

Beyond a relay nucleus: neuroimaging views on the human LGN

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Abstract: The lateral geniculate nucleus (LGN) is the thalamic station in the retinocortical projection and has traditionally been viewed as the gateway for sensory information to enter the cortex. Here, we review recent studies of the human LGN that have investigated the retinotopic organization, physiologic response properties, and modulation of neural activity by selective attention and by visual awareness in a binocular rivalry paradigm. In the retinotopy studies, we found that the contralateral visual field was represented with the lower field in the medial-superior portion and the upper field in the lateral-inferior portion of each LGN. The fovea was represented in posterior and superior portions, with increasing eccentricities represented more anteriorly. Functional MRI responses increased monotonically with stimulus contrast in the LGN and in visual cortical areas. In the LGN, the dynamic response range of the contrast function was larger and contrast gain was lower than in the cortex. In our attention studies, we found that directed attention to a spatial location modulated neural activity in the LGN in several ways: it enhanced neural responses to attended stimuli, attenuated responses to ignored stimuli, and increased baseline activity in the absence of visual stimulation. Furthermore, we showed in a binocular rivalry paradigm that neural activity in the LGN correlated strongly with the subjects' reported percepts. The overall view that emerges from these studies is that the human LGN plays a role in perception and cognition far beyond that of a relay nucleus and, rather, needs to be considered as an early gatekeeper in the control of visual attention and awareness.

Keywords: fMRI; retinotopy; magno- and parvocellular LGN; contrast response; flicker response; selective attention; binocular rivalry

Introduction

The lateral geniculate nucleus (LGN) is the thalamic station in the retinocortical projection and has traditionally been viewed as the gateway for sensory information to enter the visual cortex (Jones, 1985; Sherman and Guillery, 2001). Its topographic organization and the response properties of its neurons have been extensively studied

in nonhuman primates (e.g., Polyak, 1953; Kaas et al., 1972; Malpel and Baker, 1975; Connolly and Van Essen, 1984). The LGN is typically organized into six main layers, each of which receives input from either the contra- or ipsilateral eye and contains a retinotopic map of the contralateral hemifield. The four dorsal layers contain small (parvocellular, P) neurons characterized by sustained discharge patterns and low-contrast gain, and the two ventral layers contain large (magnocellular, M) neurons characterized by transient discharge patterns and high-contrast gain (Wiesel

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and Hubel, 1966; Dreher et al., 1976; Creutzfeldt et al., 1979; Shapley et al., 1981; Derrington and Lennie, 1984; Merigan and Maunsell, 1993). In addition to retinal afferents, which constitute only 10% of its overall afferent input, the LGN receives modulatory inputs from multiple sources including striate cortex, the thalamic reticular nucleus (TRN), and the brainstem. The LGN therefore represents the first stage in the visual pathway at which cortical top-down feedback signals could affect visual processing. The functional role of these top-down inputs to the LGN is, however, not well understood (Guillery and Sherman, 2002).

In the human brain, it has proven difficult to study subcortical nuclei because of spatial resolution and signal-to-noise limitations of brain-mapping techniques. Thus, surprisingly little is known about the functional anatomy, physiological response properties, and functional role in perception and cognition of the human LGN. Here, we review a series of studies from our laboratory that utilized optimized neuroimaging techniques at conventional or high resolution to scan the human thalamus. First, we will describe high-resolution fMRI studies on the topographic organization of the LGN and its functional subdivisions into magno- and parvocellular parts. Second, we will report its basic response properties to stimulus contrast and flicker rate. Third, we will describe our advances in understanding the role of the LGN in attentional processing, one of the better understood cognitive operations in primates. And fourth, we will report recent studies on neural correlates related to perceptual experiences in binocular rivalry, suggesting an important role of the human LGN in visual awareness and conscious perception. The overall view that emerges from these studies is that the human LGN plays a role in perception and cognition far beyond that of a relay nucleus and, rather, needs to be considered as an early gatekeeper in the control of visual attention and awareness.

We chose to provide an update on the human LGN as a tribute to Lothar Spillmann, because many of the perceptual phenomena that were at the heart of Lothar's interest and study such as the Hermann grid and the "perceptive fields" (e.g., Spillman, 1971, 1994) can be explained by

physiological response properties of retinal and geniculate neurons. Indeed, the lead author of this chapter first met Lothar in Freiburg over a discussion on neurophysiological correlates of simultaneous color contrast in LGN neurons, her graduate work at the time conducted with Otto Creutzfeldt in Goettingen (Creutzfeldt et al., 1991; Kastner et al., 1992).

Retinotopic organization

The topographic organization of the LGN has been studied extensively in macaques, using anatomical (Brouwer and Zeemann, 1926), physiological (Kaas et al., 1972; Malpeli and Baker, 1975; Connolly and Van Essen, 1984; Malpeli et al., 1996; Erwin et al., 1999), and lesion techniques (Clark and Penman, 1934). These studies have shown that the contralateral visual hemifield is represented in the LGN with the horizontal meridian dividing the structure into a superior and medial half representing the lower visual field and an inferior and lateral half representing the upper visual field. The fovea is represented medially in the posterior pole of the nucleus, whereas more peripheral visual field representations are located more anteriorly and laterally (Malpeli and Baker, 1975).

In the human LGN, anatomical studies have revealed a similar organization compared to the macaque LGN in terms of laminar patterns. The layout of the representation of the visual field, however, is less well understood because its study has been restricted to postmortem anatomical analyses of degeneration patterns following retinal or cortical lesions (Rönne, 1910; Juba and Szatmári, 1937; Kupfer, 1962; Hickey and Guillery, 1979). In one neuroimaging study, a retinotopic organization was suggested by demonstrating distinct and inverted activations associated with stimulation of the upper and lower visual hemifields in the inferior and superior parts of the LGN, respectively (Chen et al., 1999). We used high-resolution ($1.5 \times 1.5 \times 2 \text{ mm}^3$) fMRI at 3T to derive a detailed account of the retinotopic organization of the human LGN, including estimates of the eccentricity magnification factor (Schneider et al., 2004). Representations of polar

angle and eccentricity were measured within the central 15° of the visual field.

Polar-angle maps

The polar-angle component of the retinotopic map in the LGN was determined by using a smoothly rotating, flickering hemifield checkerboard stimulus. The checkerboard stimulus rotated counter-clockwise about a central fixation point, at which subjects were instructed to maintain fixation throughout the presentation, and swept through the visual field with a period of 32 s, thereby evoking waves of activation in neurons whose receptive fields (RFs) they passed. With this stimulus, bilateral activations were found in the posterior thalamus, in the anatomical location of the human LGN, in all the seven subjects tested. These

activations were strictly confined to stimulation of the contralateral hemifield in each LGN. Individual activation maps are shown for two representative subjects (S1 and S2) in the left and right columns of Fig. 1. The activation maps, overlaid on structural scans (shown in the central panel), are displayed in $15 \times 12 \text{ mm}^2$ windows for five contiguous brain slices. The color given to each voxel was determined by the phase of its response and represents the region of the visual field to which the voxel was most responsive, as indicated in the color legend at the top of each column. Regions of the upper visual field are indicated in red-yellow, regions along the horizontal meridian in green, and regions of the lower visual field in blue. In the coronal plane, the representation of the horizontal meridian was oriented at an approximately 45° angle, dividing the lower visual field,

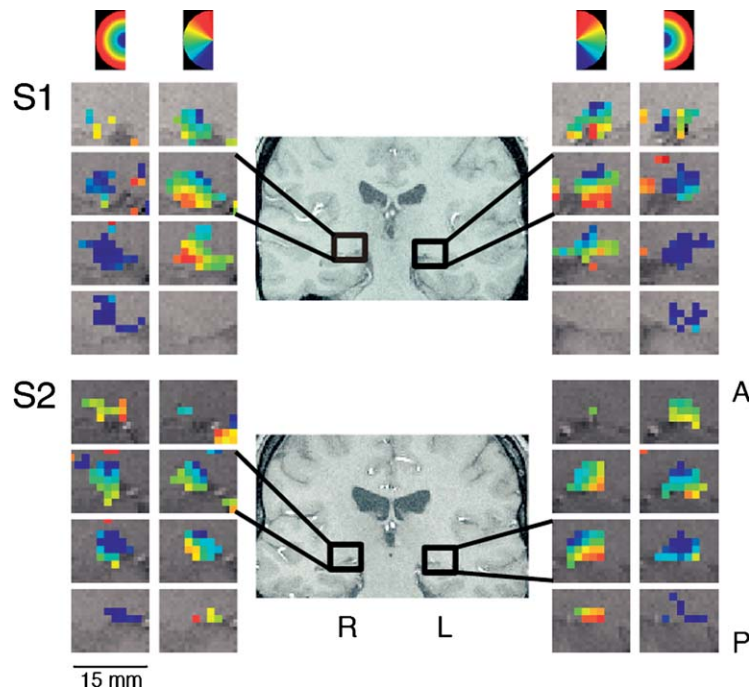


Fig. 1. Retinotopic maps in the LGN. Polar-angle and eccentricity maps are shown for two representative subjects (S1 and S2). The central panel shows an anatomical image in the coronal plane through the posterior thalamus. The boxes indicate the locations of the panels to the left and right. Details of the polar-angle maps in the right (R) and left (L) LGNs are shown in the near left and right columns, arranged in several sequential slices from anterior (A) to posterior (P). The eccentricity maps are shown in the far left and right columns and have been spatially registered with the polar-angle maps. The color code (shown for voxels whose responses were correlated with the fundamental frequency of the stimulus, $r \geq 0.25$) indicates the phase of the response and labels the region of the visual field to which the voxel is most responsive, as depicted in the visual field color legend at the top of each column. (From [Schneider et al., 2004](#), with permission.)

represented in the medial-superior section of the LGN, and the upper visual field, represented in the lateral-inferior section. Although the extent of activations varied somewhat among subjects, the overall pattern of retinotopic polar-angle organization was consistent among them.

Eccentricity maps

Eccentricity maps were measured in response to an expanding or contracting flickering checkerboard ring stimulus. The expanding ring stimulus consisted of an annulus with thickness equal to half of the radius of the visual display that expanded from the fixation point. The annulus increased in eccentricity (i.e., the distance from fixation) and wrapped around to the center once it reached the outer edge of the display, while subjects maintained fixation throughout the presentation. This stimulus activated the LGN bilaterally in all subjects ($N = 7$). Eccentricity maps are shown for the same subjects and in register with the polar-angle retinotopic maps in Fig. 1 (far away columns to the right and left). The color code, as indicated by the legend at the top of each column, indicates the region of the visual field to which each voxel was most responsive. Voxels representing the central 5° are indicated in dark to light blue; those representing 5° – 10° in cyan to green to yellow; and those representing the peripheral 10° – 15° in orange to red. The central 5° were represented mainly in the posterior portion of the LGN; in more anterior planes, the representation of the central 5° was confined to superior sections. More peripheral representations of the visual field were systematically arranged in anterior and inferior regions of the nucleus. As with the polar angle maps, the organization of the eccentricity maps was consistent across subjects.

Taken together, polar angle and eccentricity maps found in the human LGN indicate striking similarities in topographic organization compared to that reported in the macaque, as outlined above.

Eccentricity magnification factor

As in other visual areas, more LGN neurons are devoted to the representation of the fovea than to

an equivalent area of the visual periphery. This distortion can be parameterized by an eccentricity magnification factor (Talbot and Marshall, 1941; Daniel and Whitteridge, 1961), which has been measured using a number of techniques in the macaque LGN and in both macaque and human V1. In the human brain, the eccentricity magnification factor for the LGN is unknown. We estimated this magnification factor on the basis of a volumetric analysis of the data obtained with eccentricity mapping. The cumulative volumes of the right and left LGNs were plotted as a function of eccentricity, as shown for three representative subjects (S1, S2, and S6) and the group (S1–S7) in Fig. 2. The cumulative volume functions were similarly shaped among the subjects, though differing in slope and extent. For many of the subjects, the cumulative volume function was steep and nearly linear for the initial 2° – 5° of the eccentricity, after which the slope abruptly became shallower. A similar broken function has been observed in mac-

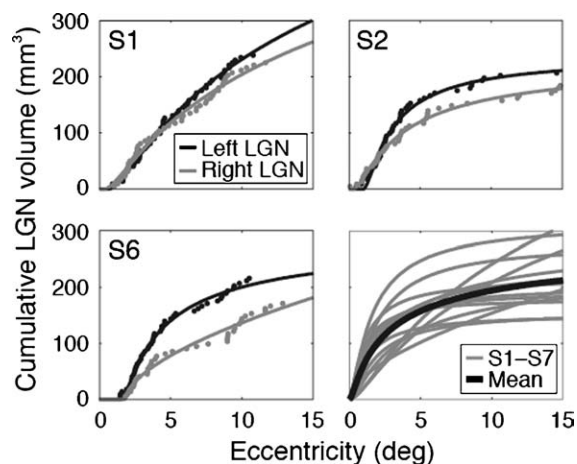


Fig. 2. Eccentricity magnification factor in the LGN. Eccentricity magnification factors for three representative subjects (S1, S2, S6) in each LGN are shown, computed on the basis of the phase responses of voxels activated by the expanding ring stimulus (see Fig. 1). The cumulative volume representing the area of the visual field from the fixation point to an eccentricity of r or less was fit to the integral of the magnification function $M(r) = A(r + B)^{-C}$ over the area of the visual hemifield (see Schneider et al., 2004 for more details). The fits for each LGN in each of the seven subjects are superimposed in the bottom right panel, along with the mean cumulative volume function fit for all subjects, which was $M(r) = 46.6(r + 0.52)^{-2.43}$. (From Schneider et al., 2004, with permission.)

aque visual cortex, where the RFs are nearly constant within the foveal 5° and begin to increase rapidly thereafter (Van Essen et al., 1984).

We then compared our estimate of the eccentricity magnification factor found in the group of seven subjects (see Fig. 2) with those obtained in macaque LGN and V1 reported in the literature. This comparison indicated a relative over-representation of the fovea in the human LGN as compared to the macaque LGN (see Fig. 6 in Schneider et al., 2004). We also compared our estimates for the human LGN with measurements of the magnification factor in human V1 that were obtained with different techniques including visually evoked potentials, fMRI, and phosphenes evoked by migraines or electrical stimulation. This comparison revealed that our estimates were similar to those obtained for human V1 (see Fig. 6 in Schneider et al., 2004). In the macaque, it is an open question whether the relative representation of the fovea expands progressively from the retina through the LGN and V1 (Malpeli and Baker, 1975; Myerson et al., 1977; Connolly and Van Essen, 1984; Van Essen et al., 1984; Perry and Cowey, 1985; Azzopardi and Cowey, 1996), or is preserved throughout the visual hierarchy with no additional magnification present at the level of the LGN or V1 (Webb and Kaas, 1976; Schein and de Monasterio, 1987; Wässle et al., 1989, 1990; Malpeli et al., 1996). In humans, our results of similar estimates of the magnification factor in LGN and V1 support the latter notion.

Magno- and parvocellular subdivisions

The spatial resolution of our imaging technique did not permit a dissociation of the parvocellular (P) and magnocellular (M) layers of the LGN. However, we attempted to dissociate the P- and M- subdivisions based upon two criteria: their anatomical locations and differences in functional properties, particularly in response sensitivity to stimulus contrast. On the basis of the anatomy, we expected M parts of the LGN to be located medially, inferiorly, and posteriorly. Typically, the M layers are flat and located on the inferior surface of the LGN, but particularly in the posterior planes,

the LGN is oriented at an angle such that the M layers are located medially. Further, the LGN often exhibits folding such that the M layers would be located in the interior of the structure (Hickey and Guillery, 1979; Andrews et al., 1997). On the basis of the physiology, we expected that M cells should respond more sensitively to stimulus contrast than P cells. In single-cell recording studies, it has been shown that P cells are typically not responsive to contrast stimuli lower than 10% and have a 10-fold lower contrast gain than M cells, which typically respond to contrast stimuli as low as 2% (Shapley et al., 1981; Lee et al., 1989; Sclar, 1990). Therefore, we assumed that the M subdivision could be identified by two functional criteria: high sensitivity in response to a low-contrast stimulus, and small or no differences in responses to a low- and a high-contrast stimulus.

To identify P and M subdivisions of the LGN, flickering checkerboard stimuli of low (10%) and high (100%) luminance contrast were used presented in alternation to the right and left hemifields, while subjects maintained fixation at a central fixation point. We assumed that the high-contrast stimulus activated both the P and the M parts of the LGN, and its evoked activity was used to define a region of interest (ROI) encompassing both. Activation maps from two representative subjects (S1 and S6) are shown in Fig. 3A. The activations in the right and left LGNs evoked by the low- and high-contrast stimuli are displayed, similar to the format used in Fig. 1, on four sequential brain slices for each LGN. Activations evoked by the high-contrast stimulus are shown in the left column of each pair. Next, we identified the regions within this ROI that were most responsive to the low-contrast stimulus, and therefore were candidate areas to contain the M subdivision. The voxels activated by the low-contrast stimulus, shown in the right column of each pair in Fig. 3A, constituted a subset of the voxels activated by the high-contrast stimulus. The voxels most responsive to the low-contrast stimulus formed clusters that varied among the subjects in location relative to the activations evoked by the high-contrast stimulus.

In addition to response sensitivity to low-contrast stimuli, the second criterion that we employed to

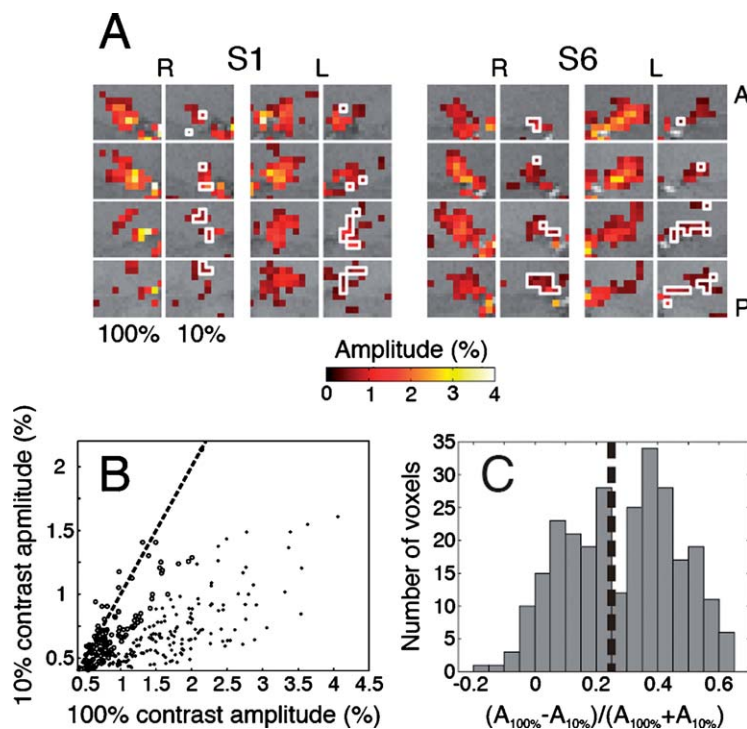


Fig. 3. Magno- and parvocellular subdivisions. Magno- and parvocellular subdivisions were functionally identified on the basis of the contrast sensitivity maps. (A) Activity evoked by an alternating hemifield stimulus in the anatomical location of the left (L) and right (R) LGNs is shown for two representative subjects. Four sequential slices are shown, ordered anterior (A) to posterior (P). The left column of each pair indicates the amplitude of the response to the high-contrast (100%) stimulus, and the right column indicates the response to the low-contrast (10%) stimulus. Only those voxels with correlations to the fundamental frequency of the stimulus, $r \geq 0.25$, are shown. Voxels surrounded by white lines responded similarly to the low- and high-contrast stimuli (see text and (B) below). On the basis of their high-contrast sensitivity, these voxels are likely dominated by magnocellular neurons. (B) For each subject ($N = 5$) and each voxel activated by both the low- and high-contrast stimuli ($r \geq 0.25$), the amplitudes of the mean fMRI time series evoked by the high- ($A_{100\%}$) and low- ($A_{10\%}$) contrast alternating hemifield stimuli are plotted against each other. The dashed diagonal line indicates equality between the amplitudes. The open circle symbols represent the voxels whose contrast modulation indices (CMI), defined as $(A_{100\%} - A_{10\%}) / (A_{100\%} + A_{10\%})$, were less than 0.25. These voxels are bordered with solid white lines in (A). (C) The distribution of CMI. Voxels predominately containing M neurons are expected to be similarly activated by both the low- and high-contrast stimuli, and hence have a small CMI. P voxels are expected to have a strong differential response to the low- and high-contrast stimuli and therefore will have a large CMI. The dotted vertical line marks the 0.25 threshold used to select the voxels in panels (A) and (B). (From Schneider et al., 2004, with permission.)

identify the M subdivisions was that the responses of M voxels evoked by the low-contrast stimulus should be nearly saturated and marginally different from the responses evoked by the high-contrast stimulus, whereas P voxels should exhibit larger differences in response to the two contrast stimuli. Therefore, we analyzed the contrast modulation for those voxels that were reliably activated by both the low- and the high-contrast stimuli and plotted the averaged response amplitudes evoked by the two stimuli (Fig. 3B). A high correlation is evident, such

that for each voxel, the larger the amplitude evoked by the high-contrast stimulus, the larger is the amplitude tended to be evoked by the low-contrast stimulus ($r = 0.59$, $p = 7.3 \times 10^{-27}$). The linear regression line has a slope of 0.22, but the population is distributed, including voxels clustered around the unity slope line, which indicates equality in the amplitudes evoked by the two contrast stimuli (see Fig. 3B). To quantify the response modulation, we calculated a contrast modulation index (CMI) for each voxel, defined as $(A_{100\%} - A_{10\%}) / (A_{100\%} + A_{10\%})$,

where $A_{100\%}$ and $A_{10\%}$ are the response amplitudes evoked by the 100% and 10% contrast stimuli, respectively. Voxels with CMI values near 0 were weakly modulated by the increase from low to high stimulus contrast, and those voxels with CMI near 1 were strongly modulated. The distribution of the CMIs is shown in Fig. 3C. The proportion of voxels with CMIs < 0.25 are indicated by open circle symbols in Fig. 3B and are bordered with white lines in Fig. 3A. We found that 16.7% of all voxels activated by the high-contrast stimulus fulfilled both criteria, exhibiting significant responses to the low-contrast stimulus and exhibiting contrast saturation (CMI < 0.25). These are the most likely candidates for voxels dominated by M responses. Although the anatomical locations of these voxels varied, when clustered, they tended to be located medially and/or posteriorly, as expected from the anatomical location of the M layers. This is also the case for the two subjects shown in Fig. 3A. In human anatomical studies, it has been shown that 19–28% of the LGN volume is occupied by the M layers (Andrews et al., 1997), which is similar to the proportion of LGN voxels identified as potential M voxel candidates using our functional criteria. It should be noted that our estimate depended on the choice of the activation and contrast modulation thresholds. Future studies using additional functional criteria will be necessary to further characterize the functional subdivisions within the human LGN.

Basic physiological response properties

Physiological response properties of LGN neurons have been extensively studied in nonhuman primates (for reviews see Jones, 1985; Sherman and Guillery, 2001). For example, P cells are characterized by sustained discharge patterns, sensitivity to color, and low-contrast gain, and M cells are characterized by transient discharge patterns and high-contrast gain (Wiesel and Hubel, 1966; Dreher et al., 1976; Creutzfeldt et al., 1979; Shapley et al., 1981; Merigan and Maunsell, 1993). In the series of studies reviewed in this section (Kastner et al., 2004), we investigated basic physiological response properties of the human LGN, specifically responses as a function of stimulus contrast and

flicker reversal rate. Collective responses of neural populations in the LGN including both P and M parts were compared with population responses obtained in visual cortical areas.

Responses to stimulus contrast

To measure responses to stimulus contrast in the LGN and visual cortex, checkerboard stimuli with a constant flicker reversal rate of 7.5 Hz encompassing the central 12° of the visual field were presented in alternation to either the left or the right visual hemifield at six different contrast levels ranging from 4 to 100%. Subjects were instructed to maintain fixation at a central cross throughout the presentations. Time series of fMRI signals evoked by checkerboard stimuli presented at 4, 9, 35, and 100% contrast, averaged across scans and subjects ($N = 6$), are presented for the LGN, V1, V4, and medial temporal area (MT) in Fig. 4A.

In the LGN and visual cortical areas except MT, fMRI responses increased monotonically but nonlinearly as a function of stimulus contrast. In the LGN, responses to stimulus contrast less than 10% amounted to 41% of the maximum response. In visual cortex, an even greater sensitivity to low-contrast stimulus was seen. In areas V1 and V4, responses to the lowest contrast stimulus tested (4%) evoked 62% of the maximum response. In area MT, responses were saturated at the lowest contrast level (Fig. 4A). These findings confirmed previous single-cell physiology and neuroimaging studies (Dean, 1981; Tolhurst et al., 1981; Albrecht and Hamilton, 1982; Sclar et al., 1990; Cheng et al., 1994; Tootell et al., 1995; Boynton et al., 1996; Carandini and Ferster, 1997; Logothetis et al., 2001; Avidan et al., 2002). In the LGN, populations of neurons with different contrast sensitivities contributed to the collective responses measured with fMRI. As discussed in the last section, P cells are typically not responsive to contrast stimuli lower than 10% and have a 10-fold lower contrast gain than M cells, which typically respond to contrast stimuli as low as 2% (Shapley et al., 1981; Lee et al., 1989; Sclar, 1990). Our previous results (Schneider et al., 2004) demonstrated response saturation in the M subdivision of the LGN with contrast stimuli of 10%, suggesting

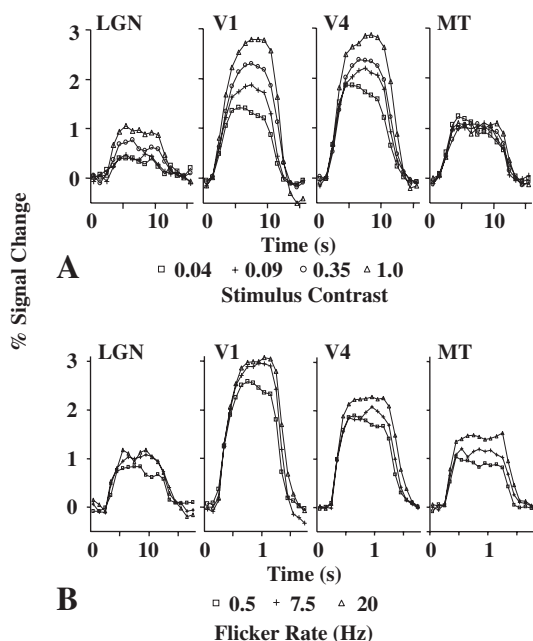


Fig. 4. Modulation by stimulus contrast (A) and flicker reversal rate (B): fMRI signals in LGN, V1, V4, and MT. Time series of fMRI signals in response to varying contrast (A) and flicker reversal rate (B) averaged over all subjects ($N = 6$) and scans. Data were combined across left and right hemispheres. (A) In the LGN, V1, and V4, responses increased monotonically with stimulus contrast. In MT, responses were saturated at the lowest contrast tested when stimuli were presented at increasing contrast levels. (B) In all areas, the 0.5 Hz stimulus evoked significantly smaller responses than the 20 Hz stimulus. In the LGN and in V1 responses evoked by the 7.5 Hz stimulus and the 20 Hz stimulus were similar, whereas in V4 and MT responses evoked by the 0.5 Hz stimulus and 7.5 Hz stimulus were similar. (From Kastner et al., 2004 with permission.)

high-contrast sensitivity for the magnocellular stream in the human visual system. Therefore, the relatively small LGN responses in the low-contrast range ($< 10\%$) may be attributed to a dominant influence from P cells, which outnumber M cells several times in the LGN (Dreher et al., 1976; Perry et al., 1984; Andrews et al., 1997).

Responses of the LGN as a function of stimulus contrast differed in several respects from cortical contrast response functions (CRFs). First, responses in the LGN were evoked by a wider range of contrast stimuli, i.e., the dynamic range of the CRF was larger (Fig. 4A). In cortical areas, CRFs were steeper and saturated more readily, thereby

reducing the dynamic range of the contrast functions. These results are in agreement with single-cell physiology studies (Sclar, 1990) and suggest that neural populations in the LGN can provide information about changes in contrast over a wider range than in cortex. Second, the contrast gain in LGN was lower than in cortical areas, as indicated by a steeper slope and a leftward shift of cortical CRFs along the contrast axis (Fig. 4A; see Fig. 4 in Kastner et al., 2004). In inactivation studies, it has been shown that cooling of V1 leads to decreases of contrast gain in LGN neurons suggesting that contrast gain in the LGN is controlled by cortical mechanisms that are mediated via corticofugal pathways (Przybylski et al., 2000). And third, LGN and V1 were significantly less sensitive to low luminance contrast than extrastriate cortex. A gradual increase of sensitivity to low luminance contrast was obtained from early to intermediate processing levels of the visual system (see also Avidan et al., 2002). These differences in contrast sensitivity may be attributed to the increasing receptive field size of neurons across visual cortex. For example, a neuron in area MT may receive inputs from as many as 10,000 M cells, which would increase its contrast sensitivity due to summation of inputs (Sclar, 1990). Similarly, the larger contrast sensitivity of M cells relative to P cells has been attributed to the larger receptive field sizes of M cells (Lennie et al., 1990).

Responses to flicker reversal rate

To measure responses to flicker reversal rate in the LGN and visual cortex, checkerboard stimuli with a constant contrast of 100% encompassing the central 12° of the visual field were presented in alternation to either the left or the right visual hemifield at three different rates: 0.5, 7.5, and 20 Hz. Subjects were instructed to maintain fixation at a central cross throughout the presentations. Time series of fMRI signals evoked by the stimuli presented at different flicker rates, averaged across sessions and subjects, are shown for the LGN, V1, V4, and MT in Fig. 4B. Differences in flicker rate modulated fMRI signals evoked by the checkerboard stimuli in the LGN and in cortical areas. In all areas, the 0.5 Hz stimulus evoked a significantly

smaller response than the 20 Hz stimulus (Fig. 4B). However, the response evoked by the 0.5 Hz stimulus was surprisingly strong and totaled about 80% of the response elicited by the 20 Hz stimulus in the LGN and in cortical areas other than MT (Fig. 4B). In MT, the 0.5 Hz stimulus was only 62% ($\pm 7\%$ S.E.M.) of the response evoked by the 20 Hz stimulus and elicited a significantly smaller response than in the other areas. In the LGN and in V1, the 7.5 and 20 Hz stimuli evoked similar responses that were significantly stronger than the response to the 0.5 Hz stimulus (Fig. 4B). In extrastriate areas V4 and MT, on the other hand, the 0.5 and 7.5 Hz stimuli evoked similar responses that were significantly smaller than the ones evoked by the 20 Hz stimulus (Fig. 4B). These results suggest that the LGN and V1 respond most sensitively to changes in flicker rate in the 0.5–7.5 Hz range. Extrastriate areas V4 and MT, on the other hand, appear to respond most sensitively within the frequency range of 7.5–20 Hz.

In the macaque monkey, P-LGN neurons have been found to respond most to stimuli at temporal frequencies close to 10 Hz, and M-LGN neurons to stimuli at frequencies close to 20 Hz (Hicks et al., 1983; Derrington et al., 1984; Merigan and Maunsell, 1990, 1993). Further, it was shown that P cells still responded to stimuli lower than 1 Hz, whereas such stimuli did not evoke responses in M cells (Hicks et al., 1983). Our results suggest that LGN responses evoked by the lowest frequency stimulus may be attributed to a predominant parvocellular influence. The low spatial frequency of the checkerboard stimulus presumably favored the activation of P cells, which, unlike M cells, do not show response attenuation at low spatial frequency (Enroth-Cugell et al., 1983; Hicks et al., 1983). In area MT, the relatively small responses evoked by the lowest frequency stimulus and the response preference in the high-frequency range are consistent with the notion that this area receives a dominant magnocellular input. Neurons in areas V1, V2, and V3 have been shown to respond optimally to temporal frequencies between 3 and 6 Hz (Foster et al., 1985; Levitt et al., 1994; Gegenfurtner et al., 1997). Despite significant differences in visual stimuli and methods to estimate neural activity, our finding of peak responses at temporal

frequencies around 4 Hz (i.e., 7.5 Hz reversal rate) in these early cortical areas is in remarkable agreement with the results from single-cell physiology.

Finally, these results can also be related to psychophysical data. At spatial frequencies around 1 cycle/deg, contrast detection curves peak at temporal frequencies of about 3 Hz (Kelly, 1979). Thus, neural responses in the LGN and V1 with peak sensitivity around 4 Hz might predict psychophysical temporal frequency functions better than neural responses in extrastriate cortex with peak sensitivity at higher frequencies. However, studies using a combination of fMRI and psychophysics in the same subjects will be needed to test this idea further.

Attentional response modulation

Thus far, we have reported evidence that fMRI can be effectively used to study the functional topography and basic response properties of thalamic nuclei such as the LGN. Because the LGN represents the first stage in the visual pathway at which cortical top-down feedback signals could affect information processing, we took another step and investigated the functional role of the human LGN in a cognitive operation, which has been well defined at the neural level in visual cortex, selective visual attention.

At the cortical level, selective attention has been shown to affect visual processing in (at least) three different ways. First, neural responses to attended visual stimuli are enhanced relative to the same stimuli when unattended (attentional enhancement; e.g., Moran and Desimone, 1985; Corbetta et al., 1990). Second, neural responses to unattended stimuli are attenuated depending on the load of attentional resources engaged elsewhere (attentional suppression; Rees et al., 1997). And third, directing attention to a location in the absence of visual stimulation and in anticipation of the stimulus onset increases neural baseline activity (attention-related baseline increases; Luck et al., 1997; Kastner et al., 1999).

It has been proven difficult to study attentional response modulation in the LGN using single-cell physiology due to the small RF sizes of LGN

neurons and the possible confound of small eye movements. Several single-cell physiology studies have failed to demonstrate attentional modulation in the LGN supporting a notion that selective attention affects neural processing only at the cortical level (e.g., Mehta et al., 2000). We revisited the role of the LGN in attentional processing using fMRI in humans (O'Connor et al., 2002; Kastner, 2004a, b). Functional MRI measures neural activity at a population level that might be better suited to uncover large-scale modulatory activity. Small modulatory effects that cannot be reliably found by measuring neural activity at the single- or multi-unit level may be revealed when summed across large populations of neurons. We investigated the three effects of selective attention demonstrated previously at the cortical level in a series of three experiments, which were designed to optimally activate the human LGN. Flickering checkerboard stimuli of high or low contrast were used in all experiments, which activated the LGN (Chen et al., 1999) and areas in visual cortex, including V1, V2, ventral and dorsal V3, V4, TEO, V3A, and MT/MST (referred to as MT), as determined on the basis of retinotopic mapping (Serenio et al., 1995; Kastner et al., 2001).

Attention effects of target enhancement, distracter suppression, and increases of baseline activity

To investigate attentional response enhancement in the LGN, checkerboard stimuli were presented to the left or right hemifield, while subjects directed attention to the stimulus (attended condition) or away from the stimulus (unattended condition). In the unattended condition, attention was directed away from the stimulus by having subjects count letters at fixation. The letter counting task ensured proper fixation and prevented subjects from covertly attending to the checkerboard stimuli (Kastner et al., 1998). In the attended condition, subjects were instructed to covertly direct attention to the checkerboard stimulus and to detect luminance changes that occurred randomly in time at 10° eccentricity. In our statistical model, stimulation of the left visual hemifield was contrasted with stimulation of the right visual hemifield. Thereby, the analysis was

restricted to voxels activated by the peripheral checkerboard stimuli and excluded foveal stimulus representations. Relative to the unattended condition, the neural activity evoked by both the high-contrast stimulus and the low-contrast stimulus increased significantly in the attended condition (Fig. 5A). The attentional response enhancement was shown to be spatially specific. These results suggest that attention facilitates visual processing in the LGN by enhancing neural responses to an attended stimulus relative to those evoked by the same stimulus when ignored.

To investigate attentional-load-dependent suppression in the LGN, high- and low-contrast checkerboard stimuli were presented to the left or right hemifield while subjects performed either an easy attention task or a hard attention task at fixation and ignored the peripheral checkerboard stimuli. During the easy attention task, subjects counted infrequent, brief color changes of the fixation cross. During the hard attention task, subjects counted letters at fixation. Behavioral performance was 99% correct on average in the easy attention task and 54% in the hard attention task, thus indicating the differences in attentional demands. Relative to the easy task condition, neural activity evoked by the high- and low-contrast stimuli decreased significantly in the hard task condition (Fig. 5B). This finding suggests that neural activity evoked by ignored stimuli was attenuated in the LGN depending on the load of attentional resources engaged elsewhere.

To investigate attention-related baseline increases in the LGN, subjects were cued to covertly direct attention to the periphery of the left or right visual hemifield and to expect the onset of the stimulus. The expectation period was followed by attended presentations of a high-contrast checkerboard stimulus during which subjects counted the occurrence of luminance changes. During the expectation period, fMRI signals increased significantly relative to the preceding blank period in which subjects were fixating but not directing attention to the periphery. Because the visual input, a gray blank screen, was identical in both conditions, the increase in baseline activity appeared to be related to directed attention and may be interpreted as a bias in favor of the attended location.

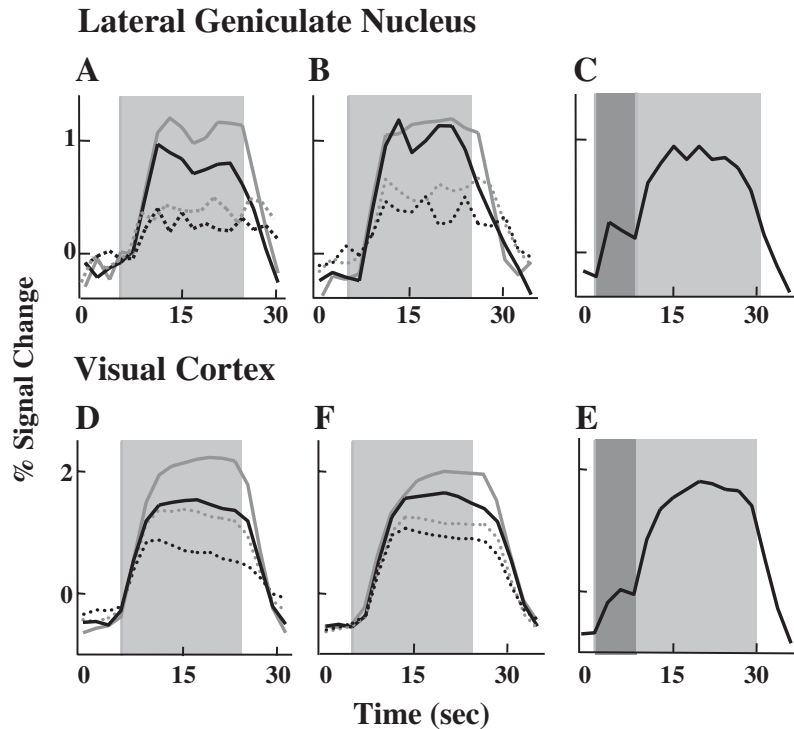


Fig. 5. Time series of fMRI signals in the LGN and in visual cortex. Group analysis ($n = 4$). Data from the LGN and visual cortex were combined across left and right hemispheres. Activity in visual cortex was pooled across areas V1, V2, V3/VP, V4, TEO, V3A, and MT/MST. (A), (D): Attentional enhancement. During directed attention to the stimuli (gray curves), responses to both the high-contrast stimulus (100%, solid curves) and low-contrast stimulus (5%, dashed curves) were enhanced relative to an unattended condition (black curves). (B), (E): Attentional suppression. During an attentionally demanding “hard” fixation task (black curves), responses evoked by both the high-contrast stimulus (100%, solid curves) and low-contrast stimulus (10%, dashed curves) were attenuated relative to an easy attention task at fixation (gray curves). (C), (F): Baseline increases. Baseline activity was elevated during directed attention to the periphery of the visual hemifield in expectation of the stimulus onset (darker gray shaded areas). The lighter gray shaded area indicates the beginning of checkerboard presentation periods. (From O’Connor et al., 2002, with permission.)

The baseline increase was followed by a further response increase evoked by the visual stimuli (Fig. 5C). It is important to note that, because of our statistical model, the increase in baseline activity was not related to the cue, which was presented at fixation. This finding suggests that neural activity in the LGN can be affected by attention-related top-down signals even in the absence of any visual stimulation whatsoever.

In summary, these studies indicate that selective attention modulates neural activity in the LGN by enhancing neural responses to attended stimuli, by attenuating those to ignored stimuli, and by increasing baseline activity in the absence of visual stimulation.

Comparison of attention effects in the LGN and the visual cortex

At the cortical level, qualitatively similar effects of attention were found, as shown in the time series of fMRI signals averaged across all activated areas in visual cortex, i.e., areas V1, V2, V3, V4, TEO, V3A, and MT (Figs. 5D–F). The attention effects found at the thalamic and at the cortical level were compared by normalizing the mean fMRI signals evoked in the LGN and in each activated cortical area and by computing index values for each attention effect and each area, which are measures of the magnitude of a given attention effect. This analysis is shown in Fig. 6; larger index values

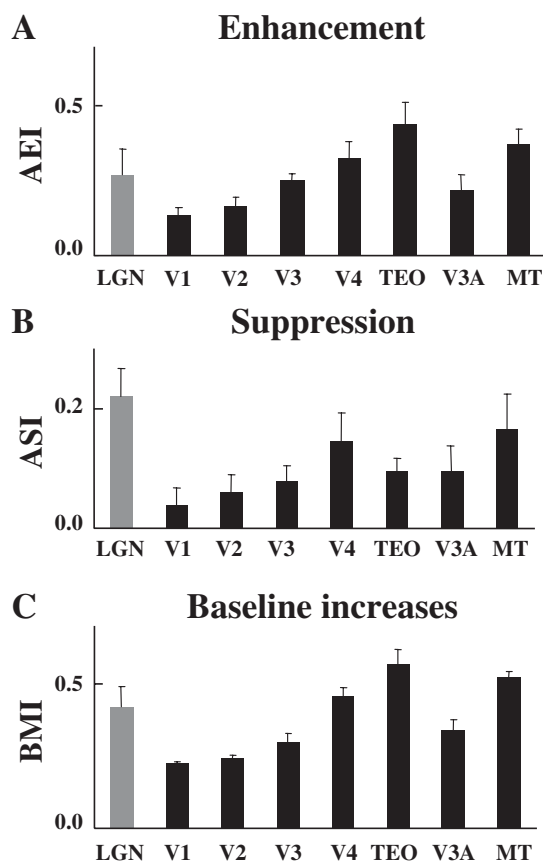


Fig. 6. Attentional response modulation in the LGN and in visual cortex. Attention effects that were obtained in the experiments presented in Fig. 1 were quantified by defining several indices: (A) attentional enhancement index (AEI), (B) attentional suppression index (ASI), (C) baseline modulation index (BMI). For all indices, larger values indicate larger effects of attention. Index values were computed for each subject based on normalized and averaged signals obtained in the different attention conditions and are presented as averaged index values from four subjects (for index definitions, see O'Connor et al., 2002). In visual cortex, attention effects increased from early to later processing stages. Attention effects in the LGN were larger than in V1. Vertical bars indicate S.E.M. across subjects. (From O'Connor et al., 2002, with permission.)

indicate larger effects of attention. It should be noted that index values cannot be easily compared across attention effects due to differences in index definitions and attention tasks. In accordance with previous findings (Kastner et al., 1998; Martinez et al., 1999; Mehta et al., 2000; Cook and Maunsell, 2002), the magnitude of all attention effects

increased from early to more advanced processing levels along both the ventral and dorsal pathways of visual cortex (Figs. 6A–C). This is consistent with the idea that attention operates through top-down signals that are transmitted via corticocortical feedback connections in a hierarchical fashion. Thereby, areas at advanced levels of visual cortical processing are more strongly controlled by attention mechanisms than are early processing levels. This idea is supported by single-cell recording studies, which have shown that attention effects in area TE of inferior temporal cortex have a latency of approximately 150 ms (Chelazzi et al., 1998), whereas attention effects in V1 have a longer latency of approximately 230 ms (Roelfsema et al., 1998). According to this account, one would predict smaller attention effects in the LGN than in striate cortex. Surprisingly, it was found that all attention effects tended to be larger in the LGN than in striate cortex (Figs. 6A–C). This finding suggests that attentional response modulation in the LGN is unlikely to be due solely to corticothalamic feedback from striate cortex, but may be further influenced by additional sources of input (see below). Other possibilities that may explain the differences in magnitude of the modulation between the LGN and V1 include regional disparities underlying the blood oxygenation level-dependent signal or nonlinearities in thalamocortical signal transmission. Further, it is possible that differences in strength of attention effects at different processing stages may reflect the degree to which multiple parallel inputs converge on a given area rather than a feedback mechanism that reverses the processing hierarchy.

Sources of modulatory influences on the LGN

The findings reviewed thus far challenge the classical notion that attention effects are confined to cortical processing. Further, they suggest the need to revise the traditional view of the LGN as a mere gateway to the visual cortex. In fact, due to its afferent input, the LGN may be in an ideal strategic position to serve as an early “gatekeeper” in attentional gain control. In addition to corticothalamic feedback projections from V1, which comprise about 30% of its modulatory input, the

LGN receives another 30% of modulatory inputs from the TRN (Sherman and Guillery, 2002). For several reasons, the TRN has long been implicated in theoretical accounts of selective attention (Crick, 1984). First, all feed-forward projections from the thalamus to the cortex as well as their reverse projections pass through the TRN. Second, the TRN receives not only inputs from the LGN and V1, but also from several extrastriate areas and the pulvinar. Thereby, it may serve as a node where several cortical areas and thalamic nuclei of the visual system can interact to modulate thalamocortical transmission through inhibitory connections to LGN neurons (Guillery et al., 1998). And third, the TRN contains topographically organized representations of the visual field and can thereby modulate thalamocortical or corticothalamic transmission in spatially specific ways. Similarly, all corticofugal projections are organized in topographic order. Other modulatory influences on the LGN stem from the parabrachial nucleus of the brainstem. These cholinergic projections, another 30% of the modulatory input to the LGN, are more diffusely organized (Erisir et al., 1997), which makes a possible role in spatially selective attention more difficult to account for.

In summary, the LGN appears to be the first stage in the processing of visual information that is modulated by attentional top-down signals. Much remains to be learnt about the complex thalamic circuitry that may subserve attentional functions related to the control of neural gain in the LGN.

Neural correlates of visual awareness

Given the modulation of LGN activity by selective attention, we considered the possibility that the LGN may play a functional role in visual awareness. An ideal paradigm to study the neural basis underlying visual awareness is binocular rivalry. In binocular rivalry, the input from the two eyes cannot be fused to a single, coherent percept. Rivalry can be induced experimentally by simultaneously presenting dissimilar stimuli to the two eyes, such as a vertical and a horizontal grating. Rather than being perceived as a merged plaid, the two stimuli compete for perceptual dominance

such that subjects perceive only one stimulus at a time while the other is suppressed from visual awareness (Levelt, 1965; Blake, 1989). Since the subjects' perceptual experiences change over time while the retinal stimulus remains constant, binocular rivalry provides an intriguing paradigm to study the neural basis of visual awareness (Crick and Koch, 1998).

Neural correlates of binocular rivalry in striate and extrastriate cortex

The neural mechanisms underlying binocular rivalry have been much debated. Single-cell physiology studies in monkeys trained to report their perceptual experiences during rivalry have identified neural correlates of binocular rivalry mainly in higher order visual areas (Sheinberg and Logothetis, 1997). Responses of about 90% of neurons in inferior temporal cortex increased when the neuron's preferred stimulus was perceived during rivalry, whereas only about 40% of neurons in areas V4 and MT showed such response enhancement, and even fewer in early visual areas V1 and V2 (Logothetis and Schall, 1989; Leopold and Logothetis, 1996). From these findings, it was concluded that binocular rivalry is mediated by competitive interactions between binocular neural populations representing the two stimuli at multiple stages of visual processing subsequent to the convergence of the input from the two eyes in V1 (pattern competition account). Alternatively, it has been suggested that binocular rivalry reflects competition between monocular channels either at the level of V1 or the LGN and is mediated by mutual inhibition and reciprocal feedback suppressing the input from one eye (Blake, 1989; Lehky and Blake, 1991). This interocular competition account has recently been supported by fMRI studies showing signal fluctuations correlated with subjects' perceptual experiences in area V1 (Polonsky et al., 2000) and more importantly in the monocular V1 neurons representing the blind spot (Tong and Engel, 2001). Given its anatomical organization and afferent projections, the LGN has often been considered as a possible site of suppression in accounts of interocular competition (Lehky, 1988; Lehky and Blake, 1991). However, single-cell

recording studies in the LGN of awake monkeys viewing rivalrous stimuli did not find evidence to support this hypothesis (Lehky and Maunsell, 1996). We recently investigated the functional role of the human LGN in binocular rivalry using fMRI in subjects viewing dichoptically presented contrast-modulated grating stimuli (Wunderlich et al., 2005).

Modulation of LGN activity during binocular rivalry

In the rivalry experiment, superimposed sinusoidal gratings were viewed through red/green filter glasses; a high-contrast, green, horizontal grating was presented to one eye and a low-contrast, red, vertical grating was presented to the other eye. The gratings filled an annular aperture centered at a fixation point and reversed contrast to minimize adaptation. Their orthogonal orientations prevented the two gratings from being fused and induced rivalrous perceptual oscillations between them. Subjects ($N = 5$) maintained fixation and reported which grating was perceived by pressing a button; periods of mixed “piecemeal” percepts of the two stimuli were indicated with a third button. The same subjects also participated in a consecutive scanning session, the physical alternation experiment, in which sequential monocular presentations of the same grating stimuli were used to produce similar perceptual but different physical stimulation than during rivalry. The low- or high-contrast gratings were presented to one eye while a uniform field was presented to the other eye using the identical temporal sequence of stimulus alternations reported by the same subject in the rivalry experiment. During these physical alternations, subjects maintained fixation and pressed buttons to indicate which grating they viewed.

In the rivalry experiment, subjects experienced vigorous perceptual alternations between the horizontal high-contrast and the vertical low-contrast gratings. The perceptual durations were random and distributed according to a gamma-shaped function for both stimuli, as typically found in rivalry studies (Levelt, 1965). In accordance with classical findings (Levelt, 1965), the perceptually more salient high-contrast grating was perceived

significantly longer than the low-contrast grating. In the group of subjects, the high-contrast stimulus was perceived on average for 5.1 ± 0.09 s (mean \pm S.E.M.) compared to 3.1 ± 0.09 s for the low-contrast stimulus ($p \leq 0.001$).

In the LGN and V1, fMRI signals increase monotonically with stimulus contrast. Reliable fMRI signals are typically evoked by stimuli of more than 10% contrast, and signal saturation occurs with stimuli of more than 35% contrast (Boynton et al., 1996; Kastner et al., 2004; Schneider and Kastner, 2005). Therefore, the different fMRI signal amplitudes evoked by low- and high-contrast stimuli can be used as a “neural signature” of the LGN and V1 populations representing these stimuli, as previously shown for physical and rivalrous alternations of contrast-modulated gratings in V1 (Polonsky et al., 2000). In the physical alternation experiment, we expected fMRI signals to increase when the high-contrast gratings were shown monocularly and to decrease when the low-contrast gratings were presented. Further, we reasoned that, if the subjects’ perceptual experiences during rivalry were reflected in fMRI signals, signal fluctuations similar to those obtained during physical alternations should occur in relation to the reported percepts despite the unchanging retinal stimulation.

Functional MRI signals in the LGN and V1 fluctuated while subjects perceived the rivalrous grating stimuli. The signals increased when subjects reported perceiving the high-contrast grating and decreased when they reported perceiving the low-contrast stimulus. To analyze the fMRI time series obtained in the rivalry experiment in relation to subjects’ behavioral responses, an event-related analysis was performed for the LGN and V1 of each subject. Mean fMRI signals were derived by averaging the fMRI time series across all events of a reported switch to the high-contrast grating and, separately, across all events of a reported switch to the low-contrast grating. The events were time-locked to the subjects’ manual responses and spanned a period of 4 s before and 9 s after each response, and the amplitude at the time of the response was subtracted to align the time series to 0. The mean fMRI signals were then averaged across subjects and are presented as group data ($N = 5$).

for the LGN and V1 in Fig. 7. Although both gratings were constantly present during rivalry, the fMRI signals in both LGN and V1 increased shortly after switches to the percept of the high-contrast grating (black lines) and decreased when the percept changed to the low-contrast grating

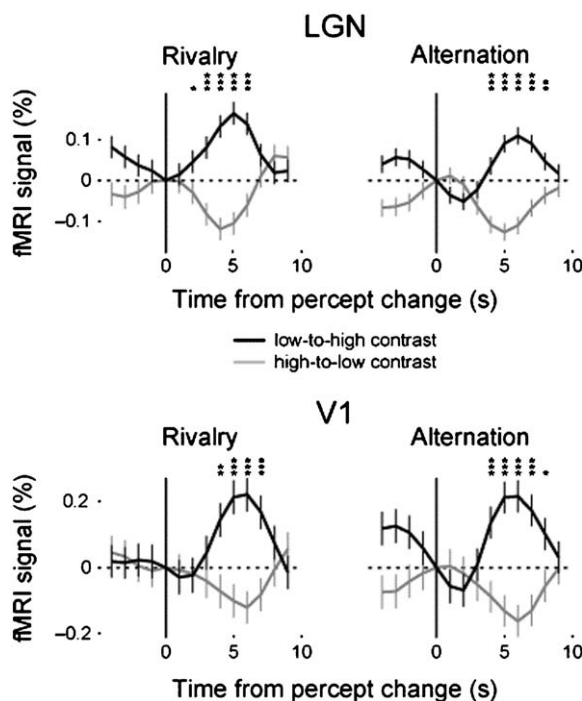


Fig. 7. fMRI signals during binocular rivalry and physical stimulus alternations in the LGN and V1 (group analysis). Data from the LGN and V1 of five subjects were combined across left and right hemispheres. Neural activity was averaged across all occurrences of perceptual switches from the low-contrast to the high-contrast grating (black curve) and across those from the high-contrast to the low-contrast grating (gray curve). The responses were time-locked to each subject's manual response, as indicated by the black vertical line at time point 0, and are shown within a relative time window of -4 to $+9$ s. All events were normalized, so that responses at time point 0 started at a value of 0% signal change. The vertical bar on each curve indicates one standard error of the mean. Asterisks indicate significant differences between data points of the two curves (one-tailed t -test, $*p < 0.05$; $**p < 0.01$; $***p < 0.001$). Left: results from rivalry scans. Right: results from physical stimulus alternation scans. Neural activity increased when subjects perceived the high-contrast stimulus and decreased when they perceived the low-contrast stimulus during rivalry conditions. A similar response pattern was found when subjects viewed physical alternations of the same gratings. (From Wunderlich et al., 2005, with permission.)

(gray lines). Activity related to the percept of the high-contrast grating was significantly different from that related to the percept of the low-contrast grating in the LGN panel (Fig. 7) and in the V1 panel (Fig. 7) (one-tailed t -test, $*p \leq .05$; $**p \leq .01$; $***p \leq .001$ in Fig. 7). A strikingly similar pattern of responses was found in the LGN and V1 in the physical alternation condition (Figs. 7). Importantly, in both the LGN and V1, the magnitude and dispersion of fMRI signals evoked during rivalry were correlated with the duration of the subjects' perceptual experience suggesting that neural activity at the earliest stages of visual processing reflect both the content and duration of the percept and is therefore closely linked to visual awareness during binocular rivalry.

Possible neural mechanisms underlying binocular rivalry in the LGN

Advocates of interocular competition accounts have considered the LGN as a possible site at which the invisible stimulus is suppressed during binocular rivalry. Neurons in the LGN are exclusively monocular, with inputs from each eye segregated into separate layers. These adjacent laminae form an ideal substrate for inhibitory interactions between the two eyes, which would allow the signal from one eye to be selectively suppressed. Binocular interactions, predominantly inhibitory, have been widely reported in both monkey (Rodieck and Dreher, 1979; Marrocco and McClurkin, 1979; Schroeder et al., 1990) and cat LGN (Singer, 1970; Sanderson et al., 1971; Schmielau and Singer, 1977; Pape and Eysel, 1986; Varela and Singer, 1987; Sengpiel et al., 1995) and might provide a neural substrate in producing rivalry. These inhibitory interactions may be mediated by several anatomical pathways including interneurons extending between LGN layers, corticogeniculate feedback from striate cortex, or modulatory input from the TRN, as discussed above. One possibility is that feedback from binocular neurons in layer 6 of V1 (Lund and Boothe, 1975; Livingstone and Hubel, 1987) to monocular LGN layers could provide a descending control signal indicating whether stimuli are binocularly fused and regulating the strength of the inhibitory

network (Lehky, 1988; Lehky and Blake, 1991). The importance of feedback from V1 in controlling the observed LGN activity cannot be overstressed. With our current temporal resolution, it is not possible to determine whether the LGN is controlling V1 activity or merely inherits the binocular resolution that might take place in a higher cortical area. Another possibility is that the TRN exerts additional control in modulating thalamocortical transmission through inhibitory connections to LGN neurons. It should be noted that these possibilities are not mutually exclusive. Taken together, based on its anatomy and the organization of its retinal and cortical feedback input, the LGN appears to be in an ideal position to play an important functional role in binocular rivalry, as suggested by our findings.

We conclude from our studies that the LGN appears to be the first stage in the processing of visual information at which neural correlates of visual awareness during binocular rivalry can be found. Our findings further suggest the need to revise the traditional view of the LGN as a mere gateway to the visual cortex. The LGN may, in fact, serve among a network of widely distributed cortical and subcortical brain systems as an early gatekeeper of visual awareness.

Conclusions

The studies reviewed in this chapter shed light on the retinotopic organization, basic response properties, and functional roles in perception and cognition of the human LGN. The LGN has been traditionally viewed as a relay nucleus, which conveys neural signals faithfully from the retina to primary visual cortex. Our studies have begun to cast doubt on this notion by demonstrating modulation of neural responses by cognitive operations such as selective attention and by perceptual content related to binocular rivalry. For example, the attentional response modulation in the LGN was on the order of that observed in extrastriate cortical areas, which have thus far been assumed to be the major sites of response modulation. We conclude from our studies thus far that the LGN plays an important role as an early gatekeeper in

controlling attentional response gain and visual awareness. Neuroimaging of the human thalamus provides an important opportunity to revisit some of the classical notions on thalamic function that were derived mainly from studies in anesthetized animals and to ultimately define the functional role of thalamic nuclei such as the LGN in cognition and perception.

Acknowledgments

We thank K. Weiner for help with manuscript preparation. The research reviewed in this chapter was supported by the National Institute of Mental Health (RO1 MH-64043, P50 MH-62196, T32 MH-065214) and the Whitehall Foundation.

References

- Albrecht, D. and Hamilton, D. (1982) Striate cortex of monkey and cat: contrast response function. *J. Neurophysiol.*, 48: 217–237.
- Andrews, T.J., Halpern, S.D. and Purves, D. (1997) Correlated size variations in human visual cortex, lateral geniculate nucleus, and optic tract. *J. Neurosci.*, 17: 2859–2868.
- Avidan, G., Harel, M., Hendler, T., Ben Bashat, D., Zohary, E. and Malach, R. (2002) Contrast sensitivity in human visual areas and its relationship to object recognition. *J. Neurophysiol.*, 87: 3102–3216.
- Azzopardi, P. and Cowey, A. (1996) The overrepresentation of the fovea and adjacent retina in the striate cortex and dorsal lateral geniculate nucleus of the macaque monkey. *Neuroscience*, 72: 627–639.
- Blake, R. (1989) A neural theory of binocular rivalry. *Psychol. Rev.*, 96: 145–167.
- Boynton, G.M., Engel, S.A., Glover, G.H. and Heeger, D.J. (1996) Linear systems analysis of functional magnetic resonance imaging in human V1. *J. Neurosci.*, 16: 4207–4221.
- Brouwer, B. and Zeemann, W.B.C. (1926) The projection of the retina in the primary optic neuron in monkeys. *Brain*, 49: 1–35.
- Carandini, M. and Ferster, D. (1997) A tonic hyperpolarization underlying contrast adaptation in cat visual cortex. *Science*, 276: 949–952.
- Chelazzi, L., Duncan, J., Miller, E.K. and Desimone, R. (1998) Responses of neurons in inferior temporal cortex during memory-guided visual search. *J. Neurophysiol.*, 80: 2918–2940.
- Chen, W., Zhu, X., Thulborn, K.R. and Ugurbil, K. (1999) Retinotopic mapping of lateral geniculate nucleus in humans using functional magnetic resonance imaging. *Proc. Natl. Acad. Sci. USA*, 96: 2430–2434.

- Cheng, K., Hasegawa, T., Saleem, K.S. and Tanaka, K. (1994) Comparison of neuronal selectivity for stimulus speed, length, and contrast in the prestriate cortical areas V4 and MT of the macaque monkey. *J. Neurophysiol.*, 71: 2269–2280.
- Clark, W.E.L.G. and Penman, G.G. (1934) The projection of the retina in the lateral geniculate body. *Proc. R. Soc. Lond. B Biol. Sci.*, 114: 291–313.
- Connolly, M. and Van Essen, D. (1984) The representation of the visual field in parvocellular and magnocellular layers of the lateral geniculate nucleus in the macaque monkey. *J. Comp. Neurol.*, 226: 544–564.
- Cook, E.P. and Maunsell, J.H. (2002) Attentional modulation of behavioral performance and neuronal responses in middle temporal and ventral intraparietal areas of macaque monkey. *J. Neurosci.*, 22: 1994–2004.
- Corbetta, M., Miezin, F.M., Dobmeyer, S., Shulman, G.L. and Petersen, S.E. (1990) Attentional modulation of neural processing of shape, color, and velocity in humans. *Science*, 248: 1556–1559.
- Creutzfeldt, O., Crook, J.M., Kastner, S., Li, C.Y. and Pei, X. (1991) The neurophysiological correlates of colour and brightness contrast in lateral geniculate neurons. *Exp. Brain Res.*, 87: 3–21.
- Creutzfeldt, O.D., Lee, B.B. and Elepfandt, A. (1979) A quantitative study of chromatic organisation and receptive fields of cells in the lateral geniculate body of the rhesus monkey. *Exp. Brain Res.*, 35: 527–545.
- Crick, F. (1984) Function of the thalamic reticular complex: the searchlight hypothesis. *Proc. Natl. Acad. Sci. USA*, 81: 4586–4590.
- Crick, F. and Koch, C. (1998) Consciousness and neuroscience. *Cereb. Cortex*, 8: 97–107.
- Daniel, P.M. and Whitteridge, D. (1961) The representation of the visual field on the cerebral cortex in monkeys. *J. Physiol.*, 159: 203–221.
- Dean, A. (1981) The relationship between response amplitude and contrast for cat striate Cortical neurons. *J. Physiol.*, 318: 413–427.
- Derrington, A.M. and Lennie, P. (1984) Spatial and temporal contrast sensitivities of neurones in lateral geniculate nucleus of macaque. *J. Physiol.*, 357: 219–240.
- Dreher, B., Fukada, Y. and Rodieck, R.W. (1976) Identification, classification and anatomical segregation of cells with X-like and Y-like properties in the lateral geniculate nucleus of old-world primates. *J. Physiol.*, 258: 433–452.
- Enroth-Cugell, C., Robson, J.G., Schweitzer-Tong, D.E. and Watson, A.B. (1983) Interactions in cat retinal ganglion cells showing linear spatial summation. *J. Physiol.*, 341: 279–307.
- Erisir, A., Van Horn, S.C. and Sherman, S.M. (1997) Relative numbers of cortical and brainstem inputs to the lateral geniculate nucleus. *Proc. Natl. Acad. Sci. USA*, 94: 1517–1520.
- Erwin, E., Baker, F.H., Busen, W.F. and Malpeli, J.G. (1999) Relationship between laminar topology and retinotopy in the rhesus lateral geniculate nucleus: results from a functional atlas. *J. Comp. Neurol.*, 407: 92–102.
- Foster, K.H., Gaska, J.P., Nagler, M. and Pollen, D.A. (1985) Spatial and temporal frequency selectivity of neurons in visual cortical areas V1 and V2 of the macaque monkey. *J. Neurophysiol.*, 365: 331–363.
- Gegenfurtner, K.R., Kiper, D.C. and Levitt, J.B. (1997) Functional properties of neurons in macaque area V3. *J. Neurophysiol.*, 77: 1906–1923.
- Guillery, R.W., Feig, S.L. and Lozsadi, D.A. (1998) Paying attention to the thalamic reticular nucleus. *Trends Neurosci.*, 21: 28–32.
- Guillery, R.W. and Sherman, S.M. (2002) Thalamic relay functions and their role in corticocortical communication: generalizations from the visual system. *Neuron*, 33: 163–175.
- Hickey, T.L. and Guillery, R.W. (1979) Variability of laminar patterns in the human lateral geniculate nucleus. *J. Comp. Neurol.*, 183: 221–246.
- Hicks, T.P., Lee, B.B. and Vidyasagar, T.R. (1983) The response of cells in macaque lateral geniculate nucleus to sinusoidal gratings. *J. Physiol.*, 337: 183–200.
- Jones, E.G. (1985) *The Thalamus*. Plenum Press, New York.
- Juba, A. and Szatmári, A. (1937) Ueber seltene hirnanatomische Befunde in Fällen von einseitiger peripherer Blindheit. *Klin. Monatsbl. Augenheilkd.*, 99: 173–188.
- Kaas, J.H., Guillery, W.R. and Allman, J.M. (1972) Some principles of organization in the dorsal lateral geniculate nucleus. *Brain Behav. Evol.*, 6: 253–299.
- Kastner, S. (2004a) Towards a neural basis of human visual attention: Evidence from functional brain imaging. In: Kanwisher, N. and Duncan, J. (Eds.), *Attention & Performance XX*. Oxford University Press, Oxford, pp. 299–318.
- Kastner, S. (2004b) Attentional response modulation in the human visual system. In: Posner, M. (Ed.), *Attention*. Guilford Press, New York, pp. 144–156.
- Kastner, S., Crook, J.M., Pei, X. and Creutzfeldt, O. (1992) Neurophysiological studies of colour induction on white surfaces. *Eur. J. Neurosci.*, 4: 1079–1086.
- Kastner, S., De Weerd, P., Desimone, R. and Ungerleider, L.G. (1998) Mechanisms of directed attention in the human extrastriate cortex as revealed by functional MRI. *Science*, 282: 108–111.
- Kastner, S., De Weerd, P., Pinsk, M.A., Elizondo, M.I., Desimone, R. and Ungerleider, L.G. (2001) Modulation of sensory suppression: implications for receptive field sizes in the human visual cortex. *J. Neurophysiol.*, 86: 1398–1411.
- Kastner, S., O'Connor, D.H., Fukui, M.M., Fehd, H.M., Herwig, U. and Pinsk, M.A. (2004) Functional imaging of the human lateral geniculate nucleus and pulvinar. *J. Neurophysiol.*, 91: 438–448.
- Kastner, S., Pinsk, M.A., De Weerd, P., Desimone, R. and Ungerleider, L.G. (1999) Increased activity in human visual cortex during directed attention in the absence of visual stimulation. *Neuron*, 22: 751–761.
- Kelly, D.H. (1979) Motion and vision. II. Stabilized spatio-temporal threshold surface. *J. Opt. Soc. Am.*, 69: 1340–1349.
- Kupfer, C. (1962) The projection of the macula in the lateral geniculate nucleus of man. *Am. J. Ophthalmol.*, 54: 597–609.

- Lee, B.B., Martin, P.R. and Valberg, A. (1989) Sensitivity of macaque retinal ganglion cells to chromatic and luminance flicker. *J. Physiol.*, 414: 223–243.
- Lehky, S.R. (1988) An astable multivibrator model of binocular rivalry. *Perception*, 17: 215–228.
- Lehky, S.R. and Blake, R. (1991) Organization of binocular pathways: Modeling and data related to rivalry. *Neural Comput.*, 3: 44–53.
- Lehky, S.R. and Maunsell, J.H. (1996) No binocular rivalry in the LGN of the alert macaque monkey. *Vision Res.*, 36: 1225–1234.
- Lennie, P., Krauskopf, J. and Sclar, G. (1990) Chromatic mechanisms in striate cortex of macaque. *J. Neurosci.*, 10: 649–669.
- Leopold, D.A. and Logothetis, N.A. (1996) Activity changes in early visual cortex reflect monkeys' percepts during binocular rivalry. *Nature*, 379: 549–553.
- Levelt, W.J. (1965) Binocular brightness averaging and contour information. *Br. J. Psychol.*, 56: 1–13.
- Levitt, J.B., Kiper, D.C. and Movshon, J.A. (1994) Receptive fields and functional architecture of macaque V2. *J. Neurophysiol.*, 71: 2517–2542.
- Livingstone, M.S. and Hubel, D.H. (1987) Psychophysical evidence for separate channels for the perception of form, color, movement, and depth. *J. Neurosci.*, 7: 3416–3468.
- Logothetis, N., Pauls, J., Augath, M., Trinath, T. and Oeltermann, A. (2001) Neurophysiological investigation of the basis of the fMRI signal. *Nature*, 412: 150–157.
- Logothetis, N.K. and Schall, J.D. (1989) Neuronal correlates of subjective visual perception. *Science*, 245: 761–763.
- Luck, S.J., Chelazzi, L., Hillyard, S.A. and Desimone, R. (1997) Neural mechanisms of spatial selective attention in areas V1, V2, and V4 of macaque visual cortex. *J. Neurophysiol.*, 77: 24–42.
- Lund, J.S. and Boothe, R.G. (1975) Interlaminar connections and pyramidal neuron organization in the visual cortex, area 17, of the Macaque monkey. *J. Comp. Neurol.*, 159: 305–334.
- Malpeli, J.G. and Baker, F.H. (1975) The representation of the visual field in the lateral geniculate nucleus of *Macaca mulatta*. *J. Comp. Neurol.*, 161: 569–594.
- Malpeli, J.G., Lee, D. and Baker, F.H. (1996) Laminar and retinotopic organization of the macaque lateral geniculate nucleus: magnocellular and parvocellular magnification functions. *J. Comp. Neurol.*, 375: 363–377.
- Marrocco, R.T. and McClurkin, J.W. (1979) Binocular interaction in the lateral geniculate nucleus of the monkey. *Brain Res.*, 168: 633–637.
- Martinez, A., Anillo-Vento, L., Sereno, M.I., Frank, L.R., Buxton, R.B., Dubowitz, D.J., Wong, E.C., Hinrichs, H., Heinze, H.J. and Hillyard, S.A. (1999) Involvement of striate and extrastriate visual cortical areas in spatial attention. *Nat. Neurosci.*, 2: 364–369.
- Mehta, A.D., Ulbert, I. and Schroeder, C.E. (2000) Intermodal selective attention in monkeys. I: distribution and timing of effects across visual areas. *Cereb. Cortex*, 10: 343–358.
- Merigan, W.H. and Maunsell, J.H. (1990) Macaque vision after magnocellular lateral geniculate lesions. *Visual Neurosci.*, 5: 347–352.
- Merigan, W.H. and Maunsell, J.H. (1993) How parallel are the primate visual pathways? *Annu. Rev. Neurosci.*, 16: 369–402.
- Moran, J. and Desimone, R. (1985) Selective attention gates visual processing in the extrastriate cortex. *Science*, 229: 782–784.
- Myerson, J., Manis, P.B., Miezin, F.M. and Allman, J.M. (1977) Magnification in striate cortex and retinal ganglion cell layer of owl monkey: a quantitative comparison. *Science*, 198: 855–857.
- O'Connor, D.H., Fukui, M.M., Pinsk, M.A. and Kastner, S. (2002) Attention modulates responses in the human lateral geniculate nucleus. *Nat. Neurosci.*, 5: 1203–1209.
- Pape, H.C. and Eysel, U.T. (1986) Binocular interactions in the lateral geniculate nucleus of the cat: GABAergic inhibition reduced by dominant afferent activity. *Exp. Brain Res.*, 61: 265–271.
- Perry, V.H. and Cowey, A. (1985) The ganglion cell and cone distributions in the monkey's retina: implications for central magnification factors. *Vision Res.*, 25: 1795–1810.
- Perry, V.H., Oehler, R. and Cowey, A. (1984) Retinal ganglion cells that project to the dorsal lateral geniculate nucleus in the macaque monkey. *Neuroscience*, 12: 1101–1123.
- Polonsky, A., Blake, R., Braun, J. and Heeger, D.J. (2000) Neuronal activity in human primary visual cortex correlates with perception during binocular rivalry. *Nat. Neurosci.*, 3: 1153–1159.
- Polyak, S. (1953) Santiago Ramon y Cajal and his investigation of the nervous system. *J. Comp. Neurol.*, 98: 3–8.
- Przybylski, A.W., Gaska, J.P., Foote, W. and Pollen, D.A. (2000) Striate cortex increases contrast gain of macaque LGN neurons. *Visual Neurosci.*, 17: 485–494.
- Rees, G., Frith, C.D. and Lavie, N. (1997) Modulating irrelevant motion perception by varying attentional load in an unrelated task. *Science*, 278: 1616–1619.
- Rodiek, R.W. and Dreher, B. (1979) Visual suppression from nondominant eye in the lateral geniculate nucleus: a comparison of cat and monkey. *Exp. Brain Res.*, 35: 465–477.
- Roelfsema, P.R., Lamme, V.A. and Spekreijse, H. (1998) Object-based attention in the primary visual cortex of the macaque monkey. *Nature*, 395: 376–381.
- Rönne, H. (1910) Pathologisch-anatomische Untersuchungen über alkoholoische Intoxikationsamblyopie. *Arch. Ophthalmol.*, 77: 1–95.
- Sanderson, K.J., Bishop, P.O. and Darian-Smith, I. (1971) The properties of the binocular receptive fields of lateral geniculate neurons. *Exp. Brain Res.*, 13: 178–207.
- Schein, S.J. and de Monasterio, F.M. (1987) Mapping of retinal and geniculate neurons onto striate cortex of macaque. *J. Neurosci.*, 7: 996–1009.
- Schmielau, F. and Singer, W. (1977) The role of visual cortex for binocular interactions in the cat lateral geniculate nucleus. *Brain Res.*, 120: 354–361.
- Schneider, K.A. and Kastner, S. (2005) Visual responses of the human superior colliculus: a high-resolution fMRI study. *J. Neurophys.*, 94: 2491–2503.

- Schneider, K., Richter, M. and Kastner, S. (2004) Retinotopic organization and functional subdivisions of the human lateral geniculate nucleus: A high-resolution fMRI study. *J. Neurosci.*, 24: 8975–8985.
- Schroeder, C.E., Tenke, C.E., Arezzo, J.C. and Vaughan Jr., H.G. (1990) Binocularity in The lateral geniculate nucleus of the alert macaque. *Brain Res.*, 521: 303–310.
- Sclar, G., Maunsell, J.H. and Lennie, P. (1990) Coding of image contrast in central visual pathways of the macaque monkey. *Vision Res.*, 30: 1–10.
- Sengpiel, F., Blakemore, C. and Harrad, R. (1995) Interocular suppression in the primary visual cortex: a possible neural basis of binocular rivalry. *Vision Res.*, 35: 179–195.
- Sereno, M.I., Dale, A.M., Reppas, J.B., Kwong, K.K., Belliveau, J.W., Brady, T.J., Rosen, B.R. and Tootell, R.B. (1995) Borders of multiple visual areas in humans revealed by functional magnetic resonance imaging. *Science*, 268: 889–893.
- Shapley, R., Kaplan, E. and Soodak, R. (1981) Spatial summation and contrast sensitivity of X and Y cells in the lateral geniculate nucleus of the macaque. *Nature*, 292: 543–545.
- Sheinberg, D.L. and Logothetis, N.K. (1997) The role of temporal cortical areas in perceptual organization. *Proc. Natl. Acad. Sci. USA*, 94: 3408–3413.
- Sherman, S.M. and Guillery, R.W. (2001) Exploring the Thalamus. Academic Press, San Diego.
- Sherman, S.M. and Guillery, R.W. (2002) The role of the thalamus in the flow of information to the cortex. *Philos. Trans. R. Soc. Lond. Ser. B: Biol. Sci.*, 357: 1695–1708.
- Singer, W. (1970) Inhibitory binocular interaction in the lateral geniculate body of the cat. *Brain Res.*, 18: 165–170.
- Spillman, L. (1971) Foveal perceptive fields in the human visual system measured with simultaneous contrast in grids and bars. *Pflügers Arch. Ges. Physiol.*, 326: 281–299.
- Spillman, L. (1994) The Hermann grid illusion: a tool for studying human perceptive field organization. *Perception*, 23: 691–708.
- Talbot, S.A. and Marshall, W.H. (1941) Physiological studies on neuronal mechanisms of visual localization and discrimination. *Am. J. Ophthalmol.*, 24: 1255–1263.
- Tolhurst, D., Movshon, J. and Thompson, I. (1981) The dependence of response amplitude and variance of cat visual cortical neurons on stimulus contrast. *Exp. Brain Res.*, 41: 414–419.
- Tong, F. and Engel, S.A. (2001) Interocular rivalry revealed in the human cortical blind-spot representation. *Nature*, 411: 195–199.
- Tootell, R.B.H., Reppas, J.B., Kwong, K.K., Malach, R., Born, R.T., Brady, T.J., Rosen, B.R. and Belliveau, J.W. (1995) Functional analysis of human MT and related visual cortical areas using magnetic resonance imaging. *J. Neurosci.*, 15: 3215–3261.
- Van Essen, D.C., Newsome, W.T. and Maunsell, J.H. (1984) The visual field representation in striate cortex of the macaque monkey: asymmetries, anisotropies, and individual variability. *Vision Res.*, 24: 429–448.
- Varela, F.J. and Singer, W. (1987) Neuronal dynamics in the visual corticothalamic pathway revealed through binocular rivalry. *Exp. Brain Res.*, 66: 10–20.
- Wässle, H., Grunert, U., Rohrenbeck, J. and Boycott, B.B. (1989) Cortical magnification factor and the ganglion cell density of the primate retina. *Nature*, 341: 643–646.
- Wässle, H., Grunert, U., Rohrenbeck, J. and Boycott, B.B. (1990) Retinal ganglion cell density and cortical magnification factor in the primate. *Vision Res.*, 30: 1897–1911.
- Webb, S.V. and Kaas, J.H. (1976) The sizes and distribution of ganglion cells in the retina of the owl monkey *Aotus trivirgatus*. *Vision Res.*, 16: 1247–1254.
- Wiesel, T.N. and Hubel, D.H. (1966) Spatial and chromatic interactions in the lateral geniculate body of the rhesus monkey. *J. Neurophysiol.*, 29: 1115–1156.
- Wunderlich, K., Schneider, K.A. and Kastner, S. (2005) Neural correlates of binocular rivalry in the human lateral geniculate nucleus. *Nat. Neurosci.*, 8: 1595–1602.