Visual Neuroscience (2017), **34**, e016, 9 pages.
Copyright © Cambridge University Press, 2017 0952-5238/17
doi:10.1017/S095252381700013X

SPECIAL ISSUE

Visual Thalamus

REVIEW ARTICLE

A cross-species comparison of corticogeniculate structure and function

J. MICHAEL HASSE[1,2] AND FARRAN BRIGGS[1,2,3,4]

[1]Program in Experimental and Molecular Medicine at Dartmouth, Hanover, New Hampshire
[2]Ernest J. Del Monte Institute for Neuroscience, University of Rochester School of Medicine, Rochester, New York
[3]Neuroscience, University of Rochester School of Medicine, Rochester, New York
[4]Center for Visual Science, University of Rochester, Rochester, New York

(RECEIVED January 19, 2017; ACCEPTED June 15, 2017)

Abstract

The corticogeniculate circuit is an evolutionarily conserved pathway linking the primary visual cortex with the visual thalamus in the feedback direction. While the corticogeniculate circuit is anatomically robust, the impact of corticogeniculate feedback on the visual response properties of visual thalamic neurons is subtle. Accordingly, discovering the function of corticogeniculate feedback in vision has been a particularly challenging task. In this review, the morphology, organization, physiology, and function of corticogeniculate feedback is compared across mammals commonly studied in visual neuroscience: primates, carnivores, rabbits, and rodents. Common structural and organizational motifs are present across species, including the organization of corticogeniculate feedback into parallel processing streams in highly visual mammals.

Keywords: Corticogeniculate, V1, LGN

Introduction

The corticogeniculate circuit is an evolutionarily conserved feedback pathway that links the visual cortex to the visual portion of the thalamus in the mammalian visual system (Jones, 1985; Sherman & Guillery, 2006; Briggs & Usrey, 2007*a*). Corticogeniculate neurons are a subpopulation of corticothalamic neurons. The term "corticothalamic" refers to all cortical neurons that project axons to thalamic structures (e.g. pulvinar, superior colliculus, basal forebrain), while "corticogeniculate" refers only to cortical neurons that project axons to the lateral geniculate nucleus (LGN) of the thalamus. The cell bodies of corticogeniculate (CG) neurons are located exclusively in layer 6 of the primary and secondary visual cortex (Gilbert & Kelly, 1975; Lund et al., 1975; Lin & Kaas, 1977; Swadlow & Weyand, 1981; Katz, 1987; Conley & Raczkowski, 1990; Jiang et al., 1993; Fitzpatrick et al., 1994; Usrey & Fitzpatrick, 1996; Brumberg et al., 2003; Ichida et al., 2014; Kim et al., 2014; Briggs et al., 2016). CG neurons often receive direct feedforward geniculocortical input (Hendrickson et al., 1978; Bullier & Henry, 1980; Blasdel & Lund, 1983; Ferster & Lindstrom, 1983; Briggs & Usrey, 2007*b*; Da Costa & Martin, 2009) as well as local input from neurons spanning the cortical layers (Lund & Boothe, 1975; Katz, 1987; Wiser & Callaway, 1996; Briggs & Callaway, 2001; Zarrinpar & Callaway, 2006; Kim et al., 2014; Briggs et al., 2016). CG neurons are all excitatory neurons, releasing glutamate as their primary neurotransmitter (Sherman & Guillery, 2006). All CG neurons project axons to the LGN and the thalamic reticular nucleus (TRN), where they form modulating synapses (Sherman & Guillery, 1998, 2006). The corticogeniculate circuit serves a vital role in visual information processing by providing the visual cortex the opportunity to dynamically influence its own input. Experimental and theoretical evidence suggests that CG feedback increases the salience of relevant visual stimuli by modulating the gain of LGN neuronal responses, altering the mode, timing, and precision of LGN spiking activity, and sharpening LGN receptive fields (Briggs & Usrey, 2008). The goal of this review is to examine similarities and differences in corticogeniculate anatomy, physiology, and function across commonly studied mammalian species: primates, carnivores, rabbits, and rodents.

Anatomy of CG neurons

Like most cortical areas, primary visual cortex (V1) is a laminar structure with 6 main cortical layers. The deepest layer of V1, layer 6, is relatively large and contains a morphologically diverse neuronal population in mammals (Tombol, 1984; Ferrer et al., 1986*a*,*b*; Briggs, 2010). In primates and insectivores, layer 6 of V1 is further subdivided into tiers based on a separation of distinct corticothalamic neuronal subpopulations with cell bodies in the upper, middle, and lower portions of layer 6 (Conley & Raczkowski, 1990; Fitzpatrick et al., 1994; Usrey & Fitzpatrick, 1996). Morphologically distinct neuronal types in layer 6 receive different patterns of local cortical input (Briggs & Callaway, 2001; Zarrinpar & Callaway, 2006). Additionally, nonoverlapping neuronal subpopulations within layer 6 project axons to different extrastriate cortical and subcortical

Address correspondence to: Farran Briggs. E-mail: farran_briggs@urmc.rochester.edu

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

targets (LeVay & Sherk, 1981; Katz, 1987; Conley & Raczkowski, 1990; Casagrande & Kaas, 1994; Usrey & Fitzpatrick, 1996; Sincich & Horton, 2005; Sherman & Guillery, 2006; Nhan & Callaway, 2012; Olsen et al., 2012).

CG neurons make up a fraction of the total population of excitatory neurons in layer 6 of V1, on the order of ~15% in primates and closer to ~50% in carnivores (Gilbert & Kelly, 1975; Ferster & Lindstrom, 1985; Fitzpatrick et al., 1994). Within the CG neuronal population, there is also diversity in local dendritic morphologies, axonal projection patterns, and stratification of cell bodies within layer 6, described in detail below. Some organizational motifs appear to be conserved across mammals. Figure 1 illustrates schematic representations of CG subtypes in primates, carnivores, and rodents, including local dendritic morphologies, putative axonal projection patterns, and stratification of cell bodies within layer 6.

Morphology and local circuit connections

CG neurons fall into three broad morphological categories: short, tall, and stellate or unusual morphology (Briggs, 2010). Short CG neurons are the most abundant morphological type with cell bodies in the upper tier of layer 6 and apical dendrites targeting layer 4. Tall CG neurons have cell bodies in either the top or bottom tier of layer 6 with apical dendrites extending into layer 2/3, sometimes including apical dendritic tufts. Less abundant and more unusual CG neuronal types include spiny stellate neurons that lack apical dendrites and tilted, sideways, or upside-down pyramidal-like neurons that have been observed in upper and lower tiers of layer 6 and also in the white matter below the cortical layers.

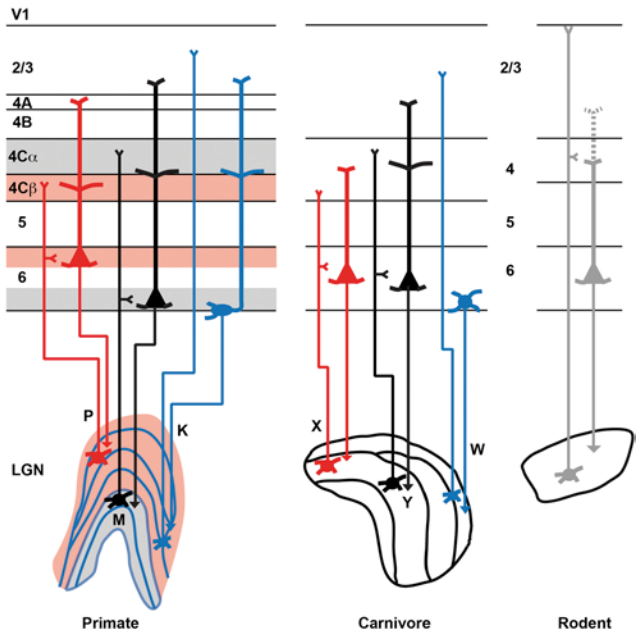


Fig. 1. Schematic representations of corticogeniculate (CG) subtypes in primates, carnivores, and rodents. Parvocellular (P), magnocellular (M), and koniocellular (K) and homologous X, Y, and W stream neurons are illustrated in red, black, and blue, respectively. Axons are thinner and dendrites thicker. Layers within V1 are indicated to the left for primate V1 and between the laminar boundaries for carnivore and rodent V1. LGN relay axons project to layers 1 and 4 in rodents (thin gray lines). Dashed gray dendrite to layer 2/3 illustrates possible, but yet unconfirmed, arborization of rodent CG neurons.

A recent anatomical study performed in macaque monkeys (Briggs et al., 2016) has expanded our understanding of the morphological diversity of CG neurons, including the presence of rare and previously unobserved CG types. In the macaque, CG cell bodies are restricted to the top and bottom tiers of layer 6 (Fitzpatrick et al., 1994). CG neurons with cell bodies in the upper tier include Iβ neurons (Wiser & Callaway, 1996), neurons with large cell bodies, and spiny stellate neurons. Following the general pattern for short CG neurons, Iβ neurons have apical dendrites that terminate in layer 4, where they preferentially target parvocellular stream input layer 4Cβ; and the basal dendrites of Iβ neurons are restricted to the upper tier of layer 6, which is the parvocellular stream input zone within layer 6 (Hubel & Wiesel, 1972; Hendrickson et al., 1978). Large neurons have tall apical dendrites with apical tufts near the pia in layer 1. Their basal dendritic arbor is more extensive than that of Iβ neurons, with basal dendrites targeting all three tiers of layer 6. Stellate CG neurons have dendrites restricted to the upper tier of layer 6.

Briggs et al. (2016) identified two distinct CG morphological subtypes with cell bodies in the bottom tier of layer 6: IC neurons (Wiser & Callaway, 1996) and tilted neurons. IC neurons follow the general pattern for tall CG neurons. Interestingly, the apical dendrites of IC neurons show no preference for the parvocellular or magnocellular stream input sublamina of layer 4C, however the basal dendrites of IC neurons are restricted to the magnocellular stream input zone at the bottom of layer 6 (Hubel & Wiesel, 1972; Hendrickson et al., 1978). Tilted neurons had not been observed previously in monkey V1, however neurons with similar morphologies have been observed in rodent and cat visual cortex (Tombol, 1984; Miller, 1988). Tilted CG neurons are observed less frequently and have unique morphology. First, their oval-shaped cell bodies are restricted to a narrow band in the deepest part of layer 6, often encroaching into the white matter. Second, the apical dendrites of tilted neurons exit at the side of the cell body (rather than the top of the cell body, as for pyramidal neurons) and turn to continue up through the cortical layers toward the pia. The dendritic and axonal analyses performed by Briggs et al. (2016) suggest that CG neurons form local connections with neurons in the same tier within layer 6 and receive segregated parvocellular or magnocellular stream input within those same tiers.

While the majority of CG neurons are in V1, CG neurons have also been identified in V2 of primates (Lin & Kaas, 1977; Briggs et al., 2016) and the homologous area 18 in cats (Gilbert & Kelly, 1975; Updyke, 1975; Murphy et al., 2000). V2 CG neurons probably made up a smaller fraction of excitatory neurons in layer 6 compared to the fraction of CG neurons in V1. V2 CG neurons also include three morphologically distinct subtypes with similar morphological features as V1 CGs. Short V2 CGs are located in the upper tier of layer 6 while tall and tilted V2 CGs are located in the lower tier (Briggs et al., 2016).

The results of most retrograde labeling studies in primates and insectivores support the notion that distinct CG subtypes are segregated into upper and lower tiers of layer 6 (Conley & Raczkowski, 1990; Fitzpatrick et al., 1994; Usrey & Fitzpatrick, 1996). However detailed data on CG dendritic morphology is only available from a limited number of primate studies. Ichida et al. (2014) performed a morphological analysis of retrogradely labeled CG neurons in galagos and observed only short dendritic morphology patterns, however technical limitations may have led to an under-sampling of superficial arbors. Still, it is possible that some species have more homogeneous CG neuronal populations than others.

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

CG neurons in cats follow many of the same organizational principals observed in primates. Cat CG neurons are pyramidal neurons with cell bodies restricted to layer 6 and the CG population does not overlap with other corticothalamic projecting neuronal populations (Gilbert & Kelly, 1975; LeVay & Sherk, 1981; Katz, 1987). Katz (1987) observed both short and tall CG neurons (called type II and type I, respectively) in cat V1. Interestingly, the cell bodies of short and tall CGs in cats do not appear to segregate into different tiers of layer 6 (Katz, 1987), suggesting that sub-laminar organization of CG subtypes may be a primate specialization.

Compared to the wealth of anatomical data available about CG neurons in primates and carnivores, relatively little is known about CG morphology in rodents. Similar to other mammals, rat and mouse CG neurons have cell bodies restricted to layer 6 in V1, however CG dendritic morphology may be more homogeneous in rodents (Jiang et al., 1993; Brumberg et al., 2003). Following the recent introduction of the Ntsr1-cre mouse line (Gong et al., 2007), which enables genetic targeting of corticothalamic neurons, more focus has been placed on the CG circuit in the mouse. Olsen et al. (2012) characterized the morphology of Ntsr1 neurons in mouse V1, observing both short and tall pyramidal neurons. It is important to note that while the Ntsr1 population includes CG neurons (Kim et al., 2014; Denman & Contreras, 2015), it also includes additional corticothalamic populations both in layer 5 and layer 6 of the cortex (Olsen et al., 2012). One notable difference between CG neurons in mice *versus* primates and carnivores involves their local connectivity. While CG neurons in primates and cats are strongly reciprocally connected with neurons in layer 4, Ntsr1 neurons in mice are more strongly connected to layer 5 and mediate inhibition across the cortical layers (Katz, 1987; Briggs & Callaway, 2001; Olsen et al., 2012; Bortone et al., 2014; Kim et al., 2014; Briggs et al., 2016). Further characterization of CG neurons in rodents is necessary before detailed comparisons can be made between rodent and primate or carnivore CG neurons. It is important to note that CG neurons in both V1 and V2 project local axons throughout the cortical depth, including the superficial layers and layer 5, both of which contain cortico-cortical projecting neurons. CG neurons are therefore positioned to influence not only visual signals relayed back to the LGN but also feedforward signals transmitted to extrastriate visual cortex.

Axon projections

By definition, CG neurons target the LGN with their axonal projections. Importantly, CG synapses onto LGN relay neurons far outnumber retinogeniculate synapses even though their influence appears to be more modulatory than driving (Guillery, 1969; Erisir et al., 1997*a*; Erisir et al., 1997*b*; Sherman & Guillery, 2006). Given the diversity of morphologically distinct CG subtypes across a variety of mammalian species, it seems reasonable to predict diverse CG axonal projection patterns within the LGN. While CG axonal projection data are largely consistent with the notion of diverse CG subtypes, it is technically challenging to confirm the actual specificity of CG-to-LGN connectivity. Interestingly, in primates, cats, and ferrets, CG axons target the LGN and TRN (Robson, 1983; Claps & Casagrande, 1990; Murphy & Sillito, 1996; Ichida & Casagrande, 2002; Ichida et al., 2014), while in rodents, some CG neurons have axons in the LGN, TRN, and/or the lateral posterior nucleus of the thalamus (Bourassa & Deschenes, 1995; Olsen et al., 2012), suggesting that CG projections in rodents may be less selective or specific than those in more visual mammals. In ferrets and cats, CG axons tend to target multiple LGN layers even though boutons are often clustered (Robson, 1983; Claps & Casagrande, 1990). In primates, CG axons are mainly restricted to individual LGN layers or to functionally-matched layers (e.g., pairs parvocellular layers or pairs of magnocellular layers) although CG axonal arbors often encroach into neighboring koniocellular layers (Ichida & Casagrande, 2002; Ichida et al., 2014). Thus at least in visual mammals such as primates and carnivores, CG axon termination patterns are consistent with distinct CG subtypes targeting select populations of LGN neurons. Whether or not CG axons make functionally stream-specific connections with LGN neurons has not yet been established.

The structure and physiological properties of CG synapses onto LGN relay neurons, LGN interneurons, and TRN neurons have been studied in a number of species, including primates, carnivores, and rodents. For thorough reviews of the ultrastructure and physiology of CG synapses across species, please refer to (Bickford, 2016) and to (Sherman & Guillery, 2006), chapters 3 and 5. The general characteristics of CG synapses appear to be largely conserved across species. While CG synapses outnumber retinal synapses, they display the characteristics of "modulating" rather than "driving" synapses. CG synapses are smaller, contain less synaptic vesicles, and are located further out along distal dendrites of LGN relay neurons compared to retinal inputs. Postsynaptic terminals of CG synapses include both ionotropic and metabotropic glutamate receptors, while postsynaptic terminals of retinal synapses contain only ionotropic glutamate receptors. The fact that these general structural characteristics are conserved across species suggests that the relative contributions of retinal and cortical inputs to LGN relay neurons are also evolutionarily conserved.

Physiology of CG neurons

In visual mammals such as primates and carnivores, there are precise relationships between CG axon conduction latency and visual physiology. Here visual physiology is used to describe the receptive field properties of neurons. One of the most common visual physiological metrics is the classification of V1 neurons as Simple or Complex. Simple cells in V1 have separate receptive field subregions that respond to opposite luminance polarity, while Complex cells respond equally well to stimuli of opposite luminance polarity within their receptive fields. The distinct CG subtypes defined by axon conduction latencies and visual response properties can be directly related to the feedforward parallel processing streams that are a hallmark of visual systems in highly visual mammals. Similar information is not available in rodents, however CG physiology has been well characterized in rabbits so comparisons between primates, carnivores, and rabbits are described below.

Axon conduction latencies

Measurements of CG axon conduction latencies provide some of the strongest, and oldest, evidence in favor of distinct CG subtypes. Antidromic stimulation studies, where CG axons in the LGN are electrically stimulated and resultant action potentials are recorded at cell bodies in layer 6 of V1, provide valuable physiological information about CG axon conduction speed. In visual mammals such as ferrets, cats, and monkeys, axon conduction latencies correlate with Simple/Complex visual response properties whereby fast-conducting CG neurons are Complex, medium-conducting CG neurons are Simple, and slowly-conducting CG neurons are Complex

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

or nonresponsive to visual stimuli (Harvey, 1978; Tsumoto & Suda, 1980; Grieve & Sillito, 1995; Briggs & Usrey, 2005, 2007*b*). In rabbits, CG axon conduction latencies are generally slower, but similar relationships exist between axon conduction speed and visual response properties (Swadlow & Weyand, 1987). In all of these species studied to date, it is clear that CG neurons with different axon conduction latencies form distinct and nonoverlapping cell types. For example, in the monkey, CG subtypes defined based on axon conduction latency are clear-cut: fast/Complex CGs always have conduction latencies <7 ms; medium/Simple CGs always have conduction latencies between 7–15 ms; and slow/Complex CGs always have conduction latencies >15 ms (Briggs & Usrey, 2007*b*, 2009). Given the diversity in CG conduction latencies that is strictly defined and conserved across many species, it is likely that CG subtypes with different axon conduction speeds contribute to different aspects of visual processing. Along these lines, only fast-conducting CG neurons in primates also receive suprathreshold feedforward input from the LGN, creating a fast, reciprocal loop for transferring visual information between LGN and V1 (Briggs & Usrey, 2007*b*). Accordingly, these fast-conducting CG neurons may contribute primarily to motion perception. The diversity in axon conduction speeds also suggests that CG circuits operate on a variety of timescales, perhaps to accommodate a variety of integration windows for accumulating visual information. As we learn more about the functional contributions of CG circuits to vision, it will be important to consider the variety of timescales over which CG circuits operate.

Receptive field properties

In carnivores, primates, and rabbits, the visual response properties of CG neurons strongly correlate with axon conduction latencies, as described above. For example, CG neurons with fast and medium conduction latencies are often tuned for orientation and direction in cats and rabbits (Tsumoto & Suda, 1980; Swadlow & Weyand, 1987; Grieve & Sillito, 1995). A more systematic study of the visual response properties of CG neurons in alert monkeys revealed that CG subtypes defined based on axon conduction latencies display unique receptive field properties that align with the feedforward magnocellular, parvocellular, and koniocellular processing streams (Briggs & Usrey, 2009). Fast-conducting Complex CGs are sensitive to low contrast and high temporal frequency stimuli, and thus optimized to process motion signals conveyed by the magnocellular stream. Medium-conducting Simple CGs are less sensitive to contrast, but are orientation tuned and responsive to red and green color signals, in line with signals conveyed by the parvocellular stream. Slow-conducting Complex CGs are poorly tuned for orientation and direction but modulated by blue color signals, aligning with signals conveyed by the koniocellular stream. These data suggest that inputs from the magnocellular, parvocellular, and koniocellular parallel processing streams are segregated through the local circuitry in V1 such that CG feedback maintains stream-specificity.

There is ongoing debate about whether some of the slowest-conducting CG neurons are visually responsive. In ferrets, cats, and rabbits, some slow-conducting CG neurons are not responsive to visual stimuli (Tsumoto & Suda, 1980; Swadlow & Weyand, 1987; Briggs & Usrey, 2005). Lack of responsiveness cannot necessarily be attributed to anesthesia as visually nonresponsive CG neurons are observed in awake rabbits (Swadlow & Weyand, 1987). Interestingly, in alert monkeys, all CG neurons, including slow-conducting CG neurons, are visually responsive (Briggs & Usrey, 2009). The utility of the slowest-conducting CG neurons and whether or not they are responsive to visual stimuli in a variety of species remain unknown.

Stream specificity

A major hallmark of retino-geniculo-cortical circuits in visual mammals is the separation of feedforward signals into parallel processing streams made up of morphologically and physiologically distinct neuronal classes. In primates, the parvocellular, magnocellular, and koniocellular parallel processing streams carry information about form/acuity, motion, and blue color, respectively (Kaplan, 2004). Homologous X, Y, and W streams are present in carnivores (Sherman & Guillery, 2006). Evidence for parallel streams in the visual systems of rodents is less clear (Krahe et al., 2011). Mounting evidence supports the notion that in visual mammals such as primates and carnivores, CG circuits are also organized into parallel streams that align with the feedforward parallel streams. The dendritic arborization and axon projection patterns of primate and carnivore CG neurons, described in detail above, support distinct CG subtypes. Similarly, physiological measurements including axon conduction latency and visual response properties also support distinct CG subtypes with physiological properties aligned with the properties of neurons in the feedforward streams. Together, these data provide strong support for the idea that separate channels of CG feedback preserve the segregation of visual information into distinct feedforward processing streams in highly visual mammals.

In the primate, the alignment of feedforward and CG feedback circuits is precise. The following predictions arise from combinations of morphological and physiological observations in monkeys. CG neurons with fast axon conduction latencies and Complex visual physiology are the presumptive magnocellular-projecting CG neurons. Magnocellular feedforward retino-geniculo-cortical and fast Complex CG neurons have the fastest conducting axons, the greatest contrast and temporal frequency sensitivity, the most surround suppression, the shortest visual response latencies, and the highest firing rates (Benardete et al., 1932; Schiller & Malpeli, 1978; Kaplan & Shapley, 1982, 1986; Maunsell et al., 1999; Usrey & Reid, 2000; White et al., 2001; Solomon et al., 2002; Briggs & Usrey, 2007*b*, 2009, 2011*b*; Alitto & Usrey, 2008). Additionally, fast Complex CG neurons have sharper orientation tuning and greater direction selectivity, reminiscent of neurons in layer 4Cα that receive direct magnocellular input from the LGN (Hawken et al., 1988; Merigan & Maunsell, 1993; Gur et al., 2005; Briggs & Usrey, 2009). The presumptive magnocellular-projecting fast Complex CG neurons are also the only CG neurons to receive direct, feedforward suprathreshold LGN input (Briggs & Usrey, 2007*b*). It is likely that the type IC CG neurons, located in the bottom tier of layer 6, are the magnocellular-projecting, fast Complex CG neurons because magnocellular LGN layers receive CG feedback from the bottom tier of layer 6 (Fitzpatrick et al., 1994).

CG neurons with medium axon conduction latencies and Simple visual physiology are the presumptive parvocellular-projecting CG neurons. Parvocellular feedforward retino-geniculo-cortical and medium Simple CG neurons have intermediary axon conduction speeds, low contrast and temporal frequency sensitivity, less surround suppression, slower visual response latencies, intermediary firing rates, and are sensitive to inputs from the L- and M-cones in the retina (Schiller & Malpeli, 1978; Bullier & Henry, 1980; Maunsell et al., 1999; Field & Chichilnisky, 2007; Briggs & Usrey, 2009). The type Iβ CG neurons, located in the top tier of layer 6 are likely the parvocellular-projecting, medium Simple CG neurons because

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

parvocellular LGN layers receive CG feedback from the top tier of layer 6 (Fitzpatrick et al., 1994).

CG neurons with the slowest conducting axons and Complex visual physiology likely project to the koniocellular LGN layers. Like the feedforward koniocellular retino-geniculo-cortical neurons, slow Complex CG neurons have slower axon conduction speeds, intermediate contrast, and temporal frequency sensitivity, some surround suppression, and sensitivity to inputs from the S-cones in the retina (Irvin et al., 1986; White et al., 1998; Solomon et al., 1999; Hendry & Reid, 2000; White et al., 2001; Solomon & Lennie, 2007; Briggs & Usrey, 2009, 2011*b*). Interestingly, slow Complex CGs are not orientation or direction tuned, unlike the other CG subtypes (Briggs & Usrey, 2009). It is likely that a number of morphologically distinct CG subtypes, including stellate, large, and tilted CG neurons, project to the various koniocellular layers in the LGN. However, the tilted CG neurons are presumably the slow Complex, koniocellular-projecting neurons encountered physiologically because these neurons were always located in the deepest part of layer 6 (Briggs & Usrey, 2009).

In primates, and possibly also in carnivores, CG neurons retain physiological signatures of the feedforward parallel processing streams in spite of the fact that V1 contains numerous local circuits that could mix information from the three input streams (Merigan & Maunsell, 1993; Douglas & Martin, 2004; Sincich & Horton, 2005; Callaway, 2014). Accordingly, a clear precedent is set to ensure that CG circuits preserve the specificity of information relayed by feedforward streams. Preservation of segregated information channels through both feedforward and feedback circuits is evident in other species and sensory systems including the whisker/barrel system of rodents and the auditory system of bats (Ghazanfar et al., 2001; Suga & Ma, 2003; Bokor et al., 2008). Stream-specific corticothalamic feedback may therefore be evolutionarily conserved for neuronal pathways that serve primary senses across a variety of species. Because stream-specificity is likely to be a critical organizational feature of CG feedback, CG function must be considered in the context of parallel processing streams.

Function of CG neurons

In the past 10 years, we have gained significant insight about the structure, organization, and visual physiology of CG neurons, especially in the primate visual system. However the functional role of CG feedback in vision has remained a particularly stubborn puzzle. It is obvious from LGN recordings that the influence of CG feedback on the visual responses of LGN neurons is subtle. The receptive fields of LGN neurons mimic their retinal inputs and not their cortical inputs. For example, individual LGN neurons are not orientation tuned even though many CG neurons are tuned for orientation. Although CG inputs onto LGN neurons are anatomically robust in terms of numbers of synapses, the smaller size and placement of CG synapses on distal dendrites of LGN relay neurons means CG influence is modulatory rather than driving (Sherman & Guillery, 1998, 2006). Until recently, it has also been technically challenging to manipulate CG neurons in a selective and reversible manner. With the advent of optogenetics (Huber et al., 2008; Gradinaru et al., 2009), it is now possible to perform a more causal test of CG function by performing reversible manipulations selectively on CG neurons in intact animals. Results of experimental examinations of CG function, varying in invasiveness and/or selectivity, converge on three general candidate functions for CG feedback: LGN gain modulation, sharpening or shifting of LGN receptive fields, and changes in LGN spiking mode, timing, and precision (Briggs & Usrey, 2008, 2011*a*).

Gain modulation

As the first feedback circuit in the visual system, CG neurons could function as filters that increase the salience of relevant visual signals and suppress the activity of non-relevant visual information. Accordingly, CG feedback could operate by increasing or decreasing the gain of LGN neuronal responses. Changes in both the magnitude and gain of LGN responses have been observed when CG feedback is manipulated (Molotchnikoff et al., 1984; Gulyas et al., 1990; Marrocco et al., 1996; Cudiero et al., 2000; Przybyszewski et al., 2000; Worgotter et al., 2002; Wolfart et al., 2005; Andolina et al., 2007; Li et al., 2011; Olsen et al., 2012; Denman & Contreras, 2015). Specifically, aspirating or cooling V1 in anesthetized cats and primates led to decreased LGN responses to moving visual stimuli without changing LGN tuning preferences (Gulyas et al., 1990; Marrocco et al., 1996). Additionally, cooling V1 in anesthetized monkeys led to a reduction in contrast gain that was specific to parvocellular LGN neurons (Przybyszewski et al., 2000). Similarly, lesioning V1 in anesthetized cats led to decreased contrast adaptation with greater effects on Y than X cells in the LGN (Li et al., 2011). These latter findings support the notion of stream-specific functions for CG subtypes. Interestingly, in the mouse, optogenetic suppression of corticothalamic feedback led to a variety of effects on LGN responses including increases, decreases, and no change in response magnitude and gain (Denman & Contreras, 2015).

A related function for CG feedback could be to convey cognitive signals about attention or arousal state from the cortex to the LGN. Corticothalamic circuits are strongly modulated by arousal state, demonstrating different spiking, and oscillatory modes during sleep and arousal (Steriade, 2001, 2003). Additionally, LGN neurons are modulated by visual attention (Vanduffel et al., 2000; O'Connor et al., 2002; McAlonan et al., 2006, 2008; Ling et al., 2015). The precise role of CG feedback in delivering arousal and/or attention signals to the LGN is not known. However, as the only path by which cortical information reaches the LGN, CG feedback is a good candidate for conveying information about cognitive state.

Receptive field changes

LGN neurons derive their receptive field properties from their retinal inputs, however it is possible that CG feedback sharpens and/or shifts the tuning properties of individual or ensembles of LGN neurons. There is evidence that the spatial receptive field of LGN neurons, with the antagonistic center/surround of the classical receptive field and the extra-classical suppressive surround, may be sharpened or modulated by CG feedback (Murphy & Sillito, 1987; Sillito & Jones, 2002; Webb et al., 2002; Jones et al., 2012; Andolina et al., 2013). CG feedback could sharpen the border between the classical and extra-classical fields (Murphy & Sillito, 1987; Jones et al., 2000; Rivadulla et al., 2002; Webb et al., 2002; Jones et al., 2012). Alternatively, CG feedback could reduce the spatial extent of the classical receptive field and enhance surround suppression as pharmacological inactivation of V1 in anesthetized cats led to an increase in LGN receptive size and a reduction in surround suppression (Andolina et al., 2013). In the mouse, corticothalamic feedback does not modulate LGN receptive field size or surround suppression (Denman & Contreras, 2015).

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

While the influence of CG feedback on the receptive fields of individual LGN neurons may be subtle, it is possible that CG feedback coordinates the activity of ensembles of LGN neurons to produce "tuning" among small groups of LGN neurons. Experimental evidence suggests that CG feedback enhances the activity of ensembles of LGN neurons with receptive fields clustered along the orientation axis of their CG inputs (Sillito et al., 1993; Wang et al., 2006; Andolina et al., 2007). Theoretical evidence also supports a role for CG feedback in enhancing the activity of ensembles of LGN neurons with retinotopically aligned receptive fields and suppressing neighboring neurons (Bickle et al., 1999). Together, these findings highlight the importance of future studies involving multielectrode recordings so that the broader impact of CG feedback on populations of LGN neurons can be examined.

A final argument in favor of a role for CG feedback in sharpening or shifting the receptive fields of LGN neurons is that similar functions have been attributed to corticothalamic circuits in other sensory systems. The term "egocentric selection" describes the enhancement and shifting of thalamic responses to match the tuning preferences of activated corticothalamic neurons and suppression of activity among thalamic neurons with nonmatched tuning (Suga & Ma, 2003). Egocentric selection by corticothalamic feedback has been described in the auditory and somatosensory systems (Krupa et al., 1999; Ghazanfar et al., 2001; Suga & Ma, 2003; Li & Ebner, 2007; Wu & Yan, 2007; Temereanca et al., 2008; Zhang & Yan, 2008).

Modulation of LGN spiking mode, timing, and precision

In addition to modulating the gain of LGN response or sharpening LGN receptive fields, CG feedback could influence the feedforward transmission of visual signals by modulating the spike timing of LGN relay neurons. By coordinating the spike latencies and/or increasing the spike timing precision for an ensemble of LGN neurons, CG feedback could enhance the efficacy of visual information conveyed by the coordinated ensemble to V1. One way in which CG feedback could coordinate the activity of LGN neurons is to shift a select group of LGN neurons between burst and tonic modes of firing (Sherman, 1996). In support of this notion is the finding that selective destruction of CG neurons led to a broadening of the inter-spike-interval distribution of tonic spikes recorded during synchronized EEG states (Eyding et al., 2003). However, in the mouse, selectively manipulating corticothalamic feedback had no net impact on tonic or burst spiking (Denman & Contreras, 2015).

Alternatively, CG feedback could coordinate slow timescale fluctuations in membrane potential, leading to an increase in coordinated spiking patterns among LGN ensembles (Destexhe et al., 1999; Bal et al., 2000; Blumenfeld & McCormick, 2000; Destexhe, 2000; Rigas & Castro-Alamancos, 2007). Both experimental and theoretical studies support the notion that CG feedback alters the timing of LGN responses in order to improve the transfer of information from the LGN to V1 (Funke et al., 1996; Bal et al., 2000; Destexhe, 2000; Worgotter et al., 2002; Wolfart et al., 2005; Andolina et al., 2007; Yousif & Denham, 2007). Specifically, Andolina and colleagues (Andolina et al., 2007) observed decreased stimulus modulation and increased response variability in LGN neurons when V1 was pharmacologically inactivated in anesthetized cats. In spite of these advances, exactly how CG feedback alters the timing and/or precision of LGN neurons to improve information transmission remains unclear.

There is some experimental evidence that CG feedback synchronizes the activity of LGN ensembles (Sillito et al., 1994), however the synchrony measurements in this study were confounded (Brody, 1999) and the manipulations of CG feedback were nonselective with limited data. Nevertheless, the hypothesis proposed in this study, that CG feedback selectively synchronizes the activity of LGN ensembles carrying feature-specific information, must be tested using modern techniques. Interestingly, somewhat parallel analyses performed in the mouse, in which pairwise correlations were measured among LGN neurons when corticothalamic feedback was manipulated, yielded no influence of corticothalamic feedback on correlated activity among LGN neurons (Denman & Contreras, 2015).

Finally, CG feedback could play a role in the arrangement of synapses onto LGN relay neurons during development—a function that could have important consequences for LGN spiking synchrony and precision throughout life. A number of recent studies examining the development of visual thalamic circuits in the mouse have provided significant new insight into the timing and influence of CG activity during development. CG axonal innervation of the LGN is delayed relative to innervation of the LGN by retinal inputs (Jacobs et al., 2007; Seabrook et al., 2013). Additionally, CG inputs become stronger during later developmental stages relative to retinal inputs (Jurgens et al., 2012). However, CG inputs are required for correct retinogeniculate innervation of the LGN as retinogeniculate afferents fail to correctly innervate the LGN in mice lacking layer 6 projection neurons (Shanks et al., 2016). Furthermore, disruptions of CG feedback during development result in overabundant retinogeniculate innervation of LGN relay neurons, similar to that observed during dark rearing (Thompson et al., 2016). Together these findings suggest that CG activity during specific developmental stages is required for correct retinal and cortical synaptic innervation of LGN neurons, perhaps setting the stage for LGN neuronal synchronization that is critical for visual function throughout life.

Concluding remarks

While a large body of work is now available describing the structure, organization, and physiology of CG neurons, the functional role of these enigmatic neurons in vision remains unresolved. A number of other important questions also remain, including the functional connectivity of CG axons with LGN relay neurons and whether or not CG feedback is functionally stream specific. Any examination of CG function must take into account the fact that CG subtypes operate on very different timescales and are specialized to convey stream-specific signals from V1 to the LGN. Additionally, it will be important to record from ensembles of neurons in the LGN to determine whether CG feedback alters the timing or population tuning properties of select groups of LGN neurons. Finally, as technical approaches improve, studies of CG circuits in alert and behaving animals will provide important new insight into the contributions of CG feedback to contextual and cognitive processes.

There are clear similarities in CG morphology and physiology across highly visual mammals such as primates and carnivores. These similarities suggest that evolution maintains a precedent for preserving the separation of visual information into parallel processing streams throughout the early visual pathways. However, this precedent is not apparent for nonvisual mammals such as rodents, as CG morphology and function appears more homogeneous and less selective. Precise and parallel organization is present in the

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

rodent somatosensory system, however. Further studies of corticothalamic feedback in a variety of sensory modalities and species may provide significant insight into the senses that are must useful for each species and the general strategies employed by corticothalamic circuits to enhance sensory perception.

References

Alitto, H.J. & Usrey, W.M. (2008). Origin and dynamics of extraclassical suppression in the lateral geniculate nucleus of the macaque monkey. *Neuron* **57**, 135–146.

Andolina, I.M., Jones, H.E. & Sillito, A.M. (2013). Effects of cortical feedback on the spatial properties of relay cells in the lateral geniculate nucleus. *Journal of Neurophysiology* **109**, 889–899.

Andolina, I.M., Jones, H.E., Wang, W. & Sillito, A.M. (2007). Corticothalamic feedback enhances stimulus response precision in the visual system. *Proceedings of the National Academy of Sciences of the United States of America* **104**, 1685–1690.

Bal, T., Debay, D. & Destexhe, A. (2000). Cortical feedback controls the frequency and synchrony of oscillations in the visual thalamus. *Journal of Neuroscience* **20**, 7478–7488.

Benardete, E.A., Kaplan, E. & Knight, B.W. (1932). Contrast gain control in the primate retina: P cells are not X-like, some M cells are. *Visual Neuroscience* **8**, 483–486.

Bickford, M.E. (2016). Thalamic circuit diversity: Modulation of the driver/modulator framework. *Frontiers in Neural Circuits* **9**, 1–8.

Bickle, J., Bernstein, M., Heatley, M., Worley, C. & Stiehl, S. (1999). A functional hypothesis for LGN-V1-TRN connectivities suggested by computer stimulation. *Journal of Comparative Neurology* **6**, 251–261.

Blasdel, G.G. & Lund, J.S. (1983). Termination of afferent axons in macaque striate cortex. *Journal of Neuroscience* **3**, 1389–1413.

Blumenfeld, H. & McCormick, D.A. (2000). Corticothalamic inputs control the pattern of activity generated in thalamocortical networks. *Journal of Neuroscience* **20**, 5153–5162.

Bokor, H., Acsady, L. & Deschenes, M. (2008). Vibrissal responses of thalamic cells that project to the septal columns of the barrel cortex and to the second somatosensory area. *Journal of Neuroscience* **28**, 5169–5177.

Bortone, D.S., Olsen, S.R. & Scanziani, M. (2014). Translaminar inhibitory cells recruited by layer 6 corticothalamic neurons suppress visual cortex. *Neuron* **82**, 474–485.

Bourassa, J. & Deschenes, 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.

Briggs, F. (2010). Organizing principles of cortical layer 6. *Frontiers in Neural Circuits* **12**, 1–8.

Briggs, F. & Callaway, E.M. (2001). Layer-specific input to distinct cell types in layer 6 of monkey primary visual cortex. *Journal of Neuroscience* **21**, 3600–3608.

Briggs, F., Kiley, C.W., Callaway, E.M. & Usrey, W.M. (2016). Morphological substrates for parallel streams of corticogeniculate feedback originating in both V1 and V2 of the macaque monkey. *Neuron* **90**, 388–399.

Briggs, F. & Usrey, W.M. (2005). Temporal properties of feedforward and feedback pathways between thalamus and visual cortex in the ferret. *Thalamus and Related Systems* **3**, 133–139.

Briggs, F. & Usrey, W.M. (2007a). Corticothalamic circuits: Structure and function. In *The New Encyclopedia of Neuroscience*, ed., Squire, L., pp. 215–219. Elsevier.

Briggs, F. & Usrey, W.M. (2007b). A fast, reciprocal pathway between the lateral geniculate nucleus and visual cortex in the macaque monkey. *Journal of Neuroscience* **27**, 5431–5436.

Briggs, F. & Usrey, W.M. (2008). Emerging views of corticothalamic function. *Current Opinion in Neurobiology* **18**, 403–407.

Briggs, F. & Usrey, W.M. (2009). Parallel processing in the corticogeniculate pathway of the macaque monkey. *Neuron* **62**, 135–146.

Briggs, F. & Usrey, W.M. (2011a). Corticogeniculate feedback and parallel processing in the primate visual system. *Journal of Physiology* **589**, 33–40.

Briggs, F. & Usrey, W.M. (2011b). Distinct mechanisms of size tuning in primate visual cortex. *Journal of Neuroscience* **31**, 12644–12649.

Brody, C.D. (1999). Correlations without synchrony. *Neural Computation* **11**, 1537–1551.

Brumberg, J.C., Hamzei-Sichani, F. & Yuste, R. (2003). Morphological and physiological characterization of layer 6 corticofugal neurons of mouse primary visual cortex. *Journal of Neurophysiology* **89**, 2854–2867.

Bullier, J. & Henry, G.H. (1980). Ordinal position and afferent input of neurons in monkey striate cortex. *Journal of Comparative Neurology* **193**, 913–935.

Callaway, E.M. (2014). Cell types and local circuits in primary visual cortex of the macaque monkey. In *The New Visual Neurosciences*, ed. Werner, J.S. & Chalupa, L.M., pp. 353–365. Cambridge, MA: MIT Press.

Casagrande, V.A. & Kaas, J.H. (1994). The afferent, intrinsic, and efferent connections of primary visual cortex in primates. In *Cerebral Cortex*, ed. Peters, A. & Rockland, K.S., pp. 201–249. New York: Plenum Press.

Claps, A. & Casagrande, V.A. (1990). The distribution and morphology of corticogeniculate axons in ferrets. *Brain Research* **530**, 126–129.

Conley, M. & Raczkowski, D. (1990). Sublaminar organization within layer 6 of the striate cortex in galago. *Journal of Comparative Neurology* **302**, 425–436.

Cudiero, J., Rivadulla, C. & Grieve, K.L. (2000). Visual response augmentation in cat (and macaque) LGN: Potentiation by corticofugally mediated gain control in the temporal domain. *European Journal of Neuroscience* **12**, 1135–1144.

Da Costa, N.M. & Martin, K.A.C. (2009). Selective targeting of dendrites of corticothalamic cells by thalamic afferents in area 17 of the cat. *Journal of Neuroscience* **29**, 13919–13928.

Denman, D.J. & Contreras, D. (2015). Complex effects on in vivo visual responses by specific projections from mouse cortical layer 6 to dorsal lateral geniculate nucleus. *Journal of Neuroscience* **35**, 9265–9280.

Destexhe, A. (2000). Modelling corticothalamic feedback and the gating of the thalamus by the cerebral cortex. *Journal of Physiology (Paris)* **94**, 391–410.

Destexhe, A., Contreras, D. & Steriade, M. (1999). Cortically-induced coherence of a thalamic-generated oscillation. *Neuroscience* **92**, 427–430.

Douglas, R.J. & Martin, K.A. (2004). Neuronal circuits of the neocortex. *Annual Review of Neuroscience* **27**, 419–451.

Erisir, A., Van Horn, S.C., Bickford, M.E. & Sherman, S.M. (1997a). Immunocytochemistry and distribution of parabrachial terminals in the lateral geniculate nucleus of the cat: A comparison with corticogeniculate terminals. *Journal of Comparative Neurology* **377**, 535–549.

Erisir, A., Van Horn, S.C. & Sherman, S.M. (1997b). Relative numbers of cortical and brainstem inputs to the lateral geniculate nucleus. *Proceedings of the National Academy of Sciences of the United States of America* **94**, 1517–1520.

Eyding, D., Macklis, J.D., Neubacher, U., Funke, K. & Worgotter, F. (2003). Selective elimination of corticogeniculate feedback abolishes the electroencephalogram dependence of primary visual cortical receptive fields and reduces their spatial specificity. *Journal of Neuroscience* **23**, 7021–7033.

Ferrer, I., Fabregues, I. & Condom, E. (1986a). A Golgi study of the sixth layer of the cerebral cortex. I. The lissencephalic brain of Rodentia, Lagomorpha, Insectivora and Chiroptera. *Journal of Anatomy* **145**, 217–234.

Ferrer, I., Fabregues, I. & Condom, E. (1986b). A Golgi study of the sixth layer of the cerebral cortex. II. The gyrencephalic brain of Carnivora, Artiodactyla and Primates. *Journal of Anatomy* **146**, 87–104.

Ferster, D. & Lindstrom, S. (1983). An intracellular analysis of geniculocortical connectivity in area 17 of the cat. *Journal of Physiology* **342**, 181–215.

Ferster, D. & Lindstrom, S. (1985). Augmenting responses evoked in area 17 of the cat by intracortical axon collaterals of cortico-geniculate cells. *Journal of Physiology* **367**, 217–232.

Field, G.D. & Chichilnisky, E.J. (2007). Information processing in the primate retina: Circuitry and coding. *Annual Reviews Neuroscience* **30**, 1–30.

Fitzpatrick, D., Usrey, W.M., Schofield, B.R. & Einstein, G. (1994). The sublaminar organization of corticogeniculate neurons in layer 6 of macaque striate cortex. *Visual Neuroscience* **11**, 307–315.

Funke, K., Nelle, E., Li, B. & Worgotter, F. (1996). Corticofugal feedback improves the timing of retino-geniculate signal transmission. *NeuroReports* **7**, 2130–2134.

Ghazanfar, A.A., Krupa, D.J. & Nicolelis, M.A.L. (2001). Role of cortical feedback in the receptive field structure and nonlinear response properties of somatosensory thalamic neurons. *Experimental Brain Research* **141**, 88–100.

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

Gilbert, C.D. & Kelly, J.P. (1975). The projections of cells in different layers of the cat's visual cortex. *Journal of Comparative Neurology* **163**, 81–106.
Gong, S., Doughty, M., Harbaugh, C.R., Cummins, A., Hatten, M.E., Heintz, N. & Gerfen, C.R. (2007). Targeting cre recombinase to specific neuron populations with bacterial artificial chromosome constructs. *Journal of Neuroscience* **27**, 9817–9823.
Gradinaru, V., Mogri, M., Thompson, K.R., Henderson, J.M. & Deisseroth, K. (2009). Optical deconstruction of parkinsonian neural circuitry. *Science* **324**, 354–359.
Grieve, K.L. & Sillito, A.M. (1995). Differential properties of cells in the feline primary visual cortex providing the corticofugal feedback to the lateral geniculate nucleus and visual claustrum. *Journal of Neuroscience* **15**, 4868–4874.
Guillery, R.W. (1969). A quantitative study of synaptic interconnections in the dorsal lateral geniculate nucleus of the cat. *Zeitschrift fuer Zellforschung und Mikroskopische Anatomie* **96**, 39–48.
Gulyas, B., Lagae, L., Eysel, U.T. & Orban, G.A. (1990). Corticofugal feedback influences the responses of geniculate neurons to moving stimuli. *Experimental Brain Research* **79**, 441–446.
Gur, M., Kagan, I. & Snodderly, D.M. (2005). Orientation and direction selectivity of neurons in V1 of alert monkeys: Functional relationships and laminar distributions. *Cerebral Cortex* **15**, 1207–1221.
Harvey, A.R. (1978). Characteristics of corticothalamic neurons in area 17 of the cat. *Neuroscience Letters* **7**, 177–181.
Hawken, M.J., Parker, A.J. & Lund, J.S. (1988). Laminar organization and contrast sensitivity of direction-selective cells in the striate cortex of the old world monkey. *Journal of Neuroscience* **8**, 3541–3548.
Hendrickson, A.E., Wilson, J.R. & Ogren, M.P. (1978). The neuroanatomical organization of pathways between the dorsal lateral geniculate nucleus and visual cortex in the old world and new world primates. *Journal of Comparative Neurology* **182**, 123–136.
Hendry, S. & Reid, R.C. (2000). The koniocellular pathway in primate vision. *Annual Review of Neuroscience* **23**, 127–153.
Hubel, D.H. & Wiesel, T.N. (1972). Laminar and columnar distribution of geniculo-cortical fibers in the macaque monkey. *Journal of Comparative Neurology* **146**, 421–450.
Huber, D., Petreanu, L., Ghitani, N., Ranade, S., Hromadka, T., Mainen, Z. & Svoboda, K. (2008). Sparse optical microstimulation in barrel cortex drives learned behavior in freely moving mice. *Nature* **451**, 61–64.
Ichida, J.M. & Casagrande, V.A. (2002). Organization of the feedback pathway from striate cortex (V1) to the lateral geniculate nucleus (LGN) in the owl monkey (*Aotus trivirgatus*). *Journal of Comparative Neurology* **454**, 272–283.
Ichida, J.M., Mavity-Hudson, J.A. & Casagrande, V.A. (2014). Distinct patterns of corticogeniculate feedback to different layers of the lateral geniculate nucleus. *Eye and Brain* **6**, 57–73.
Irvin, G.E., Norton, T.T., Sesma, M.A. & Casagrande, V.A. (1986). W-Like response properties in interlaminar zone cells in the lateral geniculate nucleus of a primate (*Galago crassicaudatus*). *Brain Research* **362**, 254–270.
Jacobs, E.C., Campagnoni, C., Kampf, K., Reyes, S.D., Kalra, V., Handley, V., Xie, Y-Y., Hong-Hu, Y., Spreur, V., Fisher, R.S., Campagnoni, A.T. (2007). Visualization of corticofugal projections during early cortical development in a T-GFP-transgenic mouse. *European Journal of Neuroscience* **25**, 17–30.
Jiang, Z., Johnson, R. & Burkhalter, A. (1993). Visualization of dendritic morphology of cortical projection neurons by retrograde axonal tracing. *Journal of Neuroscience Methods* **50**, 45–60.
Jones, E.G. (1985). *The Thalamus*. New York, NY: Plenum Press.
Jones, H.E., Andolina, I.M., Ahmed, B., Shipp, S., Clements, J.T.C., Grieve, K.L., Cudiero, J., Salt, T.E. & Sillito, A.M. (2012). Differential feedback modulation of center and surround mechanisms in parvocellular cells in the visual thalamus. *Journal of Neuroscience* **32**, 15946–15951.
Jones, H.E., Andolina, I.M., Oakely, N.M., Murphy, P.C. & Sillito, A.M. (2000). Spatial summation in lateral geniculate nucleus and visual cortex. *Experimental Brain Research* **135**, 279–284.
Jurgens, C.W.D., Bell, K.A., McQuiston, A.R. & Guido, W. (2012). Optogenetic stimulation of the corticothalamic pathway affects relay cells and GABAergic neurons differently in the mouse visual thalamus. *Public Library of Science One* **7**, 1–14.
Kaplan, E. (2004). The M, P, and K pathways of the primate visual system. In *The Visual Neurosciences*, ed. Chalupa, L. & Werner, J., pp. 481–493. Cambridge, MA: MIT Press.
Kaplan, E. & Shapley, R. (1982). X and Y cells in the lateral geniculate nucleus of macaque monkeys. *Journal of Physiology* **330**, 125–143.
Kaplan, E. & Shapley, R. (1986). The primate retina contains two types of ganglion cells, with high and low contrast sensitivity. *Proceedings of the National Academy of Sciences of the United States of America* **83**, 2755–2757.
Katz, L.C. (1987). Local circuitry of identified projection neurons in cat visual cortex brain slices. *Journal of Neuroscience* **7**, 1223–1249.
Kim, J., Matney, C.J., Blankenship, A., Hestrin, S. & Brown, S.P. (2014). Layer 6 corticothalamic neurons activate a cortical output layer, layer 5a. *Journal of Neuroscience* **34**, 9656–9664.
Krahe, T.E., El-Danaf, R.N., Dilger, E.K., Henderson, S.C. & Guido, W. (2011). Morphologically distinct classes of relay cells exhibit regional preferences in the dorsal lateral geniculate nucleus of the mouse. *Journal of Neuroscience* **31**, 17437–17448.
Krupa, D.J., Ghazanfar, A.A. & Nicolelis, M.A.L. (1999). Immediate thalamic sensory plasticity depends on corticothalamic feedback. *Proceedings of the National Academy of Sciences of the United States of America* **96**, 8200–8205.
LeVay, S. & Sherk, H. (1981). The visual claustrum of the cat I. Structure and connections. *Journal of Neuroscience* **1**, 956–980.
Li, G., Ye, X., Song, T., Yang, Y. & Zhou, Y. (2011). Contrast adaptation in cat lateral geniculate nucleus and influence of corticothalamic feedback. *European Journal of Neuroscience* **34**, 622–631.
Li, L. & Ebner, F.F. (2007). Cortical modulation of spatial and angular tuning maps in the rat thalamus. *Journal of Neuroscience* **27**, 167–179.
Lin, C.S. & Kaas, J.H. (1977). Projections from cortical visual areas 17, 18, and MT onto the dorsal lateral geniculate nucleus in owl monkeys. *Journal of Comparative Neurology* **173**, 457–474.
Ling, S., Pratte, M. & Tong, F. (2015). Attention alters orientation processing in the human lateral geniculate nucleus. *Nature Neuroscience* **18**, 496–498.
Lund, J.S. & Boothe, R.G. (1975). Interlaminar connections and pyramidal neuron organization in the visual cortex, area 17, of the macaque monkey. *Journal of Comparative Neurology* **159**, 305–334.
Lund, J.S., Lund, R.D., Hendrickson, A.E., Bunt, A.H. & Fuchs, A.F. (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. *Journal of Comparative Neurology* **164**, 287–303.
Marrocco, R.T., McClurkin, J.W. & Alkire, M.T. (1996). The influence of the visual cortex on the spatiotemporal response properties of lateral geniculate nucleus cells. *Brain Research* **737**, 110–118.
Maunsell, J.H.R., Ghose, G.M., Assad, J.A., McAdams, C.J., Boudreau, C.E. & Noerager, B.D. (1999). Visual response latencies of magnocellular and parvocellular LGN neurons in macaque monkeys. *Visual Neuroscience* **16**, 1–14.
McAlonan, K., Cavanaugh, J.R. & Wurtz, R.H. (2006). Attentional modulation of thalamic reticular neurons. *Journal of Neuroscience* **26**, 4444–4450.
McAlonan, K., Cavanaugh, J.R. & Wurtz, R.H. (2008). Guarding the gateway to cortex with attention in visual thalamus. *Nature* **456**, 391–394.
Merigan, W.H. & Maunsell, J.H.R. (1993). How parallel are the primate visual pathways. *Annual Review of Neuroscience* **16**, 369–402.
Miller, M.W. (1988). Maturation of rat visual cortex: IV. The generation, migration, morphogenesis, and connectivity of atyipcally oriented pyramidal neurons. *Journal of Comparative Neurology* **274**, 387–405.
Molotchnikoff, S., Tremblay, F. & Lepore, F. (1984). The role of the visual cortex in response properties of lateral geniculate cells in rats. *Experimental Brain Research* **53**, 223–232.
Murphy, P.C., Duckett, S.G. & Sillito, A.M. (2000). Comparison of the laminar distribution of input from areas 17 and 18 of the visual cortex to the lateral geniculate nucleus of the cat. *Journal of Neuroscience* **20**, 845–853.
Murphy, P.C. & Sillito, A.M. (1987). Corticofugal feedback influences the generation of length tuning in the visual pathway. *Nature* **329**, 727–729.
Murphy, P.C. & Sillito, A.M. (1996). Functional morphology of the feedback pathway from area 17 of the cat visual cortex to the lateral geniculate nucleus. *Journal of Neuroscience* **16**, 1180–1192.
Nhan, H.L. & Callaway, E.M. (2012). Morphology of superior colliculus- and middle temporal area-projecting neurons in primate primary visual cortex. *Journal of Comparative Neurology* **520**, 52–80.
O'Connor, D.H., Fukui, M.M., Pinsk, M.A. & Kastner, S. (2002). Attention modulates responses in the human lateral geniculate nucleus. *Nature Neuroscience* **5**, 1203–1209.

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press

Olsen, S.R., Bortone, D.S., Adesnik, H. & Scanziani, M. (2012). Gain control by layer six in cortical circuits of vision. *Nature* **483**, 47–52.
Przybyszewski, A.W., Gaska, J.P., Foote, W. & Pollen, D.A. (2000). Striate cortex increases contrast gain of macaque LGN neurons. *Visual Neuroscience* **17**, 485–494.
Rigas, P. & Castro-Alamancos, M.A. (2007). Thalamocortical up states: Differential effects of intrinsic and extrinsic cortical inputs on persistent activity. *Journal of Neuroscience* **27**, 4261–4272.
Rivadulla, C., Martinez, L.M., Varela, C. & Cudeiro, J. (2002). Completing the corticofugal loop: A visual role for the corticogeniculate type I metabotropic glutamate receptor. *Journal of Neuroscience* **22**, 2956–2962.
Robson, J.A. (1983). The morphology of corticofugal axons to the dorsal lateral geniculate nucleus in the cat. *Journal of Comparative Neurology* **216**, 89–103.
Schiller, P.H. & Malpeli, J.G. (1978). Functional specificity of lateral geniculate nuclues laminae of the rhesus monkey. *Journal of Neurophysiology* **41**, 788–797.
Seabrook, T.A., El-Danaf, R.N., Krahe, T.E., Fox, M.A. & Guido, W. (2013). Retinal input regulates the timing of corticogeniculate innervation. *Journal of Neuroscience* **33**, 10085–10097.
Shanks, J.A., Ito, S., Schaevitz, L., Yamada, J., Chen, B., Litke, A.M. & Feldheim, D.A. (2016). Corticothalamic axons are essential for retinal ganglion cell axon targeting to the mouse dorsal lateral geniculate nucleus. *Journal of Neuroscience* **36**, 5252–5263.
Sherman, S.M. (1996). Dual response modes in lateral geniculate neurons: Mechanisms and functions. *Visual Neuroscience* **13**, 205–213.
Sherman, S.M. & Guillery, R.W. (1998). On the actions that one nerve cell can have on another: Distinguishing "drivers" from "modulators". *Proceedings of the National Academy of Sciences of the United States of America* **95**, 7121–7126.
Sherman, S.M. & Guillery, R.W. (2006). *Exploring the Thalamus and its Role in Cortical Function* (2nd ed.). Boston: MIT Press.
Sillito, A.M., Cudeiro, J. & Murphy, P.C. (1993). Orientation sensitive elements in the corticofugal influence on centre-surround interactions in the dorsal lateral geniculate nucleus. *Experimental Brain Research* **93**, 6–16.
Sillito, A.M. & Jones, H.E. (2002). Corticothalamic interactions in the transfer of visual information. *Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences* **357**, 1739–1752.
Sillito, A.M., Jones, H.E., Gerstein, G.L. & West, D.C. (1994). Feature-linked synchronization of thalamic relay cell firing induced by feedback from the visual cortex. *Nature* **369**, 479–482.
Sincich, L.C. & Horton, J.C. (2005). The circuitry of V1 and V2: Intergration of color, form, and motion. *Annual Review of Neuroscience* **28**, 303–326.
Solomon, S.G. & Lennie, P. (2007). The machinery of colour vision. *Nature Reviews Neuroscience* **8**, 276–286.
Solomon, S.G., White, A.J.R. & Martin, P.R. (1999). Temporal contrast sensitivity in the lateral geniculate nucleus of a new world monkey, the marmoset *Callithrix jacchus*. *Journal of Physiology* **517**, 907–918.
Solomon, S.G., White, A.J.R. & Martin, P.R. (2002). Extraclassical receptive field properties of parvocellular, magnocellular and koniocellular cells in the primate lateral geniculate nucleus. *Journal of Neuroscience* **22**, 338–349.
Steriade, M. (2001). Impact of network activities on neuronal properties in corticothalamic systems. *Journal of Neurophysiology* **86**, 1–39.
Steriade, M. (2003). The corticothalamic system in sleep. *Frontiers in Bioscience* **8**, d878–899.
Suga, N. & Ma, X. (2003). Multiparametric corticofugal modulation and plasticity in the auditory system. *Nature Reviews Neuroscience* **4**, 783–794.
Swadlow, H.A. & Weyand, T.G. (1981). Efferent systems of the rabbit visual cortex: Laminar distribution of cells of origin, axonal conduction velocities, and identification of axonal branches. *Journal of Comparative Neurology* **203**, 799–822.
Swadlow, H.A. & Weyand, T.G. (1987). Corticogeniculate neurons, corticotectal neurons, and suspected interneurons in visual cortex of awake rabbits: Receptive-field properties, axonal properties, and effects of EEG arousal. *Journal of Neurophysiology* **57**, 977–1001.
Temereanca, S., Brown, E.N. & Simons, D.J. (2008). Rapid changes in thalamic firing synchrony during repetitive whisker stimulation. *Journal of Neuroscience* **28**, 11153–11164.
Thompson, A.D., Picard, N., Min, L., Fagiolini, M. & Chen, C. (2016). Cortical feedback regulates feedforward retinogeniculate refinement. *Neuron* **91**, 1021–1033.
Tombol, T. (1984). Layer VI cells. In *Cerebral Cortex*, ed. Peters, A. & Jones, E.G., pp. 479–519. New York: Plenum Press.
Tsumoto, T. & Suda, K. (1980). Three groups of cortico-geniculate neurons and their distribution in binocular and monocular segments of cat striate cortex. *Journal of Comparative Neurology* **193**, 223–236.
Updyke, B.V. (1975). The patterns of projection of cortical areas 17, 18, and 19 onto the laminae of the dorsal lateral geniculate nucleus in the cat. *Journal of Comparative Neurology* **163**, 377–396.
Usrey, W.M. & Fitzpatrick, D. (1996). Specificity in the axonal connections of layer 6 neurons in tree shrew striate cortex: Evidence for distinct granular and supragranular systems. *Journal of Neuroscience* **16**, 1203–1218.
Usrey, W.M. & Reid, R.C. (2000). Visual physiology of the lateral geniculate nucleus in two species of new world monkey: *Saimiri sciureus* and *Aotus trivirgatis*. *Journal of Physiology* **523**, 755–769.
Vanduffel, W., Tootell, R.B.H. & Orban, G. (2000). Attention-dependent suppression of metabolic activity in the early stages of the macaque visual system. *Cerebral Cortex* **10**, 109–126.
Wang, W., Jones, H.E., Andolina, I.M., Salt, T.E. & Sillito, A.M. (2006). Functional alignment of feedback effects from visual cortex to thalamus. *Nature Neuroscience* **9**, 1330–1336.
Webb, B.S., Tinsley, C.J., Barraclough, N.E., Easton, A., Parker, A. & Derrington, A.M. (2002). Feedback from V1 and inhibition from beyond the classical receptive field modulates the response of neurons in the primate lateral geniculate nucleus. *Visual Neuroscience* **19**, 583–592.
White, A.J.R., Solomon, S.G. & Martin, P.R. (2001). Spatial properties of koniocellular cells in the lateral geniculate nucleus of the marmoset Callithrix jacchus. *Journal of Physiology* **553**, 519–535.
White, A.J.R., Wilder, H.D., Goodchild, A.K., Sefton, A.J. & Martin, P.R. (1998). Segregation of receptive field properties in the lateral geniculate nucleus of the new-world monkey, the marmoset *Callithrix jacchus*. *Journal of Neurophysiology* **80**, 2063–2076.
Wiser, A.K. & Callaway, E.M. (1996). Contributions of individual layer 6 pyramidal neurons to local circuitry in macaque primary visual cortex. *Journal of Neuroscience* **16**, 2724–2739.
Wolfart, J., Debay, D., Le Masson, G., Destexhe, A. & Bal, T. (2005). Synaptic background activity controls spike transfer from thalamus to cortex. *Nature Neuroscience* **8**, 1760–1767.
Worgotter, F., Eyding, D., Macklis, J.D. & Funke, K. (2002). The influence of the corticothalamic projection on responses in the thalamus and cortex. *Philosophical Transactions of the Royal Society of London, Series B: Biological Sciences* **357**, 1823–1834.
Wu, Y. & Yan, J. (2007). Modulation of the receptive fields of midbrain neurons elicited by thalamic electrical stimulation through corticofugal feedback. *Journal of Neuroscience* **27**, 10561–10658.
Yousif, N. & Denham, M. (2007). The role of cortical feedback in the generation of the temporal receptive field responses of lateral geniculate nucleus neurons: A computational modelling study. *Biological Cybernetics* **97**, 269–277.
Zarrinpar, A. & Callaway, E.M. (2006). Local connections to specific types of layer 6 neurons in the rat visual cortex. *Journal of Neurophysiology* **95**, 1751–1761.
Zhang, Y. & Yan, J. (2008). Corticothalamic feedback for sound-specific plasticity of auditory thalamic neurons elicited by tones paired with basal forebrain stimulation. *Cerebral Cortex* **18**(7), 1521–1528.

https://doi.org/10.1017/S095252381700013X Published online by Cambridge University Press