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Review

Transthalamic Pathways for Cortical Function

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The cerebral cortex contains multiple, distinct areas that individually perform specific computations. A particular strength of the cortex is the communication of signals between cortical areas that allows the outputs of these compartmentalized computations to influence and build on each other, thereby dramatically increasing the processing power of the cortex and its role in sensation, action, and cognition. Determining how the cortex communicates signals between individual areas is, therefore, critical for understanding cortical function. Historically, corticocortical communication was thought to occur exclusively by direct anatomical connections between areas that often sequentially linked cortical areas in a hierarchical fashion. More recently, anatomical, physiological, and behavioral evidence is accumulating indicating a role for the higher-order thalamus in corticocortical communication. Specifically, the transthalamic pathway involves projections from one area of the cortex to neurons in the higher-order thalamus that, in turn, project to another area of the cortex. Here, we consider the evidence for and implications of having two routes for corticocortical communication with an emphasis on unique processing available in the transthalamic pathway and the consequences of disorders and diseases that affect transthalamic communication.

Key words: cortex; efference copy; thalamus

Significance Statement

The relatively recent appreciation of the presence of transthalamic pathways, which are cortico-thalamo-cortical routes for corticocortical communication and organized in parallel with direct connections, has transformed our thinking about cortical functioning. Three main questions about this loom large: Does corticocortical communication always involve both direct and transthalamic pathways? What is different in the information carried by each pathway? Why relay one communication route through the thalamus? This manuscript aims to highlight these issues, provide some speculations regarding the answers, and more generally suggest research approaches to provide more insight into relating this new appreciation of cortical organization to fundamental issues of cortical functioning writ large.

Introduction

The conventional view of cortical processing of information, as defined by textbook accounts, is illustrated in Figure 1*A*. This asserts that information is processed in a hierarchical fashion, starting with primary sensory areas to secondary areas, etc., up the chain [Felleman and Van Essen, 1991; Luo (2020), their Fig. 4.51B; Kandel et al. (2000), their Fig. 28-2; and Squire et al., (2008), their Figs. 25.12 and 27.15]. In all of these accounts, the processing of information between cortical areas involves only direct connections. Furthermore, only thalamic nuclei involved in relaying peripheral information to the cortex (e.g., the relay of retinal information by the lateral geniculate nucleus) are considered in this account: most of the thalamus by volume (Fig. 1*A*, question marks) are left out.

Figure 1*B* shows an alternative view. That is, increasing evidence indicates that information between cortical areas can arrive either directly or indirectly via higher-order thalamic nuclei (Fig. 1*B*). These feedforward cortico-thalamo-cortical, or transthalamic, pathways often if not always are present in parallel to direct pathways and have functional properties that support the fast, robust propagation of stimulus information (Sherman and Guillery, 1998, 2013; Theyel et al., 2010; Sherman, 2016; Usrey and Sherman, 2021; Miller-Hansen and Sherman, 2022; Mo et al., 2024). Feedforward transthalamic pathways are thus well-positioned to influence higher-order processing.

Note in Figure 1*B* that thalamic nuclei involved in relaying peripheral information to the cortex are called “first order (FO),” whereas those involved in transthalamic processing are “higher order (HO),” and that these latter nuclei in Figure 1*B* involve most of those indicated by question marks in Figure 1*A*, thereby indicating a real and critical function for these thalamic relays. Note also that the schemas shown in Figure 1 represent

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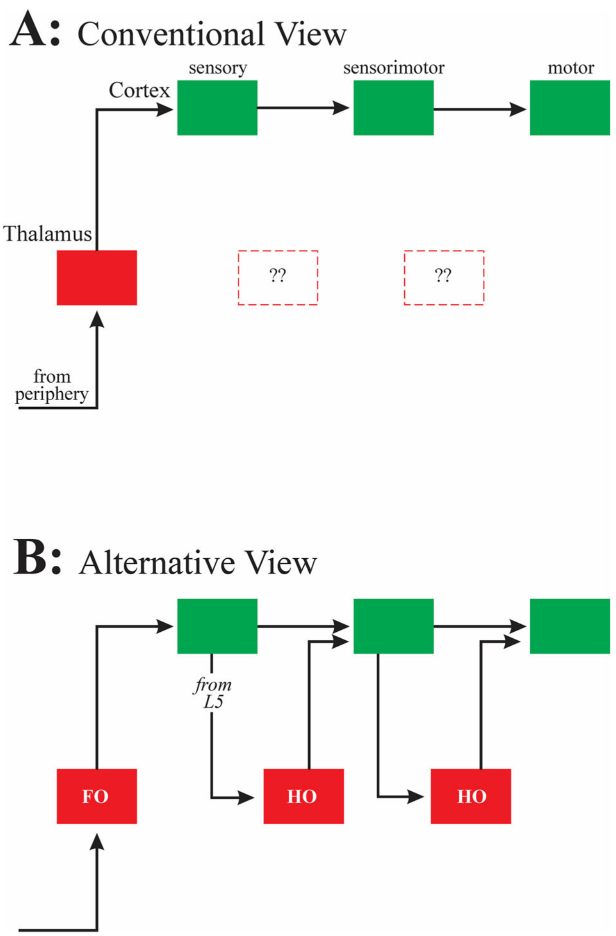

Figure 1. Comparison of conventional view (***A***) with the alternative view proposed here (***B***). The question marks in ***A*** indicate higher-order thalamic relays, for which no specific function is suggested in this scheme. Further details in text. Abbreviations, FO, first order; HO, higher order. Redrawn from Sherman (2017).

feedforward processing; feedback processing in the cortex involving direct and transthalamic pathways is discussed below under "Feedforward and feedback transthalamic pathways."

Drivers and modulators

The pathways that connect cortical areas, both directly and through the thalamus, involve excitatory neurons that use glutamate as a neurotransmitter. It is important to appreciate that glutamatergic afferents in the thalamus and cortex can be divided into two major functional classes: drivers and modulators. These have very different synaptic and thus functional properties (reviewed in Sherman and Guillery, 1998, 2013; Usrey and Sherman, 2021). The prevailing hypothesis is that drivers are used to communicate information in neuronal circuits and that modulators serve to affect the processing of driver inputs. Glutamatergic modulators act synaptically much like classical modulator systems (e.g., cholinergic or noradrenergic) with two exceptions: (1) the classic systems tend to be diffusely organized, whereas the glutamatergic ones have a high degree of topography, and (2) the classic ones originate in brainstem, whereas the glutamatergic ones have cortical (and thalamic) sources (Usrey and Sherman, 2021). Thus, the glutamatergic modulators are involved in circuits requiring topography and higher cognitive content, such as focal attention, learning, and memory. The classical modulator systems, because of their brainstem origin and diffuse projections, seem poorly suited for such topographically organized cognitive modulation.

In the feedforward transthalamic circuitry shown in Figure 1*B*, the two afferent components—from Layer 5 of a lower cortical area to the higher-order thalamus and higher-order thalamus to a higher cortical area—are both driver pathways (Theyel et al., 2010; Usrey and Sherman, 2019, 2021; Miller-Hansen and Sherman, 2022), suggesting that such transthalamic circuitry supports the transfer of information between cortical areas. Limited data suggest that the organization of direct corticocortical pathways has a more complex organization and contains both drivers and modulators (Covic and Sherman, 2011; DePasquale and Sherman, 2011).

Corticothalamic inputs

There are two very different sources of corticothalamic projections: one emanates from Layer 6 and the other from Layer 5.

Layer 6 corticothalamic pathway

To the extent that it has been studied, the Layer 6 corticothalamic pathway operates as a modulator, as opposed to the Layer 5 corticothalamic driver input, and is organized mostly in a feedback manner (Sherman and Guillery, 2013; Usrey and Sherman, 2019, 2021). A good example is the circuitry of the first-order relay, the lateral geniculate nucleus, which innervates the primary visual cortex (V1). It has two major glutamatergic inputs: the retina, which is a driver input and provides the main information to be relayed, and the Layer 6 input from V1, which provides numerous modulatory functions, affecting how retinal input is processed (Usrey and Sherman, 2019).

Every cortical area studied has a Layer 6 corticothalamic projection, and likewise, every thalamic nucleus, first order and higher order, receives such input.

Layer 5 corticothalamic pathway

Again, to the extent that it has been studied, the Layer 5 corticothalamic pathway operates as a driver, since both the Layer 5 input from a lower cortical area to a higher-order thalamic nucleus and that from the thalamic target to a higher cortical area (as in Fig. 1*B*) are drivers (Sherman and Guillery, 2013; Usrey and Sherman, 2019, 2021). Most transthalamic circuits appear to be organized in a feedforward manner, as in Figure 1*B*, but other arrangements, including feedback, have been documented (Miller-Hansen and Sherman, 2022).

Every cortical area so far studied has a Layer 5 projection that initiates transthalamic processing (Sherman and Guillery, 2013; Usrey and Sherman, 2019, 2021). However, only higher-order thalamic relays receive such a Layer 5 input.

To sum up, first-order thalamic relays receive driver input for relay from a subcortical source, whereas higher-order relays receive theirs from Layer 5 of the cortex. All thalamic nuclei receive modulatory input from Layer 6 of the cortex.

Layer 5 corticofugal cell properties

Layer 5 cells that give rise to corticothalamic innervation have several notable properties. Anatomically, they are the largest pyramidal cells in the cortex with apical dendrites that typically ascend to Layer 1 and end in branching tufts there (Larkum et al., 1999; Llano and Sherman, 2009). Physiologically, these apical dendrites have voltage-dependent Ca^{2+} channels that, when activated, lead to a large depolarization that produces high-frequency bursts of action potentials (Larkum et al., 1999;

Llano and Sherman, 2009), much like the bursting seen in thalamic relay neurons (Sherman, 2001). Of particular interest is one mechanism by which such bursts can be activated (Larkum et al., 1999; de Kock et al., 2021): an action potential in such a Layer 5 neuron will depolarize the apical dendrite through back-propagation, but by itself this does not typically elicit a Ca^{2+}-dependent burst; however, when this depolarization is coupled with a second depolarizing input to the apical dendritic tufts, a burst will often be evoked. Accordingly, inputs to the apical dendritic tuft and the basilar dendrites of Layer 5 corticothalamic neurons work together in an "AND gate" fashion for coincidence detection (Shai et al., 2015). The Layer 5 neurons that project directly to other cortical areas and those giving rise to transthalamic circuitry are effectively separate populations (Petrof et al., 2012), and only the latter express this bursting behavior (Takahashi et al., 2020). Such bursting has been seen in response to whisker deformation in these Layer 5 cells recorded in the primary somatosensory cortex of rats (de Kock et al., 2021).

Generality of transthalamic pathways in mammals

An important proviso to the above is that the vast majority of evidence for transthalamic processing derives from studies of sensory processing in mice. This raises the question as to how general this pattern is for mammalian cortical functioning. The problem is a general lack of evidence from species other than mice, but what evidence does exist supports this feature more broadly in mammals. For instance, in both cats and monkeys, morphological studies show that Layer 5 inputs target higher-order thalamic nuclei and have large terminals consistent with a driver function (Lund et al., 1975; Abramson and Chalupa, 1985; Feig and Harting, 1998; Rockland, 1998; Cappe et al., 2007; Rockland, 2019). Limited receptive field analyses in cats also support transthalamic processing in the visual system involving the pulvinar (de Souza et al., 2020). In rats, evidence exists that the higher-order somatosensory thalamic relay, the posterior medial nucleus, receives driving input from the primary somatosensory cortex (Diamond et al., 1992), suggesting this reflects transthalamic processing.

Whereas scattered and often indirect evidence supports the idea of transthalamic processing as a general property of the mammalian cortex, clearly more data are needed to establish this.

Feedforward and feedback transthalamic pathways

Figure 1 shows the corticocortical connections, both direct and transthalamic, limited to feedforward connections. Figure 2 adds feedback connections to the schema. We emphasize that Figure 2 is based on very limited data from the mouse (Theyel et al., 2010; Covic and Sherman, 2011; DePasquale and Sherman, 2011; Petrof et al., 2015; Mo and Sherman, 2019; Kirchgessner et al., 2021; Miller-Hansen and Sherman, 2022; Mo et al., 2024). With this proviso, we emphasize three points. First, direct projections contain both driver and modulator types in both directions. Second, in all cases studied so far, the Layer 5 input to the higher-order thalamus is strictly driver. Third, the feedforward transthalamic pathway is strictly driver, whereas the feedback serves a modulatory role. The difference is in the thalamocortical limb of these pathways: the feedforward limb is driver, but the feedback limb is modulator. Note that feedback transthalamic projections include two types: one that represents feedback from a higher cortical area to a lower one and the other that represents feedback from a cortical area to itself.

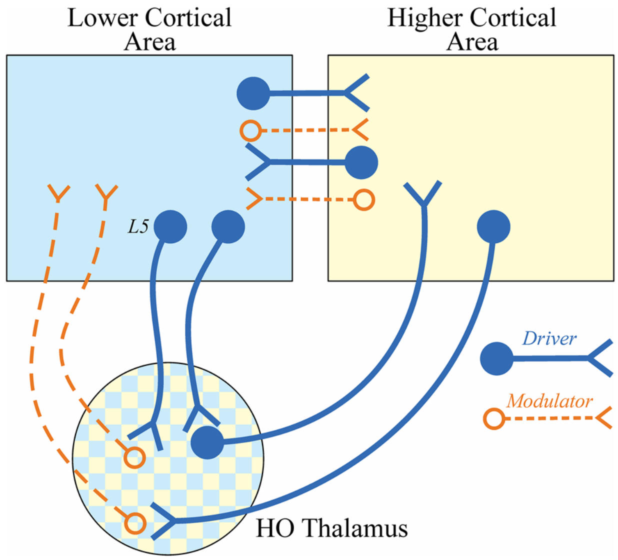

Figure 2. Transthalamic feedforward and feedback pathways. In each example, the Layer 5 input to the higher-order relay cell is driver. In the feedforward version (from lower to higher cortical area), the higher-order relay cell input to the cortex is driver, but in the feedback version (from higher to lower cortical area or from a cortical area to itself), the thalamocortical input is modulator. Layer 6 projections, which are strictly modulatory, are not shown.

An implicit view of cortical processing is that feedforward processing, which generally means connections running up a hierarchy of areas, is involved in information transfer (Felleman and Van Essen, 1991; Zagha, 2020), whereas feedback connections are largely modulatory in function (Rao and Ballard, 1999; Hupé et al., 2001; Nassi et al., 2013; Zagha, 2020; Debes and Dragoi, 2023). In the context of the driver/modulator classification, this would predict that feedforward connections are driver, and feedback, modulator. Figure 2 makes an interesting point regarding this. That is, again based on limited evidence, only the transthalamic circuits obey this prediction, whereas the direct connections contain both projection classes in both directions. Perhaps, the evidence for feedback modulation in the cortex is more dependent on transthalamic than direct connections.

Evidence and speculations regarding transthalamic functioning

Given that higher-order thalamic relays receive driving input from Layer 5 of the cortex and, in turn, project to the cortex, it follows that these relays are involved in the transfer of information between cortical areas (Sherman and Guillery, 2001, 2013; Sherman, 2016). Moreover, as most or all cortical areas have a Layer 5 projection to the thalamus, transthalamic pathways appear to be a ubiquitous feature of cortical processing. It is therefore important that we understand the functions of transthalamic circuits and the neural mechanisms that underlie these functions.

The relevant evidence for the role of transthalamic processing comes in two main forms. One involves scattered evidence based on anatomy, physiology, and/or behavior that demonstrates or strongly implies the presence of transthalamic pathways. The other involves studies of the higher-order thalamus (e.g., pulvinar), since, as noted, these thalamic relays are central elements in transthalamic processing. One problem with the latter is that many higher-order nuclei do get driver inputs from sources other than Layer 5 of the cortex; for example, there is an apparent driver input from the superior colliculus to the pulvinar (Kelly et al., 2003) and from the spinal nucleus of the fifth nerve to posterior medial nucleus (Groh et al., 2014; Mo et al., 2017). Thus, manipulations of higher-order thalamic relays do not necessarily imply effects on transthalamic function.

Insight from damage and disease

Given that the higher-order thalamus is the central link in transthalamic circuitry, insight into transthalamic communication can be gained from an examination of the behavioral/cognitive consequences following damage and disease of these thalamic nuclei. Lesion studies in humans and monkeys indicate a role for the pulvinar in orienting attention and filtering distractors. Visuospatial hemineglect is a syndrome that manifests as a failure to direct attention to contralesional visual space. Although visuospatial neglect is most prominent following lesions of the posterior parietal cortex, it is also seen following thalamic lesions, including those of the pulvinar. Consistent with an involvement of transthalamic pathways, inactivation of the dorsal pulvinar in monkeys, which has projections to the posterior parietal cortex, impairs the animals' ability to direct attention to contralateral visual space (Wilke et al., 2010). Similarly, humans with thalamic lesions often display deficits in engaging attention at cued locations in the contralateral hemifield (Rafal and Posner, 1987; Finsterwalder et al., 2017).

Individuals with pulvinar lesions also have difficulty with filtering visual distractors. For these patients, performance in discriminating target stimuli is impaired when the target stimulus is presented along with nontarget stimuli (i.e., distractors; Snow et al., 2009). Similar deficits in filtering distractor stimuli are also seen in humans with cortical lesions in the posterior parietal cortex and/or V4 (Gallant et al., 2000; Friedman-Hill et al., 2003) and in monkeys with lesions that affect area V4 (De Weerd et al., 1999). The similarity of these deficits following cortical and pulvinar lesions suggests that transthalamic pathways involving the pulvinar play a critical role in attention, as lesions to either node in the pathway have similar consequences on attention.

There is also evidence for the involvement of the higher-order thalamus in schizophrenia. Whereas first-order thalamic nuclei appear normal in patients with schizophrenia, two higher-order nuclei, the mediodorsal nucleus and the pulvinar, appear shrunken with neuronal loss (Danos et al., 2003; Brickman et al., 2004; Byne et al., 2009; Cronenwett and Csernansky, 2010; Janssen et al., 2012; Parnaudeau et al., 2013; Dorph-Petersen and Lewis, 2017; Penner et al., 2018). This finding suggests that schizophrenia may be associated with a disruption of transthalamic circuitry and, consequently, some of the cognitive defects in schizophrenia including deficits in selective attention (Gold et al., 2007) may be related, in part, to pathology in the transthalamic system.

Evidence for transthalamic pathways from studies of circuits

Selectively blocking transthalamic or direct circuits

There is a long history of using the ablation (i.e., physical lesion, cooling, and temporary chemical blockade) approach to knock out one cortical area and determine its effect on another. This has been done by silencing early visual areas and determining the effects on higher ones (Sherk, 1978; Girard and Bullier, 1989; Girard et al., 1991; Casanova et al., 1992; Salin and Bullier, 1995; Funk and Rosa, 1998); the same has been done for somatosensory cortical areas (Burton and Robinson, 1987; Garraghty et al., 1990a,b; Garraghty et al., 1991; Murray et al., 1992; Pons et al., 1992). However, because the concept of transthalamic processing was not known at the time of these experiments, the results were interpreted strictly based on removing direct corticocortical connections. Yet the ablations would necessarily have removed both direct and transthalamic inputs to the target cortical areas.

To gain insight into the separate functions of direct versus transthalamic circuits, an ablation approach is needed that selectively affects only one or the other. There have been several early efforts to do such experiments in mice.

Somatosensory processing

A number of such studies in mice have been focused on somatosensory processing. Many have been directed at the transthalamic pathway from S1 by using optogenetics to inhibit the synapse from S1 Layer 5 inputs to the posterior medial nucleus. The first clear evidence of a transthalamic pathway from S1 to S2 via the posterior medial nucleus was documented in mice (Theyel et al., 2010). When testing the effects on whisking behavior in mice, inhibition of this Layer 5 input to the posterior medial nucleus reduces their ability both to discriminate different textures (Qi et al., 2022; Mo et al., 2024) and to detect the sudden appearance of stimuli (Le Merre et al., 2018; Esmaeili et al., 2021; Mo et al., 2024). Working memory needed to successfully discriminate textures is also affected by inhibiting this synapse (Mo et al., 2024). This is interesting because working memory seems to depend on persistent activity in the cortex (Fuster and Alexander, 1971; Kubota and Niki, 1971; Funahashi et al., 1989; Christophel et al., 2017; Leavitt et al., 2017). Such activity in cortical areas relies on constant input from the higher-order thalamus (Reinhold et al., 2015; Bolkan et al., 2017; Guo et al., 2017). Thus, a simple explanation for this result is that inhibition of the transthalamic pathway, by reducing the input from the posterior medial nucleus, prevents the establishment of persistent activity in S2.

Attempts to parse the distinct functions of the direct versus transthalamic circuits are essentially limited to the comparison of Layer 5 cells that project directly to other cortical areas in mice to those that initiate transthalamic circuitry (Takahashi et al., 2020; Musall et al., 2023; Mo et al., 2024). These studies indicate that the direct Layer 5 pathway does not contribute much to sensory discrimination but that the transthalamic pathway does so.

Visual processing

Evidence from the mouse shows that multiple visual cortical areas send driver input to pulvinar cells that, in turn, project to other visual cortical areas (Miller-Hansen and Sherman, 2022), thus establishing the presence of transthalamic processing in the visual system. Furthermore, as mice move through a visual environment, it is the input from the pulvinar rather than directly from the visual cortex that more powerfully influences the response patterns of the higher-order visual cortex (Blot et al., 2021).

There is also much anatomical evidence consistent with this from other species, namely in the form of large terminals from the visual cortex in the pulvinar (Rockland, 1996), implying a driving input from the visual cortex to the pulvinar, which in turn suggests transthalamic circuitry. Finally, there is evidence from monkeys that pulvinar serves, through its widespread connections with the cortex, to coordinate multiple cortical areas subserving attention (Saalmann et al., 2012) and synchronous activity (Cortes et al., 2020; Eradath et al., 2021), as described in greater detail below in the subsection "A hub for broadcasting cognitive influences broadly across the cortex."

Auditory processing

Evidence for transthalamic processing in the auditory system is largely limited to morphological data that are consistent with such circuitry. That is, cortical inputs to the first-order auditory thalamic relay, the ventral division of the medial geniculate nucleus, contain only smaller terminals, consistent with an input strictly from Layer 6, whereas those to the higher-order relay, the dorsal division of the medial geniculate nucleus, contain both smaller and larger terminals (Bajo et al., 1995; Rouiller and Welker, 2000; Llano and Sherman, 2008; Antunes and Malmierca, 2021). The latter is consistent with Layer 5 input, which implies that transthalamic circuits exit in the cortical processing of auditory information.

Sensorimotor processing

Evidence exists in mice for a transthalamic pathway from S1 to M1 that parallels a direct projection (Petrof et al., 2015; Mo and Sherman, 2019). Prior examples of transthalamic pathways had been limited to sensory cortices, so this example suggests that transthalamic circuitry may be more general among cortical areas and not be limited to sensory processing.

Studies of the higher-order thalamus

Gating of transthalamic information

Just as the first-order thalamus (e.g., the lateral geniculate nucleus) can gate/govern the flow of peripheral signals to the cortex, the higher-order thalamus appears well suited for gating the communication of signals between cortical areas. Indeed, the higher-order thalamus has more modulatory circuitry and more extrathalamic inhibitory control than is present in the first-order thalamus. For instance, differences exist in how first-order and higher-order neurons respond to modulatory input. Whereas serotonergic and cholinergic inputs from the brainstem depolarize all first-order relay cells, these sources of input hyperpolarize a significant minority (1/4 to 1/3) of neurons in higher-order nuclei due to different receptors for the neurotransmitters (Varela and Sherman, 2007, 2008). These sources of input likely influence transthalamic corticocortical communication. Furthermore, many higher-order relays seem rather selectively targeted by GABAergic inputs that not so robustly target first-order relays. Examples are basal ganglia input to higher-order parts of the ventral anterior/ventral lateral thalamic complex, zona incerta input to the posterior medial nucleus, and pretectal input to the posterior medial nucleus and pulvinar (Power et al., 1999; Barthó et al., 2002; McFarland and Haber, 2002; Giber et al., 2008; Koster and Sherman, 2024). These extra inhibitory inputs could gate transthalamic circuits and thus determine whether cortical areas communicate directly or through both direct and transthalamic connections.

Recent evidence also points to differences in the cell and circuit properties of GABAergic projections from the thalamic reticular nucleus to the first-order and higher-order thalamus (Clemente-Perez et al., 2017; Li et al., 2020; Martinez-Garcia et al., 2020). Whereas calbindin-containing reticular cells, which occupy central core regions of the thalamic reticular nucleus, innervate the first-order thalamus, somatostatin-containing reticular cells, which occupy the surrounding edges of the nucleus, innervate the higher-order thalamus (Li et al., 2020; Martinez-Garcia et al., 2020; Carroll et al., 2022). Biologically based modeling efforts further indicate reticular inhibition can interact with transthalamic circuits to facilitate computations associated with cognition (Jaramillo et al., 2019).

While the functions and interactions from these various sources of GABAergic input may be complex, in general, these GABAergic inputs would hyperpolarize a substantial fraction of higher-order relay cells, thereby interrupting transthalamic communication or influencing ongoing rhythmic interactions. The inhibition of higher-order relay cells, if it were strong and long-lasting enough, would also deinactivate their T-type Ca^{2+} channels. Thus, when the inhibition ceases and the transthalamic gateway opens, the first significant input from Layer 5 to the affected thalamic neurons will elicit a burst, with the potential significance of such a response, such as providing a wake-up call to the targeted cortical area (Sherman, 2001; Swadlow et al., 2002; Usrey, 2002) Taking all of this together, it is noteworthy that burst firing is more prevalent in the higher-order thalamus compared with the first-order thalamus in awake, behaving monkeys (Ramcharan et al., 2005; Wei et al., 2011).

A hub for broadcasting cognitive influences broadly across the cortex

The higher-order thalamus has also been suggested to serve as an efficient hub for the rapid dispersal of cognitive influences supplied by higher cortical areas. For instance, with tasks requiring visual attention, fMRI and electrophysiological studies find increased activity in the pulvinar (Usrey and Kastner, 2020). Among the fMRI studies, results from humans show increased activity in the pulvinar with shifts of attention across the visual field (Yantis et al., 2002), attention directed to specific locations (Arcaro et al., 2018), and filtering of distracter information (Fischer and Whitney, 2012). Likewise, electrophysiological studies in monkeys show that spatial attention modulates visual responses in the dorsal, lateral, and inferior divisions of the pulvinar (Petersen et al., 1985; Saalmann et al., 2012; Zhou et al., 2016). The effects of attention include increased response magnitude and a reduction in the variability of signals communicated to the cortex (Petersen et al., 1985; Saalmann et al., 2012).

The higher-order thalamus has also been proposed to facilitate corticocortical communication by synchronizing oscillatory activity between the cortical areas (reviewed in Shipp, 2003; Buschman and Kastner, 2015; Fries, 2015; Kastner and Usrey, 2023). This idea is based on the view that synaptic communication is enhanced when source and target neurons are similarly depolarized (in phase with each other) and has led researchers to investigate whether the pulvinar is involved in synchronizing oscillatory cortical activity, as well as whether attention plays a role. In a series of technically challenging experiments conducted in macaque monkeys performing a visual attention task, simultaneous recordings were made from two interconnected cortical areas, V4 and TEO, as well as from the region of the pulvinar connected with both cortical areas (Saalmann et al., 2012). These experiments revealed synchronization in V4 and TEO in the alpha frequency range and, to a smaller extent, in the gamma frequency range when animals engaged in the spatial attention task. Results further revealed that the pulvinar causally influenced the oscillatory activity in both V4 and TEO, supporting the idea that the pulvinar can coordinate oscillatory activity between cortical areas as a function of attention to facilitate the communication of signals between cortical areas.

It should be noted that suggestions above that HO nuclei like the pulvinar may be involved in broadcasting information and/or synchronizing rhythmic behavior across wide areas of the cortex suggest thalamocortical axons that branch extensively to innervate multiple cortical areas, particularly in upper layers (Jones, 1998). A subset of HO thalamocortical cells do so, but this is also true for a subset of FO thalamic cells (Sherman and Usrey, 2024).

Layer 5 corticothalamic afferents are branches

All available evidence indicates a crucial feature of transthalamic processing: the Layer 5 corticothalamic axons that initiate this processing stream typically branch to innervate other subcortical sites (Deschênes et al., 1994; Bourassa and Deschênes, 1995; Bourassa et al., 1995; Kita and Kita, 2012; Economo et al., 2018). An important implication here is that branching axons in mammals means that the actual message projected to their targets is the same along all branches of an axon (Cox et al., 2000; Raastad and Shepherd, 2003).

Layer 5 projections to subcortical motor sites

As has been noted elsewhere (Prasad et al., 2020; Sherman and Usrey, 2021), the only route by which the cortex can fairly directly control or affect behavior is via Layer 5 subcortical projections that innervate brainstem motor centers (e.g., the superior colliculus or red nucleus) or the spinal cord. Furthermore, every cortical area so far studied, including primary sensory areas, has a Layer 5 projection to subcortical motor centers (Sherman and Guillery, 2013; Usrey and Sherman, 2021). One conclusion from this anatomical fact is that the distinction between the "sensory" and "motor" cortex seems obsolete, since all areas possess potential motor outputs. For instance, electrical stimulation of deep layers (e.g., Layer 5) of V1 in monkeys elicits short latency saccadic eye movements (Tehovnik et al., 2003). Figure 3 illustrates the subcortical targets of Layer 5 axons from four representative cortical areas in the mouse. As noted above, these extensive subcortical targets of Layer 5 are accomplished by axons with extensive branching, meaning that individual axons generally if not always innervate several of these targets; furthermore, many or most of these branching axons target both the thalamus and one or more subcortical motor centers.

Speculations regarding the functional significance of transthalamic pathways

Obvious questions are as follows: what is the point of transthalamic circuitry? Why cannot any such information relayed through the thalamus be sent directly, removing the need for transthalamic

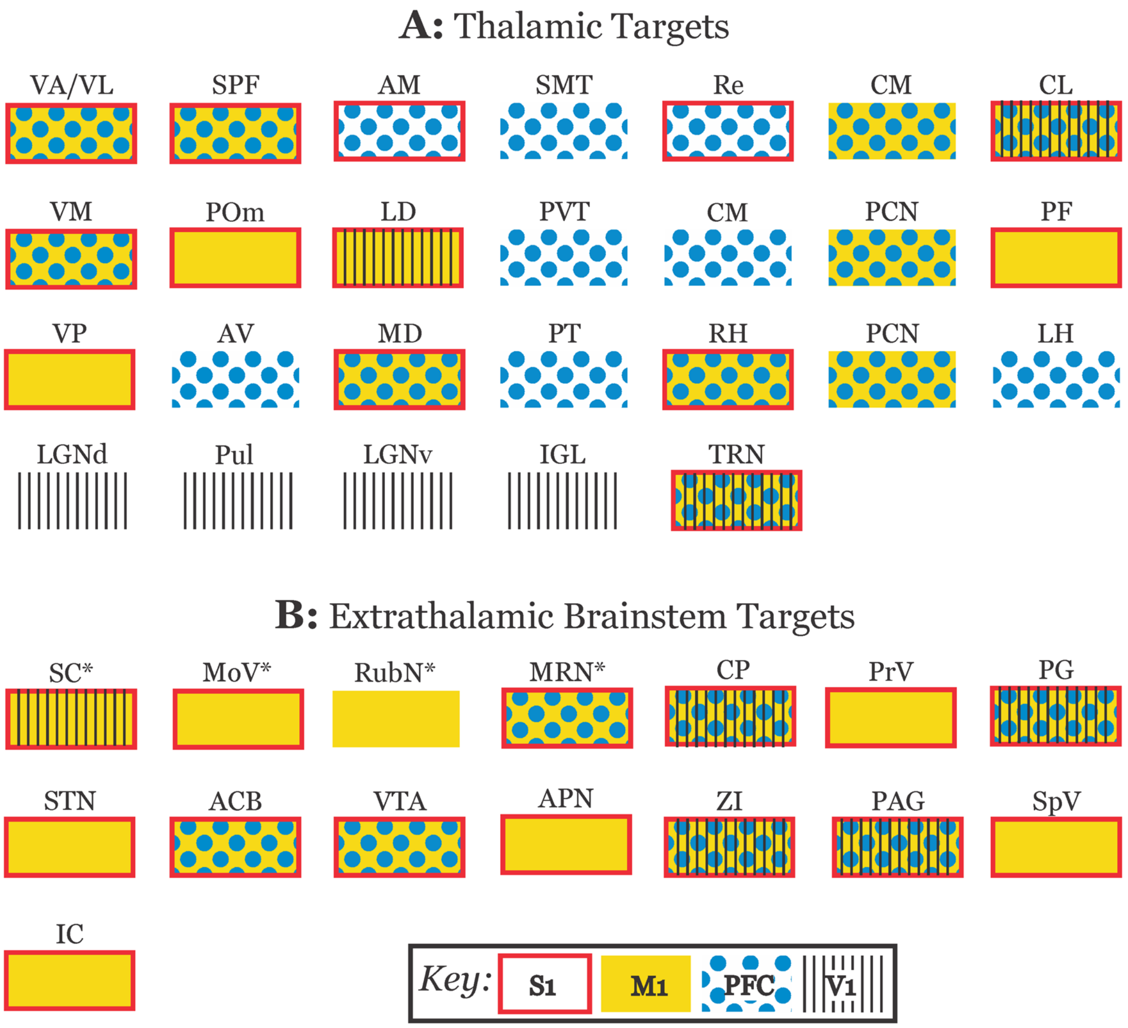

Figure 3. Widespread cortical L5 projections to the thalamus and select extrathalamic areas. For each cortical injection site from four representative cortical areas (indicated in the Key), filled boxes represent terminals in subcortical sites. ***A***, Thalamic targets. ***B***, Extrathalamic brainstem targets. Asterisks indicate subcortical motor centers. Abbreviations: ACB, nucleus accumbens; AM, anteromedial nucleus; APN, anterior prectectal nucleus; AV, anteroventral nucleus; CL, central lateral nucleus; CM, central medial nucleus; CP, caudoputamen; IC, inferior colliculus; IGL, intergeniculate leaflet; LD, lateral dorsal nucleus; LGNd, dorsal lateral geniculate nucleus; LGNv, ventral lateral geniculate nucleus; LH, lateral habenula; M1, primary motor cortex; MD, mediodorsal nucleus; MoV, motor nucleus of the fifth nerve; RN, midbrain reticular nucleus; PAG, periaqueductal gray; PCN, paracentral nucleus; PFC, prefrontal cortex; PG, pontine gray; PF, parafascicular nucleus; POm, posterior medial nucleus; PrV, principal trigeminal nucleus; PT, parataenial nucleus; Pul, pulvinar; PVT, paraventricular nucleus; Re, nucleus reuniens; RH, rhomboid nucleus; RubN, red nucleus; S1, primary somatosensory cortex; SC, superior colliculus; SMT, submedial nucleus; SPF, subparafascicular nucleus; SpV, spinal trigeminal nucleus; STN, subthalamic nucleus; TRN, thalamic reticular nucleus; V1, primary visual cortex; VA/VL, ventral anterior/ventral lateral nucleus; VM, ventral medial nucleus; VP, ventral posteromedial and posterolateral nuclei; VTA, ventral tegmental area; ZI, zona incerta. Redrawn from Prasad et al., (2020) and Sherman and Usrey (2021).

pathways? We offer two speculative ideas, and we emphasize that these are not mutually exclusive, and, of course, others may also be contemplated.

Do transthalamic circuits carry an efference copy message?

Not all branching Layer 5 corticofugal axons innervate the thalamus, although most do, and many or most of those that do innervate the thalamus also branch to innervate one or more subcortical motor centers (Deschênes et al., 1994; Bourassa and Deschênes, 1995; Bourassa et al., 1995; Kita and Kita, 2012; Economo et al., 2018). That is, based on an analysis of Layer 5 subcortical projections from the motor cortex in mice, there is a minority that innervates only the HO thalamus or extrathalamic targets (Economo et al., 2018). Also, for those neurons with branching axons, this means that the message sent to the thalamus to initiate transthalamic processing is a copy of that sent through the branching to motor center(s). In other words, the transthalamic message is a copy of a motor message, which is a definition of an efference copy (Guillery and Sherman, 2011; Sherman and Guillery, 2013).

Efference copies (also known as "corollary discharges") are universally present in the brains of any animal that actively moves through its environment. Readers are directed elsewhere for a detailed discussion of efference copies (Crapse and Sommer, 2008; Sommer and Wurtz, 2008; Wolpert and Flanagan, 2010); such a description is beyond the scope of this account. Efference copies allow the animal to disambiguate sensory stimuli due to the animal's own movements from those reflecting actual environmental changes. This is an absolute necessity, since an animal's survival frequently depends on sensing actual changes in the environment.

A good example of efference copy in action occurs with eye movements. When we smoothly track a moving object, the purpose is to keep that object imaged in or near the fovea. The result is visual stimulation of the retina in which the object being tracked seems to move little if at all, and the background moves instead. However, because the efference copy signal accounts for the eye movement during the tracking, the perception is of a moving object and stationary background. Similarly, when we move our hand across a textured surface, the perception is of the hand moving and the surface remaining stationary.

Figure 4, *A* and *B*, shows the logic of suggesting an efference copy function for some transthalamic circuits, and it is based on the functional significance of branching axons. Figure 4*A* shows a drawing from Cajal based on Golgi impregnations of primary afferents to the spinal cord (Cajal, 1911). He emphasized that every such axon branched, with one branch entering the spinal gray matter and the other ascending to the brain. Figure 4*B* illustrates a diagram view of this in which the lower branch innervates a motoneuron directly to activate a monosynaptic reflex movement. This branch, then, conveys a motor message. The branch directed to the brain is an exact copy of that motor message, and this defines an efference copy message. But this is a singular message that can be read by some postsynaptic circuits as an efference copy, and by others, as, perhaps, a sensory message about the movement of a joint angle, etc.

A simple analogy may serve to elucidate this latter point of a single message being read out with different meanings. Think of an army commander who receives intelligence that the enemy is advancing toward the river and so a key bridge must be destroyed before the enemy can use it. To deal with this, he sends a single message to two subordinates. One is to the officer concerned with the control of river crossings and is read as a command to blow up the bridge immediately: this is the "motor" message. The other is to the officer in charge of observing the progress of the imminent action: this is the "efference copy." Thus, each of the subordinates will read the whole message and react in accordance with their particular responsibilities, and the latter officer can correctly interpret the impending events.

Figure 4, *C–E*, extends this logic to transthalamic pathways. Figure 4*C* is an analog of Figure 4*B*, one branch of the Layer 5 axon carries a motor message to a subcortical motor center, and the other branch carries a copy of this message—the efference copy—to the higher-order thalamus for transthalamic processing. As noted above (Fig. 2), transthalamic processing can take two forms: feedforward and feedback. The efference copy message transmitted in the feedforward configuration provides driving input to the higher target cortical area (Fig. 4*D*), whereas the feedback version leads to a modulatory function in the target lower cortical area (Fig. 4*E*; Miller-Hansen and Sherman, 2022). Frankly, it is not clear what this distinction means for the functioning of efference copies, but the general idea is that if an area sends out a Layer 5 command to initiate a movement, this leads to a powerful thalamocortical input to a higher area, allowing it to keep track of any actions initiated by lower areas, whereas a command initiated higher in the hierarchy leads to modulation of processing in lower areas.

We emphasize that, as is the case for the example of Figure 4*B*, the message carried by the thalamic branch of the Layer 5 axon is a singular message that can be read by some recipients as an efference copy, and by others, as a different product of processing in the afferent cortical area.

One might ask: if the message sent via transthalamic pathways is an efference copy, why not send this message directly instead of through the thalamus? One possibility relates to the idea that a transthalamic route can be blocked via GABAergic input targeting the thalamic relay, and this would be useful if the presumptive transthalamic message would carry an incorrect efference copy signal. That is, while it seems obvious why appropriate efference copy information is needed to disambiguate sensory input due to one's own movements versus those caused by environmental events, it also follows that an efference copy message that is not tied to an actual movement would be problematic. Such rogue efference copy messages, if they existed, and if they were routed via transthalamic pathways, could be blocked at the thalamus; this could not be easily accomplished if the efference copy message were conveyed via a direct corticocortical route.

We argue that it is plausible for Layer 5 projections to subcortical motor centers to be active and yet not lead to any motor result. Such activity should then not be relayed through transthalamic circuits as an efference copy. We have previously argued for this scenario based on arguments related to attention (Sherman and Usrey, 2021). That is, there is tremendous convergence of Layer 5 inputs to subcortical motor sites from multiple cortical areas. The superior colliculus, for example, is innervated by Layer 5 inputs from most or all cortical areas tested (Prasad et al., 2020), and this represents a major bottleneck through which the cortex must operate to control behavior. Imagine, for instance, that an animal attends to visual stimuli (e.g., a rabbit scanning the skies for potential avian predators), relatively ignoring sounds in the environment, then it seems likely that Layer 5 projections from the visual cortex and not the auditory cortex would dominate circuits in the superior colliculus. Thus, we argue, a filtering must take place that allows only certain cortical areas through their Layer 5 projections to activate subcortical motor centers and affect behavior.

This filtering could take place in the cortex, by inhibiting Layer 5 activity in areas not privileged via attentional mechanisms to control behavior, or it could occur at the subcortical

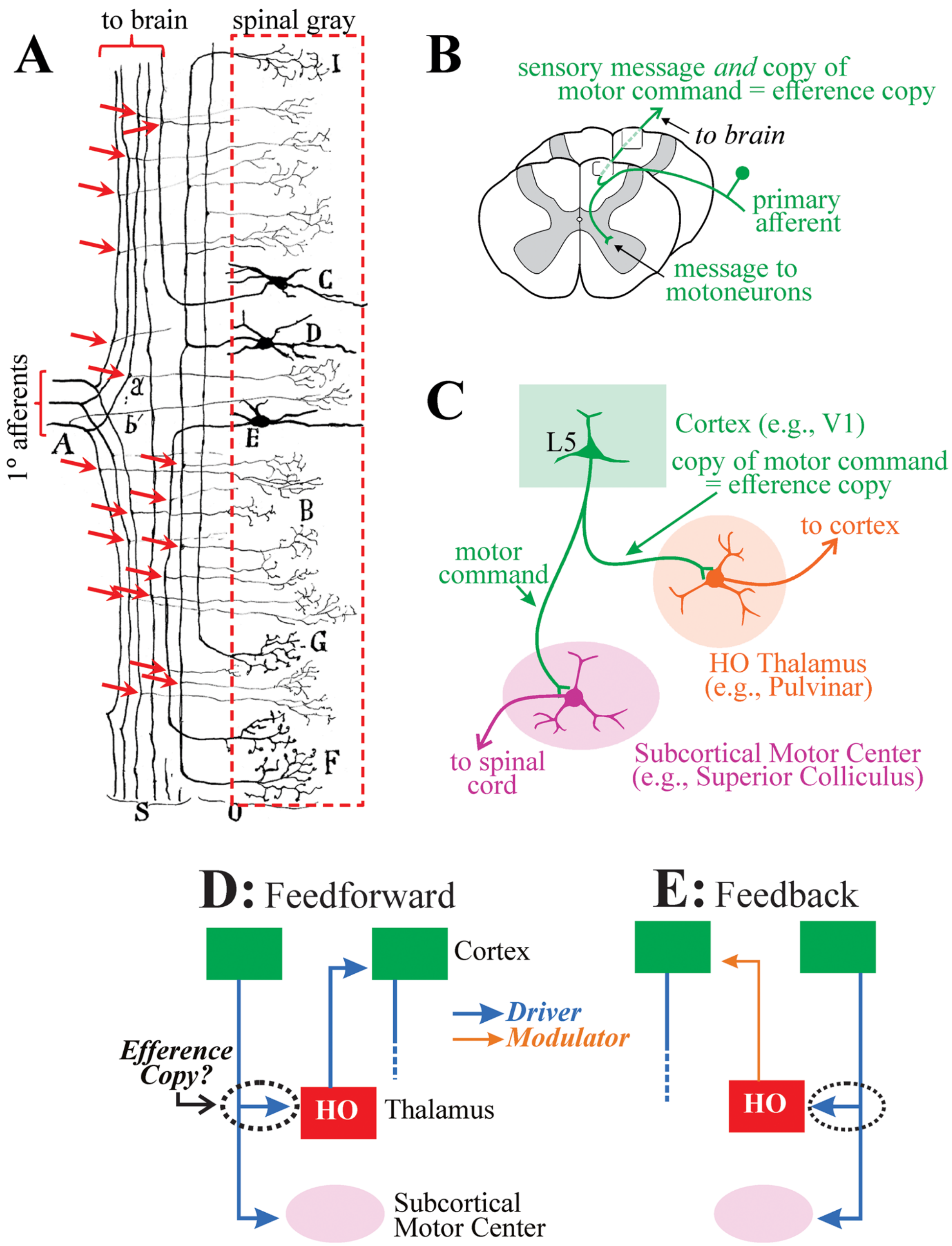

Figure 4. Branching axons and efference copy. ***A***, Cajal illustration of primary axons entering the spinal cord and branching to innervate the spinal gray matter and brain areas (Cajal, 1911). The red arrows indicate the branch points. ***B***, Schematic interpretation of ***A***. Because of the branching axon, the message carried by the ascending branch to the brain can be read as a copy of the motor message carried by the branch entering the ventral horn of the spinal cord; such a copy can be considered an efference copy. ***C***, Analog of ***B*** for transthalamic processing. Again, because of the branching axon, the message carried by the branch innervating the higher-order thalamus can be read as a copy of the motor message carried by the branch innervating a subcortical motor center; and again, such a copy can be considered an efference copy. ***D***, ***E***, The difference in the feedforward and feedback versions of transthalamic circuitry is that the feedforward efference copy message drives its cortical target, whereas the feedback one modulates its target (Fig. 2).

motor site. For two reasons, we favor the latter scenario. The first reason comes from an evolutionary perspective. In nonmammalian vertebrates with little or no telencephalic contribution to behavior, the most advanced sensorimotor structure is the midbrain tectum and associated circuits. As is the case for the mammalian homolog of this structure, the superior colliculus, the tectum does multimodal sensorimotor integration (Stein et al., 2009) and thus has to do the same sort of filtering suggested for mammalian Layer 5 projections. If this view is correct, it seems likely that the filtering is done within the midbrain, and since such filtering was successful in our nonmammalian vertebrate ancestors, it seems likely that it would have survived further evolution to filter Layer 5 inputs. Second, cortical areas not enhanced by attentional mechanisms continue to respond to sensory inputs. Thus, in the above example of the rabbit attending with vision to the skies, its auditory pathways would continue to respond to sounds, although presumably not as vigorously as its visual pathways. It follows that its auditory cortex would continue to generate some activity in its Layer 5 projections to subcortical motor centers, an activity that needs to be filtered out when vision is meant to dominate.

So even though Layer 5 axons from the auditory cortex fire, they would not generate a movement, and it would create a problem if their firing was treated anywhere as an efference copy.

To the extent that this scenario is realistic, it follows that an advantage of passing Layer 5 messages from one cortical area to another through the thalamus, where they may be blocked, makes sense so that these messages do not create efference copies unrelated to imminent motor actions. Whereas this scenario suggests that such transthalamic pathways would not be operative under these conditions, recall that evidence suggests that some Layer 5 inputs to the higher-order thalamus do not have branches innervating extrathalamic motor centers (Economo et al., 2018). These could thus represent transthalamic avenues that continue to operate and provide an avenue for corticocortical communication.

These are admittedly speculative ideas, and experiments are needed to test the idea that Layer 5 signals from axon branches innervating subcortical motor centers but not associated with the motor activity are blocked or at least differentially relayed through the higher-order thalamus. Experiments are also needed to determine whether signals conveyed via transthalamic circuits lacking branching axons differ from those with branching axons. There may indeed be parallel transthalamic pathways, one associated with motor behavior and one independent of behavior.

Do transthalamic circuits support the coordination and synchrony of cortical areas?

A given cortical area projects directly to numerous other cortical areas. Detailed studies in the monkey indicate that 15–20 targets for single visual areas are common (Markov et al., 2014). If many, or even perhaps all, of these direct connections are paralleled by transthalamic ones, an interesting possibility emerges. This is illustrated by Figure 5. There is no known plausible route by which the direct connections can be much affected or gated. However, as noted above, the higher-order relays through which transthalamic circuitry operates receive strong GABAergic inputs that, when active, can gate transthalamic processing. Thus, as shown in Figure 5, the pattern of activity among these GABAergic inputs can determine which cortical areas are functionally connected by just direct connections and which communicate through both direct and transthalamic connections.

It seems plausible that areas connected by both pathways can more effectively cooperate functionally. We discussed above how higher-order thalamocortical circuits can act to synchronize cortical areas, which is simply another way of looking at this suggestion. The point emphasized here and in Figure 5 is that circuitry is available to gate transthalamic pathways in a way that can determine the pattern of cortical areas communicating through both direct and transthalamic pathways versus just direct ones.

Classification of Layer 5 projections and transthalamic circuits

A major challenge to progress in understanding transthalamic processing derives from the great diversity in projection patterns of the Layer 5 axons involved. An analysis of a population of the Layer 5 projecting axons from the motor cortex in the mouse shows the tremendous variability among the population as regards branching patterns and subcortical targets, including those that innervate the thalamus (Kita and Kita, 2012; Economo et al., 2018).

The Layer 5 projection overall is thus a complex system, and the first step in analyzing a complex system is to classify its distinct components. An example is the value of such classification in research to understand retinal functioning. That is, early analysis of retinal organization first defined the component neuronal types—receptor, interneuron, and ganglion cell—each of which has been classified into distinct subtypes, and such classification has been a sine qua non for further insights into retinal functioning. Therefore, we assert such a classification is an absolute necessity and an early step for understanding how the cortex controls behavior and communicates among its areas via transthalamic pathways. In short, we need to know how many distinct motifs and submotifs exist for these Layer 5 projections and types of transthalamic circuits, how these vary across cortical areas, and the relationship of this overall classification to transthalamic circuits, which presumably also include multiple distinct classes that need to be identified.

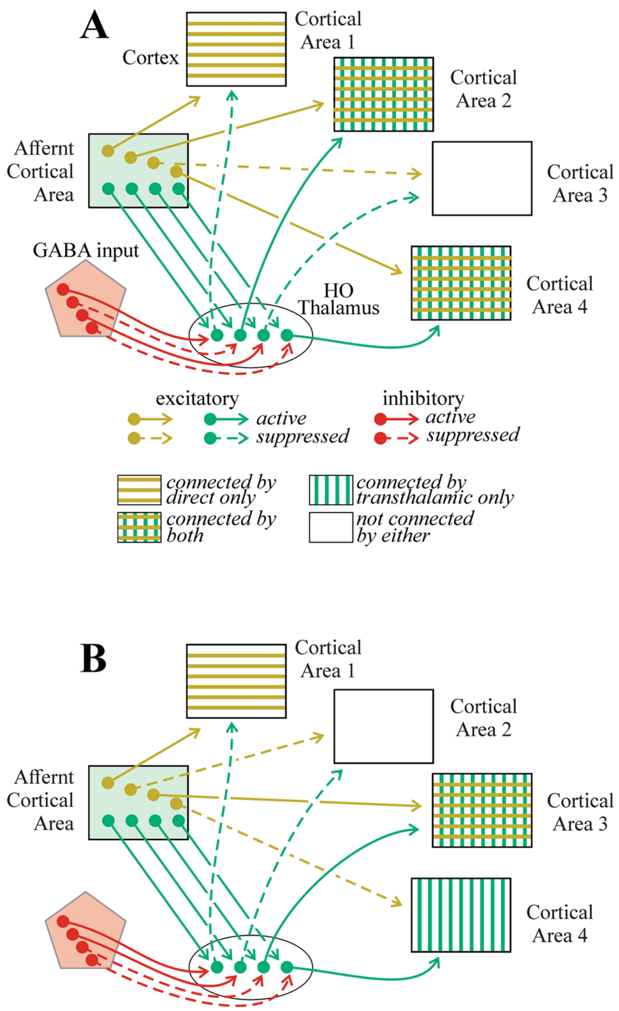

Figure 5. A cortical area connects to multiple other cortical areas via both direct and transthalamic pathways. In this example, four such parallel pathways are shown, but cortical areas may contact many more (e.g., 15–20 or more; Markov et al., 2014). GABAergic inputs to the higher-order thalamic relays can determine which areas are functionally connected by both pathways or just by direct ones. ***A***, The activity pattern of the GABAergic input results in the afferent cortical area functionally connected by both pathways only with Cortical areas 2 and 4. ***B***, A pattern of active GABAergic input different from that in ***A*** leads to a different pattern of functional joint connectivity.

Relationship to the core and matrix classification

Thalamic projections have been divided into core and matrix types (Jones, 1998; Halassa and Sherman, 2019; Usrey and Sherman, 2021). Core projections are said to be highly topographical, target only the cortex, and terminate in middle layers.

In contrast, matrix projections are described as topographically quite diffuse, targeting upper cortical layers and especially Layer 1, and some also target subcortical structures such as the amygdala, hippocampus, and basal ganglia. We have argued elsewhere that the core and matrix classification is fundamentally flawed and should be discontinued. The main problem is that, whereas many thalamocortical projections seem to follow the core description, there is no clear grouping of the remainder into any one class that can be considered matrix (Sherman and Usrey, 2024).

We assert that not only is the core/matrix classification unsound, but it has also led to misunderstanding and confusion. This is evident regarding its relationship to the thalamocortical division into first and higher order and implications for transthalamic functioning. For instance, some suggest that first-order relays are core, and higher-order relays, matrix (Harris and Shepherd, 2015; La Terra et al., 2022; Aru et al., 2023; Munn et al., 2023). However, an examination of the literature reveals no clear differences in thalamocortical projection patterns between first and higher-order relays that would correspond to the imagined core/matrix moiety (Sherman and Usrey, 2024). For instance, much, if not most, higher-order nuclei are core based on topographic projections that target middle layers (Niimi et al., 1974; Benevento and Rezak, 1976; Symonds et al., 1981; Dick et al., 1991; Krubitzer and Kaas, 1992; Huang and Winer, 2000; Lyon et al., 2003; Bureau et al., 2006; Mundinano et al., 2019; El-Boustani et al., 2020; Juavinett et al., 2020; Wang et al., 2023; reviewed in Usrey and Sherman, 2021).

An evolutionary perspective on the higher-order thalamus and transthalamic communication

In the textbook view of cortical processing, as indicated in Figure 1*A*, information enters the cortex and travels sequentially up the cortical hierarchy via direct connections until it reaches the highest areas for analysis and/or a motor response. This seems an unlikely product of evolution, because the animal's response to a novel and possibly hazardous stimulus would be dangerously slow. Furthermore, motor responses would become increasingly slower in more advanced animals with larger cortices as the signals work their way up the hierarchy before eventually reaching executive motor areas in the cortex. The increased time needed for these activities would seemingly have a negative impact on survival, as the likelihood of reaching sexual maturity would be diminished in animals with slower decision/reaction times. With transthalamic pathways as shown in Figure 4*C*, however, processing time is reduced as (1) the transthalamic pathways do not appear to be as restricted to following the sequential order of cortical processing as is seen with direct pathways, thereby reducing the number of nodes required for signals to reach the higher cortex, and (2) the Layer 5 projections from each cortical area to the higher-order thalamus has branches that target subcortical motor structures, allowing even the earliest cortical area in a series to influence motor responses (Tehovnik et al., 2003).

An indication of the importance of the partnership between the cortex and higher-order thalamus is also evident from comparisons of the relative sizes of the higher-order thalamus with the first-order thalamus across species with varying cortical sizes. Specifically, there is a significant relationship between the size of the cortex (and number of cortical areas) and the size of the higher-order thalamus. Moreover, as the thalamus becomes larger, more space is occupied by higher-order nuclei compared with first-order nuclei (Armstrong, 1979, 1980a,b, 1981; reviewed in Halley and Krubitzer, 2023). Thus, as a general rule, as brains increase in size and the number of higher cortical areas increases, the relative size of first-order thalamic nuclei and the cortical areas they innervate become relatively smaller, and the thalamus becomes dominated by higher-order nuclei (Halley and Krubitzer, 2023).

Summary and concluding remarks

We argue that the current understanding of thalamocortical relationships has advanced to the point where we must put to rest the old ideas about corticocortical communication expressed in Figure 1*A*. The major insight driving this view involved the discovery of transthalamic pathways and how this has changed our thinking about cortical functioning.

New views of thalamocortical relationships

The appreciation of transthalamic processing and its continued exploration has led to several new and related ideas, some of which are summarized in Figures 1*B* and 4. Three in particular stand out:

1. A first approximation of the functioning of a thalamic relay involves identifying the informational input it relays to a particular cortical area or set of areas. For decades, we have known this for several such relays: for example, the primary sensory thalamic nuclei such as the lateral geniculate nucleus relaying retinal input and the ventral posterior nucleus relaying somatosensory information from the head and body. This left the vast bulk of the thalamus, including examples such as the pulvinar and medial dorsal nucleus, as a conundrum, because whereas their cortical targets were known, exactly what information they relayed was not clear. We now suggest that most of this previously enigmatic mass of thalamic nuclei serves to relay information from one cortical area to another, often organized in parallel with direct connections between the same cortical areas. We thus divide the thalamus into first order—nuclei relaying subcortical information and whose general functioning has long been appreciated—and higher order—those nuclei newly appreciated as hubs in transthalamic processing.
2. The Layer 5 cortical neurons that give rise to transthalamic circuitry do so via branching axons that typically if not always branch to innervate numerous extrathalamic subcortical motor targets (Figs. 3, 4). We have argued that these Layer 5 projections to these motor centers represent the routes by which the cortex influences behavior, and thus the messages transmitted by these axons can be regarded as motor commands. Because of the branching axons, this in turn means that the message sent through transthalamic pathways is an exact copy of that command, which implies that it may serve as an efference copy. Note that in suggesting this hypothesis, we emphasize that this same transthalamic message can be interpreted by some of the cortical targets as an efference copy and by others with a different meaning.
3. As noted, these Layer 5 corticofugal projections represent the motor output of the cortex. To the extent that data are available, every cortical area so far studied has such motor outputs. This includes what is normally regarded as primary sensory cortices. We have argued that a major result of evolution of nervous systems is to produce rapid and efficient sensorimotor transformations to ensure fast responses to a changing environment. One implication of this is that

dividing the cortex into sensory and motor areas is misleading: all cortical areas are organized as sensorimotor processing machines.

Three key questions

Finally, we stress that appreciation that transthalamic pathways exist is just the beginning. Like much scientific endeavor, such a finding generates new questions that cry out for answers. We could list many, but we leave the reader with the three that we consider the most vital.

Are transthalamic and direct pathways between cortical areas always present and organized in parallel?

As indicated in Figure 1*B*, cortical areas can communicate either directly or via the thalamus. In the examples so far documented, every time a direct projection is seen between two cortical areas, a transthalamic pathway is also present. Is this always the case, or to rephrase, are cortical areas ever connected only directly or via the thalamus? The examples currently available are relatively few, dominated by studies of mice, and are mostly limited to visual and somatosensory areas. Again, we need more data to answer this question.

What is different in the information transmitted by each pathway?

An implicit assumption regarding the schema shown in Figure 1*B* is that the information transmitted by each pathway must be different, but there is precious little evidence to address this issue. One obvious difference is suggested by anatomy (Petrof et al., 2012): the transthalamic projection involves Layer 5 axons that branch repeatedly, with one or more branch(es) innervating thalamus, and others, a variety of subcortical targets, but these typically do not project to other cortical areas; direct projections appear to involve axons that distribute only within the cortex and do not innervate brainstem or spinal cord. Thus, the information transmitted by direct connections is contained within the cortex, whereas that initiated by transthalamic processing is shared with additional subcortical centers.

Why is one information route sent via the thalamus?

One logical reason to have a thalamic relay for information between cortical areas is that it allows for gating and/or modulation not available in direct connections. We have offered two different but not mutually exclusive hypotheses for this routing: such an arrangement could be key to the underlying circuitry required for different combinations of cortical areas to cooperate in synchrony, and it could be used to cancel rogue efference copy messages. The same argument could be made generally for first-order thalamic relays as well. That is, the retina does not project directly to the cortex, and thus relaying its information through the lateral geniculate nucleus allows for gating and/or modulation. However, until we have a better understanding of the nature of the information carried by transthalamic pathways, we cannot fully appreciate what value is added by thalamic filtering.

References

Abramson BP, Chalupa LM (1985) The laminar distribution of cortical connections with the tecto- and cortico-recipient zones in the cat's lateral posterior nucleus. Neuroscience 15:81–95.

Antunes FM, Malmierca MS (2021) Corticothalamic pathways in auditory processing: recent advances and insights from other sensory systems. Front Neural Circuits 15:721186.

Arcaro MJ, Pinsk MA, Chen J, Kastner S (2018) Organizing principles of pulvino-cortical functional coupling in humans. Nat Commun 9:5382.

Armstrong E (1979) Quantitative comparison of the hominoid thalamus. I. Specific sensory relay nuclei. Am J Phys Anthropol 51:365–382.

Armstrong E (1980a) A quantitative comparison of the hominoid thalamus: III. A motor substrate—the ventrolateral complex. Am J Phys Anthropol 52:405–419.

Armstrong E (1980b) A quantitative comparison of the hominoid thalamus: II. Limbic nuclei anterior principalis and lateralis dorsalis. Am J Phys Anthropol 52:43–54.

Armstrong E (1981) A quantitative comparison of the hominoid thalamus. IV. Posterior association nuclei-the pulvinar and lateral posterior nucleus. Am J Phys Anthropol 55:369–383.

Aru J, Larkum ME, Shine JM (2023) The feasibility of artificial consciousness through the lens of neuroscience. Trends Neurosci 46:1008–1017.

Bajo VM, Rouiller EM, Welker E, Clarke S, Villa AEP, De Ribaupierre Y, De Ribaupierre F (1995) Morphology and spatial distribution of corticothalamic terminals originating from the cat auditory cortex. Hear Res 83: 161–174.

Barthó P, Freund TF, Acsády L (2002) Selective GABAergic innervation of thalamic nuclei from zona incerta. Eur J Neurosci 16:999–1014.

Benevento LA, Rezak M (1976) The cortical projections of the inferior pulvinar and adjacent lateral pulvinar in the rhesus monkey (*Macaca mulatta*): an autoradiographic study. Brain Res 108:1–24.

Blot A, Roth MM, Gasler IT, Javadzadeh M, Imhof F, Hofer SB (2021) Visual intracortical and transthalamic pathways carry distinct information to cortical areas. Neuron 109:1996–2008.

Bolkan SS, Stujenske JM, Parnaudeau S, Spellman TJ, Rauffenbart C, Abbas AI, Harris AZ, Gordon JA, Kellendonk C (2017) Thalamic projections sustain prefrontal activity during working memory maintenance. Nat Neurosci 20:987–996.

Bourassa J, Deschênes M (1995) Corticothalamic projections from the primary visual cortex in rats: a single fiber study using biocytin as an anterograde tracer. Neuroscience 66:253–263.

Bourassa J, Pinault D, Deschênes M (1995) Corticothalamic projections from the cortical barrel field to the somatosensory thalamus in rats: a single-fibre study using biocytin as an anterograde tracer. Eur J Neurosci 7: 19–30.

Brickman AM, Buchsbaum MS, Shihabuddin L, Byne W, Newmark RE, Brand J, Ahmed S, Mitelman SA, Hazlett EA (2004) Thalamus size and outcome in schizophrenia. Schizophr Res 71:473–484.

Bureau I, von Saint PF, Svoboda K (2006) Interdigitated paralemniscal and lemniscal pathways in the mouse barrel cortex. PLoS Biol 4:e382.

Burton H, Robinson CJ (1987) Responses in the first or second somatosensory cortical area in cats during transient inactivation of the other ipsilateral area with lidocaine hydrochloride. Somatosens Res 4:215–236.

Buschman TJ, Kastner S (2015) From behavior to neural dynamics: an integrated theory of attention. Neuron 88:127–144.

Byne W, Hazlett EA, Buchsbaum MS, Kemether E (2009) The thalamus and schizophrenia: current status of research. Acta Neuropathol 117:347–368.

Cajal SRy (1911) *Histologie du Système Nerveaux de l'Homme et des Vertébrés*. Paris: Maloine.

Cappe C, Morel A, Rouiller EM (2007) Thalamocortical and the dual pattern of corticothalamic projections of the posterior parietal cortex in macaque monkeys. Neuroscience 146:1371–1387.

Carroll BJ, Sampathkumar V, Kasthuri N, Sherman SM (2022) Layer 5 of cortex innervates the thalamic reticular nucleus in mice. Proc Natl Acad Sci U S A 119:e2205209119.

Casanova C, Michaud Y, Morin C, McKinley PA, Molotchnikoff S (1992) Visual responsiveness and direction selectivity of cells in area 18 during local reversible inactivation of area 17 in cats. Visual Neurosci 9: 581–593.

Christophel TB, Klink PC, Spitzer B, Roelfsema PR, Haynes JD (2017) The distributed nature of working memory. Trends Cogn Sci 21:111–124.

Clemente-Perez A, et al. (2017) Distinct thalamic reticular cell types differentially modulate normal and pathological cortical rhythms. Cell Rep 19: 2130–2142.

Cortes N, de Souza BOF, Casanova C (2020) Pulvinar modulates synchrony across visual cortical areas. Vision 4:22.

Covic EN, Sherman SM (2011) Synaptic properties of connections between the primary and secondary auditory cortices in mice. Cereb Cortex 21: 2425–2441.

Cox CL, Denk W, Tank DW, Svoboda K (2000) Action potentials reliably invade axonal arbors of rat neocortical neurons. Proc Natl Acad Sci U S A 97:9724–9728.

Crapse TB, Sommer MA (2008) Corollary discharge across the animal kingdom. Nat Rev Neurosci 9:587–600.

Cronenwett WJ, Csernansky J (2010) Thalamic pathology in schizophrenia. Curr Top Behav Neurosci 4:509–528.

Danos P, Baumann B, Kramer A, Bernstein HG, Stauch R, Krell D, Falkai P, Bogerts B (2003) Volumes of association thalamic nuclei in schizophrenia: a postmortem study. Schizophr Res 60:141–155.

Debes SR, Dragoi V (2023) Suppressing feedback signals to visual cortex abolishes attentional modulation. Science 379:468–473.

de Kock CPJ, Pie J, Pieneman AW, Mease RA, Bast A, Guest JM, Oberlaender M, Mansvelder HD, Sakmann B (2021) High-frequency burst spiking in layer 5 thick-tufted pyramids of rat primary somatosensory cortex encodes exploratory touch. Commun Biol 4:709.

DePasquale R, Sherman SM (2011) Synaptic properties of corticocortical connections between the primary and secondary visual cortical areas in the mouse. J Neurosci 31:16494–16506.

Deschênes M, Bourassa J, Pinault D (1994) Corticothalamic projections from layer V cells in rat are collaterals of long-range corticofugal axons. Brain Res 664:215–219.

de Souza BOF, Cortes N, Casanova C (2020) Pulvinar modulates contrast responses in the visual cortex as a function of cortical hierarchy. Cereb Cortex 30:1068–1086.

De Weerd P, Peralta MR III, Desimone R, Ungerleider LG (1999) Loss of attentional stimulus selection after extrastriate cortical lesions in macaques. Nat Neurosci 2:753–758.

Diamond ME, Armstrong-James M, Budway MJ, Ebner FF (1992) Somatic sensory responses in the rostral sector of the posterior group (POm) and in the ventral posterior medial nucleus (VPM) of the rat thalamus: dependence on the barrel field cortex. J Comp Neurol 319:66–84.

Dick A, Kaske A, Creutzfeldt OD (1991) Topographical and topological organization of the thalamocortical projection to the striate and prestriate cortex in the marmoset (Callithrix jacchus). Exp Brain Res 84:233–253.

Dorph-Petersen KA, Lewis DA (2017) Postmortem structural studies of the thalamus in schizophrenia. Schizophr Res 180:28–35.

Economo MN, et al. (2018) Distinct descending motor cortex pathways and their roles in movement. Nature 563:79–84.

El-Boustani S, Sermet BS, Foustoukos G, Oram TB, Yizhar O, Petersen CCH (2020) Anatomically and functionally distinct thalamocortical inputs to primary and secondary mouse whisker somatosensory cortices. Nat Commun 11:3342.

Eradath MK, Pinsk MA, Kastner S (2021) A causal role for the pulvinar in coordinating task-independent cortico-cortical interactions. J Comp Neurol 529:3772–3784.

Esmaeili V, et al. (2021) Rapid suppression and sustained activation of distinct cortical regions for a delayed sensory-triggered motor response. Neuron 109:2183–2201.e2189.

Feig S, Harting JK (1998) Corticocortical communication via the thalamus: ultrastructural studies of corticothalamic projections from area 17 to the lateral posterior nucleus of the cat and inferior pulvinar nucleus of the owl monkey. J Comp Neurol 395:281–295.

Felleman DJ, Van Essen DC (1991) Distributed hierarchical processing in the primate cerebral cortex. Cereb Cortex 1:1–47.

Finsterwalder S, Demeyere N, Gillebert CR (2017) Deficit in feature-based attention following a left thalamic lesion. Neuropsychologia 102:1–10.

Fischer J, Whitney D (2012) Attention gates visual coding in the human pulvinar. Nat Commun 3:1051.

Friedman-Hill SR, Robertson LC, Desimone R, Ungerleider LG (2003) Posterior parietal cortex and the filtering of distractors. Proc Natl Acad Sci U S A 100:4263–4268.

Fries P (2015) Rhythms for cognition: communication through coherence. Neuron 88:220–235.

Funahashi S, Bruce CJ, Goldman-Rakic PS (1989) Mnemonic coding of visual space in the monkey's dorsolateral prefrontal cortex. J Neurophysiol 61: 331–349.

Funk AP, Rosa MG (1998) Visual responses of neurones in the second visual area of flying foxes (*Pteropus poliocephalus*) after lesions of striate cortex. J Physiol 513:507–519.

Fuster JM, Alexander GE (1971) Neuron activity related to short-term memory. Science 173:652–654.

Gallant JL, Shoup RE, Mazer JA (2000) A human extrastriate area functionally homologous to macaque V4. Neuron 27:227–235.

Garraghty PE, Florence SL, Kaas JH (1990a) Ablations of areas 3a and 3b of monkey somatosensory cortex abolish cutaneous responsivity in area 1. Brain Res 528:165–169.

Garraghty PE, Florence SL, Tenhula WN, Kaas JH (1991) Parallel thalamic activation of the first and second somatosensory areas in prosimian primates and tree shrews. J Comp Neurol 311:289–299.

Garraghty PE, Pons TP, Kaas JH (1990b) Ablations of areas 3b (SI proper) and 3a of somatosensory cortex in marmosets deactivate the second and parietal ventral somatosensory areas. Somatosens Mot Res 7:125–135.

Giber K, Slézia A, Bokor H, Bodor AL, Ludányi A, Katona I, Acsády L (2008) Heterogeneous output pathways link the anterior pretectal nucleus with the zona incerta and the thalamus in rat. J Comp Neurol 506:122–140.

Girard P, Bullier J (1989) Visual activity in area V2 during reversible inactivation of area 17 in the macaque monkey. J Neurophysiol 62:1287–1302.

Girard P, Salin PA, Bullier J (1991) Visual activity in macaque area V4 depends on area 17 input. Neuro Rep 2:81–84.

Gold JM, Fuller RL, Robinson BM, Braun EL, Luck SJ (2007) Impaired top-down control of visual search in schizophrenia. Schizophr Res 94:148–155.

Groh A, Bokor H, Mease RA, Plattner VM, Hangya B, Stroh A, Deschenes M, Acsády L (2014) Convergence of cortical and sensory driver inputs on single thalamocortical cells. Cereb Cortex 24:3167–3179.

Guillery RW, Sherman SM (2011) Branched thalamic afferents: what are the messages that they relay to cortex? Brain Res Brain Res Rev 66:205–219.

Guo ZV, Inagaki HK, Daie K, Druckmann S, Gerfen CR, Svoboda K (2017) Maintenance of persistent activity in a frontal thalamocortical loop. Nature 545:181–186.

Halassa MM, Sherman SM (2019) Thalamocortical circuit motifs: a general framework. Neuron 103:762–770.

Halley AC, Krubitzer L (2023) The coevolution of the neocortex and dorsal thalamus in mammals: scaling relationships between and within structures. In: *The cerebral cortex and thalamus* (Usrey WM, Sherman SM, eds), pp 585–595. New York, NY: Oxford University Press.

Harris KD, Shepherd GM (2015) The neocortical circuit: themes and variations. Nat Neurosci 18:170–181.

Huang CL, Winer JA (2000) Auditory thalamocortical projections in the cat: laminar and areal patterns of input. J Comp Neurol 427:302–331.

Hupé JM, James AC, Girard P, Lomber SG, Payne BR, Bullier J (2001) Feedback connections act on the early part of the responses in monkey visual cortex. J Neurophysiol 85:134–145.

Janssen J, et al. (2012) Regional specificity of thalamic volume deficits in male adolescents with early-onset psychosis. Br J Psychiatry 200:30–36.

Jaramillo J, Mejias JF, Wang XJ (2019) Engagement of pulvino-cortical feedforward and feedback pathways in cognitive computations. Neuron 101: 321–336.

Jones EG (1998) Viewpoint: the core and matrix of thalamic organization. Neuroscience 85:331–345.

Juavinett AL, Kim EJ, Collins HC, Callaway EM (2020) A systematic topographical relationship between mouse lateral posterior thalamic neurons and their visual cortical projection targets. J Comp Neurol 528:95–107.

Kandel ER, Schwartz JH, Jessell TM (2000) *Principles of neural science.* New York: McGraw Hill.

Kastner S, Usrey WM (2023) Attention and thalamocortical interactions. In: *The cerebral cortex and thalamus* (Usrey WM, Sherman SM, eds). New York, NY: Oxford University Press.

Kelly LR, Li J, Carden WB, Bickford ME (2003) Ultrastructure and synaptic targets of tectothalamic terminals in the cat lateral posterior nucleus. J Comp Neurol 464:472–486.

Kirchgessner MA, Franklin AD, Callaway EM (2021) Distinct "driving" versus "modulatory" influences of different visual corticothalamic pathways. Curr Biol 31:5121–5137.

Kita T, Kita H (2012) The subthalamic nucleus is one of multiple innervation sites for long-range corticofugal axons: a single-axon tracing study in the rat. J Neurosci 32:5990–5999.

Koster KP, Sherman SM (2024) Convergence of inputs from the basal ganglia with layer 5 of motor cortex and cerebellum in mouse motor thalamus. eLife 13:e97489.

Krubitzer LA, Kaas JH (1992) The somatosensory thalamus of monkeys: cortical connections and a redefinition of nuclei in marmosets. J Comp Neurol 319:123–140.

Kubota K, Niki H (1971) Prefrontal cortical unit activity and delayed alternation performance in monkeys. J Neurophysiol 34:337–347.

Larkum ME, Zhu JJ, Sakmann B (1999) A new cellular mechanism for coupling inputs arriving at different cortical layers. Nature 398:338–341.

La Terra D, Bjerre AS, Rosier M, Masuda R, Ryan TJ, Palmer LM (2022) The role of higher-order thalamus during learning and correct performance in goal-directed behavior. eLife 11:e77177.

Leavitt ML, Mendoza-Halliday D, Martinez-Trujillo JC (2017) Sustained activity encoding working memories: not fully distributed. Trends Neurosci 40:328–346.

Le Merre P, Esmaeili V, Charrière E, Galan K, Salin PA, Petersen CCH, Crochet S (2018) Reward-based learning drives rapid sensory signals in medial prefrontal cortex and dorsal hippocampus necessary for goal-directed behavior. Neuron 97:83–91.e85.

Li Y, et al. (2020) Distinct subnetworks of the thalamic reticular nucleus. Nature 583:819–824.

Llano DA, Sherman SM (2008) Evidence for nonreciprocal organization of the mouse auditory thalamocortical-corticothalamic projection systems. J Comp Neurol 507:1209–1227.

Llano DA, Sherman SM (2009) Differences in intrinsic properties and local network connectivity of identified layer 5 and layer 6 adult mouse auditory corticothalamic neurons support a dual corticothalamic projection hypothesis. Cereb Cortex 19:2810–2826.

Lund JS, Lund RD, Hendrickson AE, Bunt AH, Fuchs AF (1975) The origin of efferent pathways from the primary visual cortex, area 17, of the macaque monkey as shown by retrograde transport of horseradish peroxidase. J Comp Neurol 164:287–303.

Luo L (2020) *Principles of neurobiology*, Ed 2. CRC Press.

Lyon DC, Jain N, Kaas JH (2003) The visual pulvinar in tree shrews II. Projections of four nuclei to areas of visual cortex. J Comp Neurol 467:607–627.

Markov NT, et al. (2014) A weighted and directed interareal connectivity matrix for macaque cerebral cortex. Cereb Cortex 24:17–36.

Martinez-Garcia RI, Voelcker B, Zaltsman JB, Patrick SL, Stevens TR, Connors BW, Cruikshank SJ (2020) Two dynamically distinct circuits drive inhibition in the sensory thalamus. Nature 583:813–818.

McFarland NR, Haber SN (2002) Thalamic relay nuclei of the basal ganglia form both reciprocal and nonreciprocal cortical connections, linking multiple frontal cortical areas. J Neurosci 22:8117–8132.

Miller-Hansen AJ, Sherman SM (2022) Conserved patterns of functional organization between cortex and thalamus in mice. Proc Natl Acad Sci U S A 119:e2201481119.

Mo C, McKinnon C, Sherman SM (2024) A transthalamic pathway crucial for perception. Nat Commun 15:6300.

Mo C, Petrof I, Viaene AN, Sherman SM (2017) Synaptic properties of the lemniscal and paralemniscal pathways to the mouse somatosensory thalamus. Proc Natl Acad Sci U S A 114:E6212–E6221.

Mo C, Sherman SM (2019) A sensorimotor pathway via higher-order thalamus. J Neurosci 39:692–704.

Mundinano IC, Kwan WC, Bourne JA (2019) Retinotopic specializations of cortical and thalamic inputs to area MT. Proc Natl Acad Sci U S A 116:23326–23331.

Munn BR, Müller EJ, Aru J, Whyte CJ, Gidon A, Larkum ME, Shine JM (2023) A thalamocortical substrate for integrated information via critical synchronous bursting. Proc Natl Acad Sci U S A 120:e2308670120.

Murray GM, Zhang HQ, Kaye AN, Sinnadurai T, Campbell DH, Rowe MJ (1992) Parallel processing in rabbit first (SI) and second (SII) somatosensory cortical areas: effects of reversible inactivation by cooling of SI on responses in SII. J Neurophysiol 68:703–710.

Musall S, et al. (2023) Pyramidal cell types drive functionally distinct cortical activity patterns during decision-making. Nat Neurosci 26:495–505.

Nassi JJ, Lomber SG, Born RT (2013) Corticocortical feedback contributes to surround suppression in V1 of the alert primate. J Neurosci 33:8504–8517.

Niimi K, Kadota M, Matsushita Y (1974) Cortical projections of the pulvinar nuclear group of the thalamus in the cat. Brain Behav Evol 9:422–457.

Parnaudeau S, O'Neill PK, Bolkan SS, Ward RD, Abbas AI, Roth BL, Balsam PD, Gordon JA, Kellendonk C (2013) Inhibition of mediodorsal thalamus disrupts thalamofrontal connectivity and cognition. Neuron 77:1151–1162.

Penner J, Osuch EA, Schaefer B, Théberge J, Neufeld RWJ, Menon RS, Rajakumar N, Bourne JA, Williamson PC (2018) Higher order thalamic nuclei resting network connectivity in early schizophrenia and major depressive disorder. Psychiatry Res Neuroimaging 272:7–16.

Petersen SE, Robinson DL, Keys W (1985) Pulvinar nuclei of the behaving rhesus monkey: visual responses and their modulation. J Neurophysiol 54:867–886.

Petrof I, Viaene AN, Sherman SM (2012) Two populations of corticothalamic and interareal corticocortical cells in the subgranular layers of the mouse primary sensory cortices. J Comp Neurol 520:1678–1686.

Petrof I, Viaene AN, Sherman SM (2015) Properties of the primary somatosensory cortex projection to the primary motor cortex in the mouse. J Neurophysiol 113:2652.

Pons TP, Garraghty PE, Mishkin M (1992) Serial and parallel processing of tactual information in somatosensory cortex of rhesus monkeys. J Neurophysiol 68:518–527.

Power BD, Kolmac CI, Mitrofanis J (1999) Evidence for a large projection from the zona incerta to the dorsal thalamus. J Comp Neurol 404:554–565.

Prasad JA, Carroll BJ, Sherman SM (2020) Layer 5 corticofugal projections from diverse cortical areas: variations on a pattern of thalamic and extrathalamic targets. J Neurosci 40:5785–5796.

Qi J, Ye C, Naskar S, Inácio AR, Lee S (2022) Posteromedial thalamic nucleus activity significantly contributes to perceptual discrimination. PLoS Biol 20:e3001896.

Raastad M, Shepherd GM (2003) Single-axon action potentials in the rat hippocampal cortex. J Physiol (Lond) 548:745–752.

Rafal RD, Posner MI (1987) Deficits in human visual spatial attention following thalamic lesions. Proc Natl Acad Sci U S A 84:7349–7353.

Ramcharan EJ, Gnadt JW, Sherman SM (2005) Higher-order thalamic relays burst more than first-order relays. Proc Natl Acad Sci U S A 102:12236–12241.

Rao RP, Ballard DH (1999) Predictive coding in the visual cortex: a functional interpretation of some extra-classical receptive-field effects. [see comments]. Nat Neurosci 2:79–87.

Reinhold K, Lien AD, Scanziani M (2015) Distinct recurrent versus afferent dynamics in cortical visual processing. Nat Neurosci 18:1789–1797.

Rockland KS (1996) Two types of corticopulvinar terminations: round (type 2) and elongate (type 1). J Comp Neurol 368:57–87.

Rockland KS (1998) Convergence and branching patterns of round, type 2 corticopulvinar axons. J Comp Neurol 390:515–536.

Rockland KS (2019) Corticothalamic axon morphologies and network architecture. Eur J Neurosci 49:969–977.

Rouiller EM, Welker E (2000) A comparative analysis of the morphology of corticothalamic projections in mammals. Brain Res Bull 53:727–741.

Saalmann YB, Pinsk MA, Wang L, Li X, Kastner S (2012) The pulvinar regulates information transmission between cortical areas based on attention demands. Science 337:753–756.

Salin PA, Bullier J (1995) Corticocortical connections in the visual system: structure and function. Physiol Rev 75:107–154.

Shai AS, Anastassiou CA, Larkum ME, Koch C (2015) Physiology of layer 5 pyramidal neurons in mouse primary visual cortex: coincidence detection through bursting. PLoS Comput Biol 11:e1004090.

Sherk H (1978) Area 18 cell responses in cat during reversible inactivation of area 17. J Neurophysiol 41:204–215.

Sherman SM (2001) Tonic and burst firing: dual modes of thalamocortical relay. Trends Neurosci 24:122–126.

Sherman SM (2016) Thalamus plays a central role in ongoing cortical functioning. Nat Neurosci 19:533–541.

Sherman SM (2017) Functioning of circuits connecting thalamus and cortex. Compr Physiol 7:713–739.

Sherman SM, Guillery RW (1998) On the actions that one nerve cell can have on another: distinguishing "drivers" from "modulators". Proc Natl Acad Sci U S A 95:7121–7126.

Sherman SM, Guillery RW (2001) *Exploring the thalamus*. San Diego: Academic Press.

Sherman SM, Guillery RW (2013) *Functional connections of cortical areas: a new view from the thalamus*. Cambridge, MA: MIT Press.

Sherman SM, Usrey WM (2021) Cortical control of behavior and attention from an evolutionary perspective. Neuron 109:3048–3064.

Sherman SM, Usrey WM (2024) A reconsideration of the core and matrix classification of thalamocortical projections. J Neurosci 44:e0163242024.

Shipp S (2003) The functional logic of cortico-pulvinar connections. Philos Trans R Soc Lond B Biol Sci 358:1605–1624.

Snow JC, Allen HA, Rafal RD, Humphreys GW (2009) Impaired attentional selection following lesions to human pulvinar: evidence for homology between human and monkey. Proc Natl Acad Sci U S A 106:4054–4059.

Sommer MA, Wurtz RH (2008) Brain circuits for the internal monitoring of movements. Annu Rev Neurosci 31:317–338.

Squire LR, Berg D, Bloom FE, du Lac S, Ghosh A, Spitzer NC (2008) *Fundamental neuroscience*, Ed 3. Academic Press.

Stein BE, Stanford TR, Rowland BA (2009) The neural basis of multisensory integration in the midbrain: its organization and maturation. Hear Res 258:4–15.

Swadlow HA, Gusev AG, Bezdudnaya T (2002) Activation of a cortical column by a thalamocortical impulse. J Neurosci 22:7766–7773.

Symonds LL, Rosenquist AC, Edwards SB, Palmer LA (1981) Projections of the pulvinar-lateral posterior complex to visual cortical areas in the cat. Neuroscience 6:1995–2020.

Takahashi N, Ebner C, Sigl-Glöckner J, Moberg S, Nierwetberg S, Larkum ME (2020) Active dendritic currents gate descending cortical outputs in perception. Nat Neurosci 10:1277–1285.

Tehovnik EJ, Slocum WM, Schiller PH (2003) Saccadic eye movements evoked by microstimulation of striate cortex. Eur J Neurosci 17:870–878.

Theyel BB, Llano DA, Sherman SM (2010) The corticothalamocortical circuit drives higher-order cortex in the mouse. Nat Neurosci 13:84–88.

Usrey WM (2002) Spike timing and visual processing in the retinogeniculocortical pathway. Philos Trans R Soc Lond B Biol Sci 357:1729–1737.

Usrey WM, Kastner S (2020) Functions of the visual thalamus in selective attention. In: *The cognitive neurosciences* (Poeppel D, Gazzaniga MS, eds). Ed 6, pp. 369–377. Cambridge, MA: MIT Press.

Usrey WM, Sherman SM (2019) Corticofugal circuits: communication lines from the cortex to the rest of the brain. J Comp Neurol 527:640–650.

Usrey WM, Sherman SM (2021) *Exploring thalamocortical interactions: circuitry for sensation, action, and cognition*. New York: Oxford University Press.

Varela C, Sherman SM (2007) Differences in response to muscarinic agonists between first and higher order thalamic relays. J Neurophysiol 98:3538–3547.

Varela C, Sherman SM (2008) Differences in response to serotonergic activation between first and higher order thalamic nuclei. Cereb Cortex 19:1776–1786.

Wang Q, Stepniewska I, Kaas JH (2023) Thalamic connections of the caudal part of the posterior parietal cortex differ from the rostral part in galagos (*Otolemur garnettii*). J Comp Neurol 531:1752–1771.

Wei H, Bonjean M, Petry HM, Sejnowski TJ, Bickford ME (2011) Thalamic burst firing propensity: a comparison of the dorsal lateral geniculate and pulvinar nuclei in the tree shrew. J Neurosci 31:17287–17299.

Wilke M, Turchi J, Smith K, Mishkin M, Leopold DA (2010) Pulvinar inactivation disrupts selection of movement plans. J Neurosci 30:8650–8659.

Wolpert DM, Flanagan JR (2010) Motor learning. Curr Biol 20:R467–R472.

Yantis S, Schwarzbach J, Serences JT, Carlson RL, Steinmetz MA, Pekar JJ, Courtney SM (2002) Transient neural activity in human parietal cortex during spatial attention shifts. Nat Neurosci 5:995–1002.

Zagha E (2020) Shaping the cortical landscape: functions and mechanisms of top-down cortical feedback pathways. Front Syst Neurosci 14:33.

Zhou H, Schafer RJ, Desimone R (2016) Pulvinar-cortex interactions in vision and attention. Neuron 89:209–220.