Corticothalamic feedback and sensory processing

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Although nearly half of the synaptic input to neurons in the dorsal thalamus comes from the cerebral cortex, the role of corticothalamic projections in sensory processing remains elusive. Although sensory afferents certainly establish the basic receptive field properties of thalamic neurons, increasing evidence indicates that feedback from the cortex plays a crucial role in shaping thalamic responses. Here, we review recent work on the corticothalamic pathways associated with the visual, auditory, and somatosensory systems. Collectively, these studies demonstrate that sensory responses of thalamic neurons result from dynamic interactions between feedforward and feedback pathways.

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Abbreviations
BF   best frequency
LGN lateral geniculate nucleus
MGB medial geniculate body
RTN reticular nucleus
VB   ventrobasal complex

Introduction

The cerebral cortex receives almost all of its sensory input from the thalamus. With the exception of olfaction, sensory information is delivered to cortical neurons through excitatory connections made by thalamic cells known as relay neurons. Although the name relay neuron might suggest that these cells simply pass the baton of sensory activity from the periphery to the cortex, it has become increasingly clear that these neurons are members of a complex circuit that involves ascending, descending, and recurrent sets of neuronal connections (Figure 1; [1–3]).

The major source of descending input to thalamic relay neurons comes from neurons with cell bodies located in layer 6 of the cerebral cortex (Figure 1). These corticothalamic neurons exert both an excitatory and an inhibitory influence on relay neurons, and it is the balance of this excitation and inhibition that is thought to influence many of the activity patterns and sensory response properties of relay neurons (reviewed in [4–6]). The excitatory influence of the cortex is achieved by monosynaptic connections that are markedly robust in number. Indeed, the number of corticothalamic synapses made onto a relay neuron is much greater than the number of synapses made from any other single source, including the ascending pathways from the periphery [7–9]. The inhibitory influence of the cortex, on the other hand, is achieved by polysynaptic connections either with intrinsic γ-amino butyric acid (GABA)ergic interneurons within the relay nuclei or with GABAergic neurons with cell bodies located in the reticular nucleus (RTN) of the thalamus [1–3].

Given the number of inputs provided to thalamic relay cells by corticothalamic neurons, it has been tempting to speculate what functional role these corticothalamic pathways could serve. Despite the certain importance of the corticothalamic pathway for thalamic processing, a consensus about its function has been elusive. Proposed roles for cortical feedback fall into two general categories: first, to effect sensory responses and receptive field properties, and second, to effect firing mode and/or activity state. Several excellent reviews discussing this second category of proposed roles have recently been published [4–6, 10–16]. In this review, we focus our discussion on the first category — the effects of cortical feedback on sensory responses and receptive field properties. As the anatomical properties of cortical feedback are so similar for the visual, auditory, and somatosensory systems, it seems reasonable to suggest that the role(s) of feedback should generalize across systems. By identifying the effects of corticothalamic input that are shared by multiple sensory systems, we hope to present results that will foster a consensus in thinking about corticothalamic function. Thus, our approach will be to identify and describe effects of feedback that are shared by more than one sensory system. In particular, we focus our discussion of the role of corticothalamic feedback for visual, auditory, and somatosensory processing by examining results from studies of sensory responses in the lateral geniculate nucleus (LGN), medial geniculate body (MGB), and ventrobasal complex (VB).

Corticothalamic feedback, receptive fields and sensory filtering

Before describing the influence of cortical feedback on sensory responses in the thalamus, it is important to review briefly the receptive field properties of thalamic neurons (Figure 2). In general, neurons in the LGN, MGB, and VB have receptive fields that can be described

Figure 1
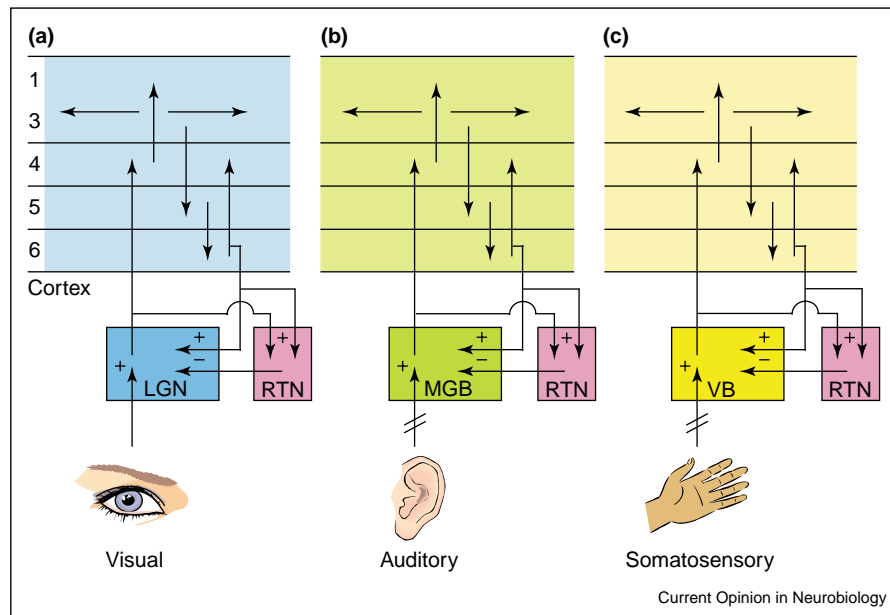
Corticothalamic circuitry for the **(a)** visual, **(b)** auditory, and **(c)** somatosensory systems. All three systems share a similar basic organization. Thalamocortical interactions begin with excitatory projections from thalamic relay neurons – located in the LGN, MGB, and VB — to neurons in layer 4 of primary visual, auditory, and somatosensory cortex. Neurons in cortical layer 6 in turn give rise to excitatory feedback to the thalamus. Corticothalamic feedback axons terminate directly onto relay neurons and interneurons in thalamic relay nuclei. Corticothalamic axons also extend collateral projections into the reticular nucleus (RTN). RTN neurons then give rise to inhibitory projections that terminate on thalamic relay neurons.

in terms of a discrete region in sensory space in which appropriate stimuli evoke an excitatory response. In addition to this excitatory region, neurons in all three thalamic nuclei often display a larger and more subtle suppressive surround (yellow regions in Figures 2a and b). In the visual system, LGN neurons have time-varying, center-surround receptive fields — the classical receptive field. Surrounding this classical center/surround receptive field, LGN neurons also have a larger more widespread surround in which visual stimulation serves to suppress responses to stimuli presented within the classical receptive field (reviewed in [17•]). In the auditory system, MGB neurons have receptive fields that can be described in terms of the range of frequencies — centered on a best frequency (BF) — that exert an excitatory influence over individual neurons [18,19•]. MGB neurons also often display a suppressive surround that serves to reduce the responsiveness of neurons to stimuli that extend beyond the classical receptive field (in frequency space) [18,19•]. In the somatosensory system, VB neurons have excitatory receptive fields centered on discrete regions of the body surface [20–22]. Finally, indirect evidence suggests that the spatial extent of VB receptive fields is partly determined by the existence of a suppressive surround [23,24•].

Although the basic properties of thalamic receptive fields are undoubtedly established by feedforward sensory

afferents [25,26], evidence from the visual, auditory, and somatosensory systems suggests that cortical feedback serves to amplify the effects of sensory stimulation both to the classical receptive field and to the suppressive surround (Figure 3). For instance, responses of LGN neurons to visual stimuli restricted to the classical receptive field are reduced following cortical inactivation [27], whereas responses to stimuli extending into the extra-classical surround display a release of suppression in the absence of cortical feedback [17•,28–31,32•]. These results suggest that cortical feedback normally serves to enhance the excitatory response of LGN neurons to stimuli restricted within the classical receptive field, as well as to enhance the suppressive effects of stimuli that extend into the extra-classical surround (Figure 3a). The combination of these two effects could be viewed as complementary mechanisms that serve to increase the spatial filtering properties and/or sharpen the receptive fields of LGN neurons.

In the auditory system, cortical feedback can influence the selectivity of MGB neurons in a manner analogous to that of the visual system (Figure 3b). For instance, focal activation of auditory cortex in the mustached bat enhances the responsiveness of individual MGB neurons if the BF of the thalamic neuron matches the BF of the activated region of cortex [33–35]. If the BFs do not match, then the responsiveness of MGB neurons

Figure 2
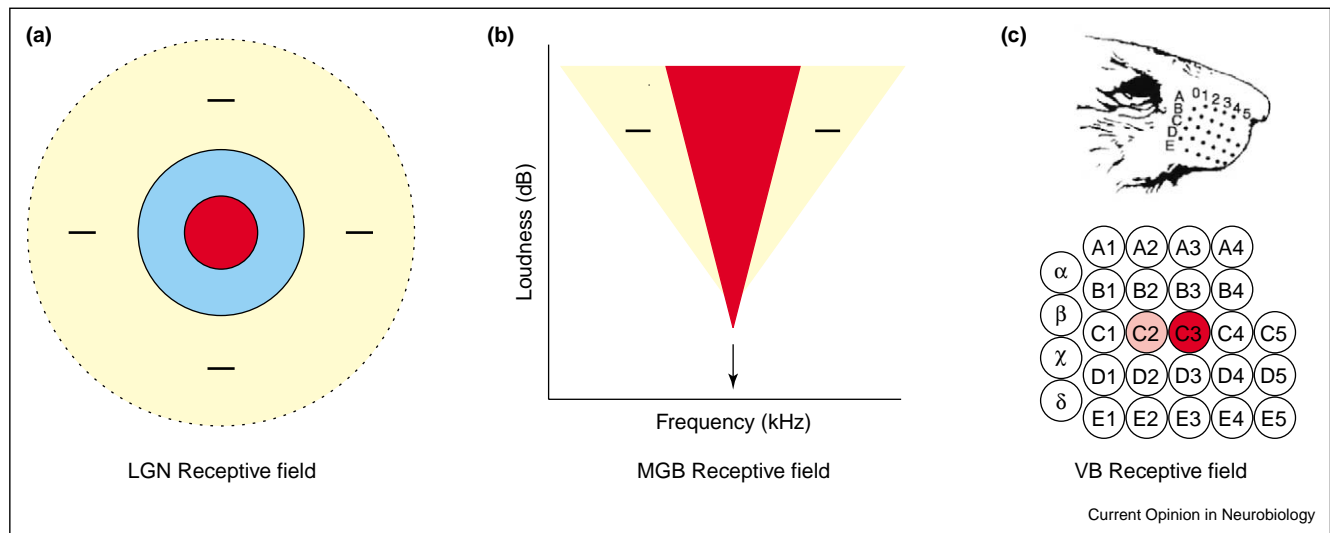
Receptive field structure of neurons in the LGN, MGB, and VB. Thalamic neurons in these relay nuclei have receptive fields that represent discrete regions of **(a)** retinotopic, **(b)** tonotopic, and **(c)** somatotopic space. (a) Surrounding the 'classical receptive field' (center and surround, indicated in red and blue) of LGN neurons is a larger suppressive region (yellow) in which visual stimuli inhibit neuronal activity. (b) MGB neurons have excitatory receptive fields centered on a best frequency (BF; arrow). Surrounding this excitatory receptive field, some MGB neurons also display inhibitory zones. (c) VB neurons that carry information about whisker stimulation have receptive fields that correspond to one or just a few whiskers. The figure is formed on the basis of results from [17•,19•,23,24•,31].

decreases. In addition, tuning curves of mismatched MGB neurons shift away from the BF of the stimulated region of cortex. Experiments that utilize cortical inactivation find complementary results [33,34]. Taken together, these results indicate that one role of cortical feedback is to adjust the tuning of thalamic input to the cortex.

Less is known about the suppressive surrounds of somatosensory neurons in the VB. Although neurons in area 3b of primate somatosensory cortex are known to have both excitatory and inhibitory regions within their receptive fields [36,37], identifying suppressive regions of VB receptive fields has been more difficult. Nevertheless, studies have shown that the spatial profile of VB receptive fields can expand (and sometimes contract) following inactivation of primary somatosensory cortex (Figure 3c [23,24•]). Thus, at least for some VB neurons, corticothalamic input appears to serve a similar role to that seen in the visual and auditory systems — corticothalamic input serves to sharpen and adjust the profile of thalamic receptive fields.

Thus far, we have discussed the enhanced suppression supplied by corticothalamic feedback as a means to sharpen receptive fields or increase the filtering properties of thalamic neurons. A related, yet different, view of corticothalamic feedback suggests that the increased filtering supplied by feedback might serve to improve the saliency of specific sensory stimuli, allowing these stimuli to 'pop out' of a noisy or inhomogeneous surround. Using separate but spatially adjacent gratings to stimulate cen-

ter and surround regions of individual LGN receptive fields, experiments in cats and primates have shown that surround suppression is strongest when the two gratings are similar (reviewed in [17•]). If the gratings differ in orientation, temporal, or spatial frequency, then the suppressive effects of surround stimulation are attenuated [29,32•,38]. In other words, although large homogenous stimulus patterns are maximally suppressive to LGN neurons, discrete stimulus patches embedded in a field of non-matching stimuli exhibit minimal suppression, and therefore 'pop out' from the surrounding stimuli.

Corticothalamic feedback and egocentric selection

In addition to sharpening thalamic receptive fields by increasing the effectiveness of center (excitatory) and surround (suppressive) mechanisms, corticothalamic feedback could also play a role in what has been termed 'egocentric selection'. Egocentric selection refers to the ability of cortical neurons to analyze thalamic input, determine which sensory features are encoded in the thalamic response, and then amplify the transmission of these selected features by feedback to the thalamus. This hypothesis was initially put forward by Suga and co-workers [34,39•] to explain plasticity in the auditory system; however, the fundamental premise of egocentric selection is also applicable to more general sensory processing.

At the heart of egocentric selection is the ability of cortical neurons to 'adjust and improve their own inputs' [34].

Figure 3
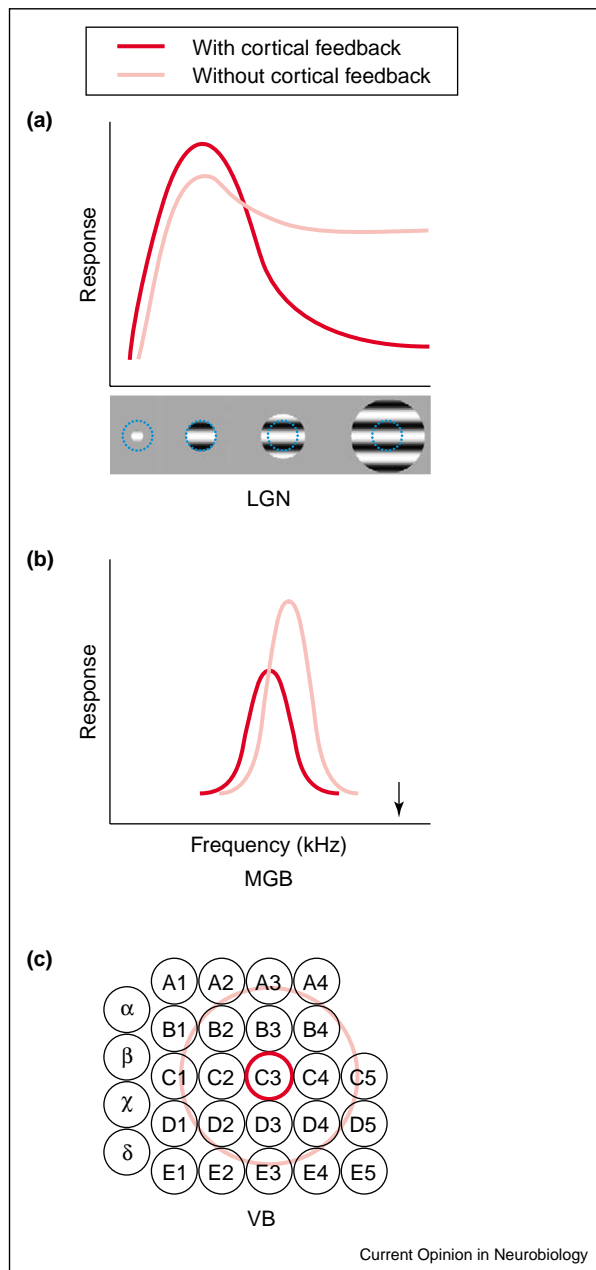
Corticothalamic feedback plays a role in sharpening thalamic receptive fields by amplifying excitatory and suppressive responses. In the visual, auditory, and somatosensory systems, cortical feedback modulates thalamic responses in similar ways. **(a)** In the visual system, the peak response in an area summation tuning curve (the point representing the optimal size of a visual stimulus) is decreased when cortical feedback is removed. In addition, the amount of suppression resulting from visual stimulation beyond the classical receptive field is reduced in the absence of cortical feedback. The approximate size of the classical receptive field is indicated in blue. **(b)** In the auditory thalamus, inactivating cortical regions (arrow) outside the best frequency of an MGB neuron shift the tuning of MGB neurons towards the inactivated frequency. This shift could be due to a release of cortically induced surround suppression. **(c)** In the somatosensory system, receptive fields of VB neurons carrying information about whisker stimulation can change size (i.e. the number of whiskers that drive a neuron can

Egocentric selection in the auditory system can be demonstrated by revisiting the experiments of Suga and co-workers [33–35]. Once a sensory signal is initially transmitted from the MGB to the cortex, further activity in the MGB (and other corticofugal targets [39[•]]) is markedly modified by feedback from the activated regions of cortex. The activation of a particular region of cortex leads to an initial assessment that the BF of that area of cortex is present in the sensory signal. By amplifying the responses of thalamic neurons that best encode the predicted signal (i.e. the BF) and inhibiting the responses of thalamic neurons that do not, the cortex thus sharpens its own response profile through feedback projections.

Whether or not corticothalamic feedback serves a similar role in egocentric selection in the visual and somatosensory systems is an open question, however, results from recent work in the visual system may support the idea of egocentric selection [17[•]]. Although this line of thinking is certainly speculative, it represents a novel means for viewing corticothalamic function for vision. In the visual system, the initial transmission of a visual signal through the LGN leads to the activation of a limited region of cortex that is selective for stimulus orientation. As is the case in the auditory system, further activity in the LGN is then modified by feedback from the activated cortical area. Part of this modification could take the form of increased temporal coherence among ensembles of LGN neurons that are co-activated by a common oriented stimulus [17[•],40]. Along these lines, orientation tuning curves that are generated from the joint activity of two LGN neurons — tuning curves that represent patterns of activity sent to the cortex — are more tightly tuned in the presence of corticothalamic feedback than in its absence [17[•]]. Although the mechanisms that are responsible for enhancing the temporal coherence among LGN neurons are unknown (and disputed; see [41]), they could involve: first, an anisotropic distribution of synapses from individual corticothalamic axons across the LGN linking retinotopic regions of LGN that correspond to the orientation preference of the corticothalamic axon [42], and/or second, a reduction in the temporal jitter of LGN responses. Regardless of the underlying mechanism, by increasing the correlated activity of LGN neurons corticothalamic input could serve to increase the transfer of sensory information from thalamus to cortex, as converging LGN spikes interact in a positive reinforcing fashion over short temporal intervals to drive cortical responses [43,44].

Conclusions and future directions

It has become increasingly clear that thalamic neurons are not mere relays of sensory activity, but, rather, components of an elaborate circuit designed to perform complex computations for sensory processing. By comparing

increase) in the absence of cortical feedback. This figure is formed on the basis of results from [17[•],24[•],31,33].

results from the visual, auditory, and somatosensory systems, corticothalamic feedback has been found to function in both the sharpening of thalamic receptive fields and the packaging of sensory information most suited for cortical processing.

Future studies that are aimed at understanding the functions served by corticothalamic feedback are likely to rely more heavily on experiments with alert animals performing behaviorally relevant tasks. These experiments are promising for two reasons. First, any concerns over anesthesia-dependent activity patterns are eliminated. Second, several recent studies have shown that thalamic activity can be markedly modulated by behaviorally relevant tasks [45–48,49•,50,51]. For most of these tasks, it is difficult, if not impossible, to imagine how the measured effects could result from simple feedforward processing. Determining the contributions made by corticothalamic feedback to task-dependent thalamic processing therefore represents an important next step in our understanding of sensory processing, and will lead to a more complete picture of the dynamic relationship that exists between the thalamus and the cortex.

Acknowledgements

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