striatum is much less clear (the lack of palisades of oriented dendritic trees tends to generate 'closed' fields, rendering LFPs more difficult to measure and interpret), LFPs can be readily recorded in both the amygdala⁶ and the striatum⁷, and these areas show learning-related changes in local power and long-distance coupling with other brain areas^{6,8}.

It was previously reported that correlations between spiking activity in the BLA and rhinal cortices increase during appetitive learning⁹, and that this increased correlation is also observed between fast oscillations (35–45 Hz) in LFPs recorded in the same brain areas⁶, suggesting that the gamma coherence might be a marker for learning-related interactions between the amygdala and its cortical and subcortical targets. Consistent with this idea, Popescu *et al.*¹ found that gamma band coherence was also present between the BLA and ventral striatum during attentive waking. Moreover, gamma power in the ventral striatum was attenuated by muscimol inactivation of BLA outputs, indicating that fast oscillations in the striatum are driven in part by BLA inputs. Notably, spiking activity in both the BLA and the ventral striatum are phase-locked with gamma oscillations in each respective area (arguing against volume conduction as an explanation for the coherence), and coordinated spiking between the BLA and the ventral striatum occurs preferentially during periods of high gamma power. These data support the idea that gamma oscillations in the BLA drive a coherent increase in gamma oscillations in the ventral striatum during natural behavior and that gamma coherence is a useful marker for enhanced spike transmission between the BLA and the ventral striatum. This may explain an earlier observation that gamma power is graded across the striatum, with the lowest gamma power occurring in the dorsal striatum and the highest gamma power occurring in the ventral/medial striatum⁷, similar to the gradient in the density of BLA projections to the striatum.

Interestingly, Popescu *et al.*¹ found much weaker gamma coherence between the BLA and primary or secondary auditory cortex

or intralaminar thalamic nuclei, all of which project to the amygdala. This suggests that gamma coherence is not derived from these areas, which leaves open the possibility that gamma oscillations are generated by neural networks intrinsic to the amygdala or that one of the numerous other inputs to the BLA are externally driving gamma oscillations.

An important question is whether gamma coherence between the BLA and the ventral striatum has a functional role during learning or whether coherence emerges without any substantial relationship to behavior, like two dancers who rehearse together, but never perform. Popescu *et al.*¹ addressed this question by training cats to discriminate between two tones, only one of which predicted food availability. They found that, in the later stages of training, gamma coherence between the BLA and ventral striatum was enhanced specifically during stimulus presentation, with the greatest coherence being measured when the stimulus paired with reward was presented (Fig. 1). This difference in gamma coherence cannot be accounted for by differences in the sensory properties of the cues, as reversing the reinforcement contingencies switched which stimulus evoked the greatest gamma coherence. Moreover, the difference in gamma coherence for the two tones was well correlated with the degree to which the animals' anticipatory licking differed for the two stimuli. These data suggest that the amygdala and ventral striatum learn in rhythm; gamma coherence reflects coordinated activity in these brain areas that is important for learning to respond to reward-predictive stimuli.

The observations of learning-related increases in gamma coherence complement previous experiments showing increased spiking activity to reward-predictive cues observed separately in the BLA^{4,10,11} and the ventral striatum¹², providing evidence that increases in spiking activity in the BLA lead to increases in activity in the ventral striatum. This is consistent with recent experiments showing that cue-related spiking activity in the BLA precedes activity in the nucleus accumbens and that BLA inactivation substantially attenuates cue responses in the latter structure¹³. Serial transmission of value information from the BLA to the ventral striatum is also consistent with experiments showing that asymmetrical unilateral inactivation of the BLA and the nucleus accumbens disrupts conditioned operant responding¹³ and conditioned place preference¹⁴. Together with the physiological data, these disconnection experiments support a model in which information about cue-outcome associations is transmitted from

the BLA to the ventral striatum, where it is used to guide behavior.

If gamma coherence is a physiological marker for communication between the BLA and the ventral striatum, what is the function of this communication during learning? One possibility is that BLA inputs facilitate synaptic plasticity. Indeed, *in vitro* experiments show that BLA stimulation facilitates long-term potentiation at corticostriatal synapses of projection neurons¹⁵. Thus, the BLA may facilitate learning-related interactions between the cortex and the ventral striatum. However, there must be more to the story, as the disconnection experiments mentioned previously were performed post-training, after learning-related synaptic plasticity is presumably complete. This implies that the BLA and the ventral striatum continue to interact during the expression of conditioned behavior. That this pathway would have multiple functions is not surprising, as it is clear that the projection from the BLA to the ventral striatum is comprised of numerous anatomically and chemically distinct circuits and that lesions of different parts of the ventral striatum have distinct behavioral effects⁵.

The elegant work of Popescu *et al.*¹ raises the intriguing possibility that gamma coherence may be used to detect coordinated neural activity in specific circuits in the broader BLA to ventral striatum pathway. Future experiments must explore this notion in more detail. Does gamma coherence underlie learning in more complex tasks or learning that occurs very rapidly? In short, does the stunning observation by Popescu *et al.*¹ mean that gamma coherence will provide a means by which neuroscientists can further dissect the various functions of the BLA to ventral striatum pathway in a variety of goal-directed behaviors?

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