Visual response latencies of magnocellular and parvocellular LGN neurons in macaque monkeys

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Abstract

Signals relayed through the magnocellular layers of the LGN travel on axons with faster conduction speeds than those relayed through the parvocellular layers. As a result, magnocellular signals might reach cerebral cortex appreciably before parvocellular signals. The relative speed of these two channels cannot be accurately predicted based solely on axon conduction speeds, however. Other factors, such as different degrees of convergence in the magnocellular and parvocellular channels and the retinal circuits that feed them, can affect the time it takes for magnocellular and parvocellular signals to activate cortical neurons. We have investigated the relative timing of visual responses mediated by the magnocellular and parvocellular channels. We recorded individually from 78 magnocellular and 80 parvocellular neurons in the LGN of two anesthetized monkeys. Visual response latencies were measured for small spots of light of various intensities. Over a wide range of stimulus intensities the fastest magnocellular response latencies preceded the fastest parvocellular response latencies by about 10 ms. Because parvocellular neurons are far more numerous than magnocellular neurons, convergence in cortex could reduce the magnocellular advantage by allowing parvocellular signals to generate detectable responses sooner than expected based on the responses of individual parvocellular neurons. An analysis based on a simple model using neurophysiological data collected from the LGN shows that convergence in cortex could eliminate or reverse the magnocellular advantage. This observation calls into question inferences that have been made about ordinal relationships of neurons based on timing of responses.

Keywords: Latency, Single unit, LGN, Magnocellular, Parvocellular, Macaque

Introduction

The magnocellular, parvocellular, and koniocellular (interlaminar) neurons in the lateral geniculate nucleus (LGN) differ markedly in their anatomy and physiology (see Kaplan et al., 1990; Valberg & Lee, 1992). One prominent difference is the speed with which their axons conduct action potentials. The fastest conducting axons are those of magnocellular LGN neurons, followed by the parvocellular and then koniocellular neurons. The conduction times for magnocellular and parvocellular pathways have received far more attention than those of the koniocellular pathway, and we focus on those two pathways here.

Several studies have attributed psychophysical or neurophysiological effects to differences in the relative speed of the magnocellular and parvocellular pathways. For example, neurophysiological studies have suggested that differences in the speed of the magnocellular and parvocellular pathways contribute to differences in activation times between cortical areas (Maunsell, 1987; Petersen et al., 1988) or between different compartments within an area (Munk et al., 1995). It has been proposed that differences between the pathways could be used for temporal interpolation and prediction of the trajectories of moving stimuli (Barlow, 1981). Delays between the magnocellular and parvocellular channels have also been put forth to explain differences in behavioral reaction times (Breitmeyer, 1975; Todd & Van Gelder, 1979) and backward masking (Breitmeyer & Ganz, 1976).

Differences in axonal conduction speeds in the retina, optic nerve, and optic radiation (Dreher et al., 1976; Schiller & Malpeli, 1977, 1978; Kaplan & Shapley, 1982) should cause parvocellular signals to take about 3 ms longer than magnocellular signals to travel to the LGN and about 5 ms longer to reach the cerebral cortex. However, several factors other than axonal conduction speeds may influence how quickly the different channels activate cortical neurons. The magnocellular and parvocellular channels are fed by different retinal circuits. Greater convergence in the circuits leading to the magnocellular channel could produce responses that start earlier. This difference in processing time would add to the difference arising from axonal conduction speed, and might be the larger of the two (Troy & Lennie, 1987; Nowak & Bullier, 1997). Differences in the response latencies between magnocellular and parvocellular neurons could also vary with stimulus intensity. Response latencies are typically shorter for stimuli that generate stronger

responses. The differences in the sensitivities of magnocellular and parvocellular neurons will cause some stimuli to be more or less effective in driving one pathway, affecting the relative timing of their responses.

Although the differences in axonal conduction speed between the magnocellular and parvocellular pathways have been established for decades, few studies have provided information concerning other factors that contribute to visual response latencies. These other factors might contribute to discrepancies in reported response latencies. For example, some studies have reported measurements from the LGN or the LGN-recipient layers of V1 that suggest visual response latencies of magnocellular and parvocellular neurons in the LGN differ by less than 10 ms (Marrocco, 1976; Schroeder et al., 1989; Maunsell & Gibson, 1992). On the other hand, a recent study of visual response latencies in V1 has suggested that this difference might be larger, about 20 ms (Nowak et al., 1995).

The current study addresses how the temporal properties of these two major visual pathways contribute to the timing of neurophysiological signals. We have recorded the responses of populations of isolated magnocellular and parvocellular LGN neurons to compare directly their visual response latencies across a range of visual stimuli.

Methods

Physiological preparation

Recordings were made from individual LGN neurons in two anesthetized adult male *Macaca mulatta* (4-year-old, 4 kg; and 7-year-old, 14 kg) using conventional extracellular recording techniques. Each animal was premedicated with atropine (50 μg/kg, i.m.) and then sedated with ketamine (15 mg/kg, i.m.) and diazepam (0.5 mg/kg, i.m.). The animal was intubated and a catheter was inserted in a leg vein. Surgical anesthesia was induced with sufentanil (4–6 μg/kg/h). The head was held in a stereotaxic that allowed a wide field of view. The scalp was incised and a craniotomy and duratomy were made dorsal to the left LGN. An electrode guide tube on a micropositioner was inserted until its tip was about 6 mm above the LGN. Skeletal muscles were paralyzed (vecuronium bromide 100 μg/kg/h, i.v.). Anesthesia was maintained during the experiment using an infusion of sufentanil determined to be adequate for anesthesia during the initial surgery. ECG, heart rate, body temperature, and expired CO_2 were monitored continuously. Ophthalmic atropine was applied to dilate the pupils and relax accommodation. Gas-permeable contact lenses protected the corneas and focused the eyes on a tangent screen 115 cm away. A reversing ophthalmoscope was used to plot each eye's line of sight on the screen at regular intervals throughout the experiments, which lasted about 75 h. Extracellular recordings were made using glass insulated Pt/Ir microelectrodes ($\sim$1 MΩ at 1 kHz). Signals were amplified, filtered, and monitored on an oscilloscope and speaker. Signals from individual units were isolated based on waveform and converted to pulses with a window discriminator.

Stimulus presentation and data analysis

Stimulus presentation and data collection were under computer control. The stimuli were small spots (0.25-deg radius) presented for 250 ms with a period of 1000 ms. The spots were generated on a video monitor with a 120-Hz frame rate. ON-cells were stimulated with bright spots presented on a dark background (0.2 cd/

m^2), and OFF-cells were stimulated with dark spots presented on a bright background (43 cd/m^2). We did not optimize the color or size of the spot for individual cells because we wanted to compare how different cells responded to a given stimulus. The monitor was calibrated to produce linear steps of luminance, and different luminance levels were presented in randomly interleaved sequences.

The time of each action potential was recorded with a precision of 1 ms. The time base for action potentials was synchronized with the vertical retrace of the video display, and all neuronal response latencies were compensated for the delay between the vertical retrace and the time that the raster scan reached the center of a unit's receptive field on the face of the display. The fidelity of the time-stamping and methods of analysis was confirmed by recording and analyzing signals taken from a photodiode placed on the face of the video display.

Many different methods have been used for measuring the response latency of visual neurons. While various methods generally give different absolute values, most lead to similar conclusions about the relative timing of responses (Lennie, 1981). The primary analysis used here is that described in Maunsell and Gibson (1992), which we refer to as onset latency. A peristimulus time histogram with 1-ms bins was compiled from the responses to 100 stimulus presentations. Baseline activity was then estimated by examining 200 bins before stimulus onset. The onset of response was assigned to the first bin that contained a number of spikes that exceeded a probability of 0.01 (assuming a Poisson distribution of spike counts), and was immediately followed by one bin that exceeded a probability of 0.01 and then one that exceeded 0.05.

As a check on the generality of some results, two other measures of latency were also computed. One, peak latency, was the latency to the peak of the neuronal response in the peristimulus time histogram that had 1-ms bins and included responses from 100 stimulus presentations. The other determined a latency to half-peak response. This entailed converting the spike train from each stimulus presentation into a spike density function and finding the first time that the function reached half its peak value. The latency of the half-peak time for a unit is the average of this value across all presentations of a particular stimulus. This method is described by Lu and colleagues (1995), and is a variation on a method introduced by Levick (1973).

Results

We collected data from 158 isolated LGN neurons in two monkeys. Efforts were made to test the same number of magnocellular and parvocellular neurons (78 and 80 units, respectively). The range of receptive-field eccentricities was 4 deg to 22 deg for parvocellular neurons (median 9 deg), and 5 deg to 35 deg for magnocellular neurons (median 9 deg). It was straightforward to assign recording sites to specific LGN layers during the recording sessions based on alternations in the driving eye, temporal aspects of the response (Schiller & Malpeli, 1978), and the characteristic physical arrangement of the layers. Each assignment was confirmed in detailed histological reconstructions. On some penetrations electrolytic lesions were placed at the transition between parvocellular and magnocellular responses. These were found in the expected location on histological sections. One such lesion is marked in Fig. 1.

Magnocellular and parvocellular latencies

For latency measurements to be reliable, responses must have a clear onset. Every unit isolated had an obvious visual response,
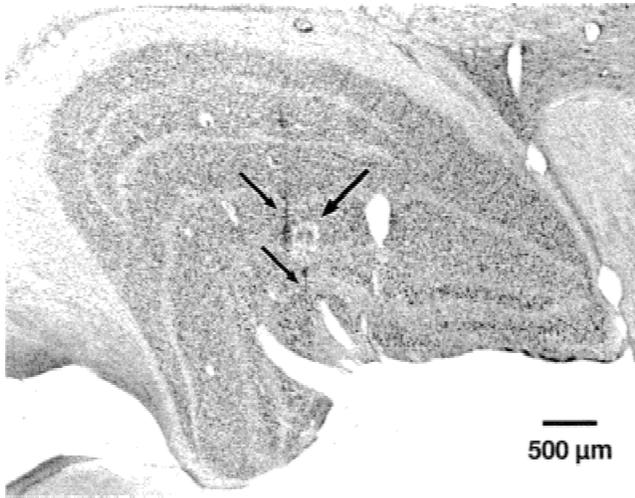
Fig. 1. Nissl-stained coronal section through the LGN of Animal 1. The large arrow points to a small electrolytic lesion (10 μA for 10 s) made during recording near the transition from parvocellular to magnocellular responses. As expected, such lesions were found close to the border between layers 2 and 3. Smaller arrows mark portions of two electrode tracks, including the one associated with the lesion. Dorsal is up and medial is to the right.

and for most the response rose rapidly from baseline. The overall responsiveness of magnocellular and parvocellular neurons to high luminance stimuli is shown in the population response histograms in Figs. 2A and 2B. These were constructed by averaging responses from magnocellular and parvocellular neurons separately. The average peak response was over 100 spikes/s for cells in both populations. As expected, the responses of magnocellular neurons were more transient.

Because the histograms in Figs. 2A and 2B average together the activity of neurons that have different response latencies, they do not necessarily provide a good representation of a typical response profile for individual neurons. The plots in Figs. 2C and 2D are population averages constructed by aligning the response onset for each individual histogram at zero before averaging. These plots show the average rise time and transience of individual magnocellular and parvocellular neurons. As expected, these average response profiles have a slightly faster rise time, higher peak response, and are more transient than the population averages made without aligning latencies.

We selected two subjects that differed in age and weight. In both animals, magnocellular neurons tended to have shorter latencies than parvocellular neurons. The distributions of visual response latencies for magnocellular and parvocellular neurons from both animals are plotted in Fig. 3. We did not combine the distri-
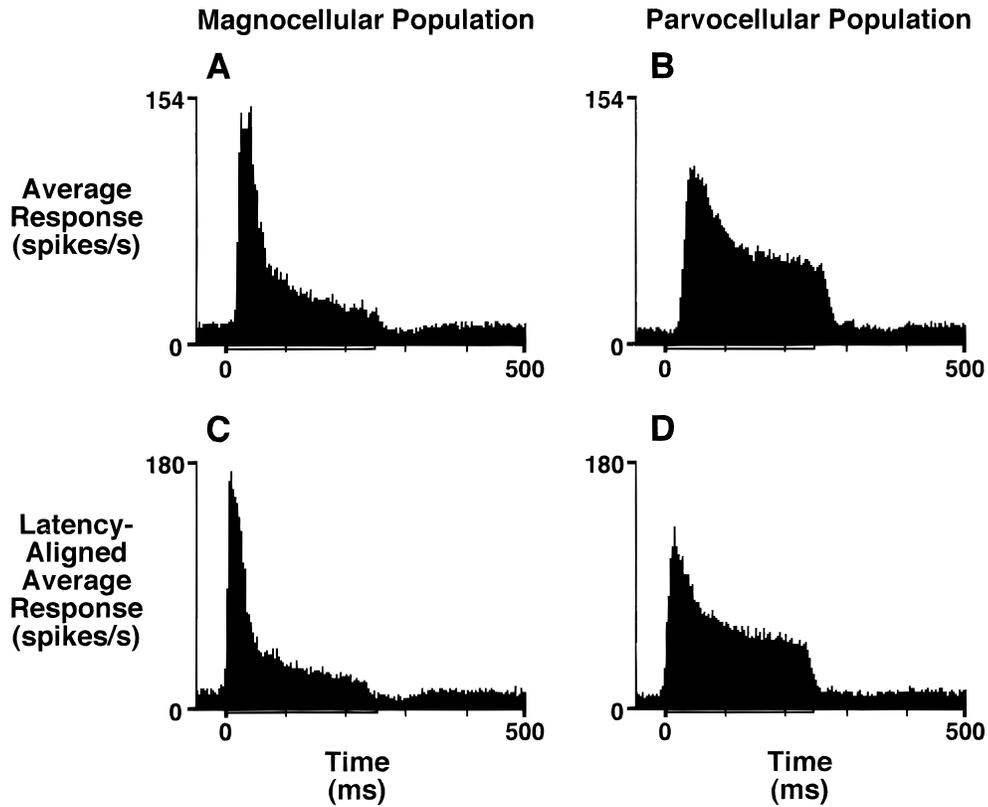

Fig. 2. Average response histograms. Responses from individual units (78 magnocellular and 80 parvocellular) were combined. A,B: Population response histograms were computed for magnocellular and parvocellular responses by averaging the responses of each neuron to a stimulus that was 28 cd/m^2 brighter (ON cells) or dimmer (OFF cells) than background. Each neuron's response was based on 100 stimulus repetitions. Neurons in both subdivisions responded strongly, with magnocellular responses being more transient. C,D: Average response profiles. These profiles were computed by shifting each unit's response histogram so that its onset latency was at zero, and then averaging the individual histograms. This compensates for the different response latencies among the neurons, which round the population response histograms.
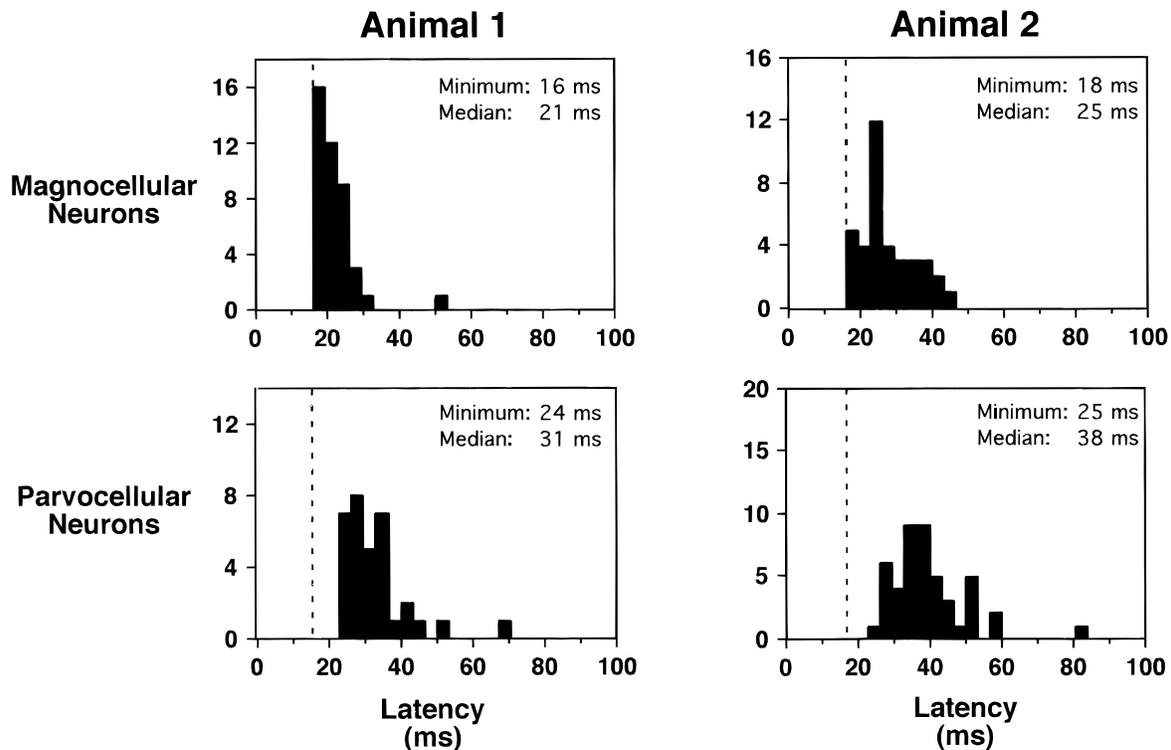
Fig. 3. Distributions of response latencies for both animals. The latency for flashed 28 cd/m^2 stimuli is plotted separately for magnocellular and parvocellular neurons. Parvocellular latencies were longer, and latencies in the larger animal (Animal 2) were slower overall.

butions of individual neurons' latencies from the animals because there were significant differences in the absolute latencies. Although there was little difference between the shortest response latencies between the two animals (1 to 2 ms), median latencies in the larger subject (Animal 2) were about 5 ms longer than those of the smaller animal. This difference was highly significant (Mann-Whitney test, $P < 0.001$ for each LGN population). An earlier study of visual response latencies in macaque V1 found overall latency differences of up to 10 ms between individuals, and suggested that latency may increase with size and age (Maunsell & Gibson, 1992).

The earliest parvocellular responses lagged the earliest magnocellular responses by 7 and 8 ms in the two subjects. The differences between the median magnocellular and parvocellular latencies were larger (10 and 13 ms). Percentile plots of the same data (Fig. 4) show that for most percentiles the difference between the magnocellular and parvocellular latencies is less than 15 ms. Responses overall were slower in the larger animal, but the separation between magnocellular and parvocellular latencies was not very different. The larger animal had more units with long latency responses (for example, compare the 75 through 100 percentiles). These tended to be neurons with weaker responses: responses in the quartile of parvocellular neurons with the longest latencies averaged 64% as strong as faster parvocellular neurons; responses in the slowest magnocellular quartile averaged about 55% as strong as other magnocellular neurons.

There were no statistically significant differences between the latencies of ON- and OFF-cells in either LGN subdivision for either animal (Mann-Whitney, $P > 0.10$ in all cases). There was also no obvious relationship between latency and receptive-field eccentricity: The latencies of neurons with receptive-field eccentricities below 9 deg were not significantly different from those

with more eccentric receptive fields for either LGN subdivision or either animal (Mann-Whitney, $P > 0.25$ in all cases).

Neurons in LGN layers receiving input from the contralateral eye had slightly faster latencies than those in layers innervated by the ipsilateral eye. The median contralateral magnocellular latency was 4 ms faster than the median ipsilateral magnocellular latency ($P < 0.001$, Mann-Whitney), and the median contralateral parvocellular latency was 3 ms faster than the median ipsilateral parvocellular latency ($P > 0.15$, Mann-Whitney). These trends might be related to intraretinal distances. Because the head of the optic nerve lies in the nasal retina, retinal ganglion cell axons in the contralateral eye will generally have a shorter distance to travel to the optic nerve than those in the ipsilateral eye. Because intraocular axons are unmyelinated and conduct slowly (parvocellular 0.9 m/s, magnocellular 1.3 m/s, Schiller & Malpeli, 1978), this difference could have measurable effects on conduction times. Linear regression showed that latencies within our LGN populations increased with intraocular axon length (computed based on receptive-field location: 220 μm/deg; Perry & Cowey, 1985) by amounts corresponding to 1.0 ms/mm (parvocellular) and 1.1 ms/mm (magnocellular). The correlation was weak, but statistically significant ($r = 0.28$, $P = 0.01$ magnocellular; $r = 0.22$, $P = 0.05$ parvocellular). In our sample, contralateral receptive fields were an average of 11 deg ($\sim$2.5 mm) from the optic nerve, while ipsilateral fields averaged 27 deg ($\sim$6.0 mm). The extra length of the axons in the ipsilateral eye might therefore contribute to the differences in latency that we measured at the LGN (but see Stanford, 1987). Because the populations of magnocellular and parvocellular neurons contained comparable numbers of contralateral and ipsilateral receptive fields, their relative latencies are unlikely to be affected by differences in the eye of origin.
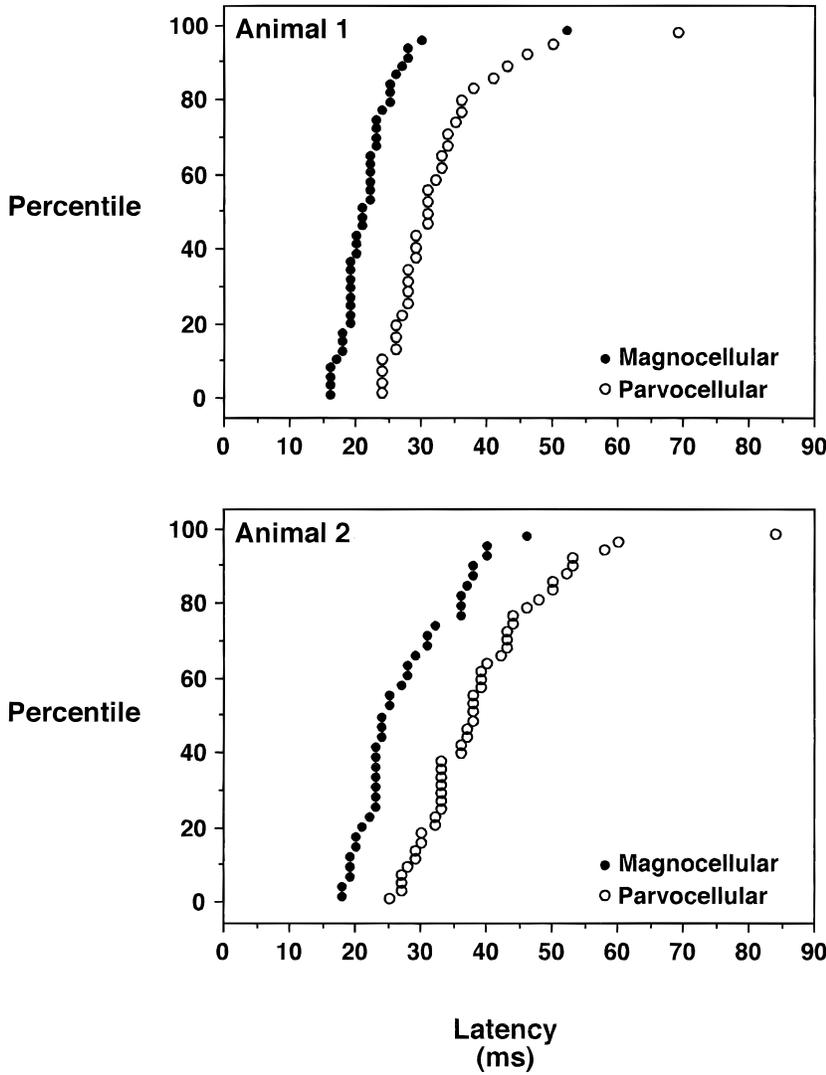
Fig. 4. Percentile plot of response latencies for both subjects. Over most of the range, parvocellular onset latencies lagged by less than 15 ms. The stimulus luminance was 28 cd/m^2.

Latencies at different stimulus luminances

A neuron's visual response latency is not fixed. Neurons throughout the visual system typically respond to different stimuli with different latencies, with shorter latencies generally associated with stimuli that produce stronger responses (Levick & Zacks, 1970; Levick, 1973; Shapley & Victor, 1978; Lennie, 1981; Sestokas & Lehmkuhle, 1988; Maunsell & Gibson, 1992; Oram & Perrett, 1992; Celebrini et al., 1993; Givre et al., 1995; but see Gawne et al., 1996). The data presented so far were collected using high luminance stimuli. Because the difference between magnocellular and parvocellular latencies might vary with stimulus strength, we tested every neuron with a range of stimulus intensities.

Fig. 5 shows the responses of a representative parvocellular unit to stimulus spots of different luminances. The response to each stimulus intensity is plotted twice, once showing the entire stimulus presentation (right column) and once with an expanded representation of the onset of the response (left column). Responses were stronger and latencies shorter for stimuli of higher luminance. The plot at the bottom of the figure summarizes response latency as a function of stimulus intensity for this unit. The three lines correspond to three different methods for computing latency (onset, which is our standard measure, halfpeak and peak; see Methods). Each measure yielded longer values for weaker stimuli. This relationship was observed for all LGN neurons.

The effects of stimulus intensity on magnocellular and parvocellular response latencies are summarized in Fig. 6, which includes all the data from Animal 1. Similar results were obtained from Animal 2, but we have not combined the data due to differing absolute latency values between the two animals (see above). The latency distributions for both magnocellular and parvocellular neurons shifted to longer times and broadened when stimulus intensity was reduced. For most stimuli, however, the difference between the earliest magnocellular and parvocellular activity did not change much. The arrows mark the medians of the distributions, and the vertical line in each plot marks the earliest *magnocellular* response observed for that stimulus luminance. Although the absolute latencies changed greatly as stimulus intensity was reduced, parvocellular responses lagged by 5 to 10 ms over much of the range. At luminances below 1.7 cd/m^2 differences between magnocellular and parvocellular latencies appeared greater, but responses were weak in this range (e.g. Fig. 5) and many neurons did not have a detectable response.
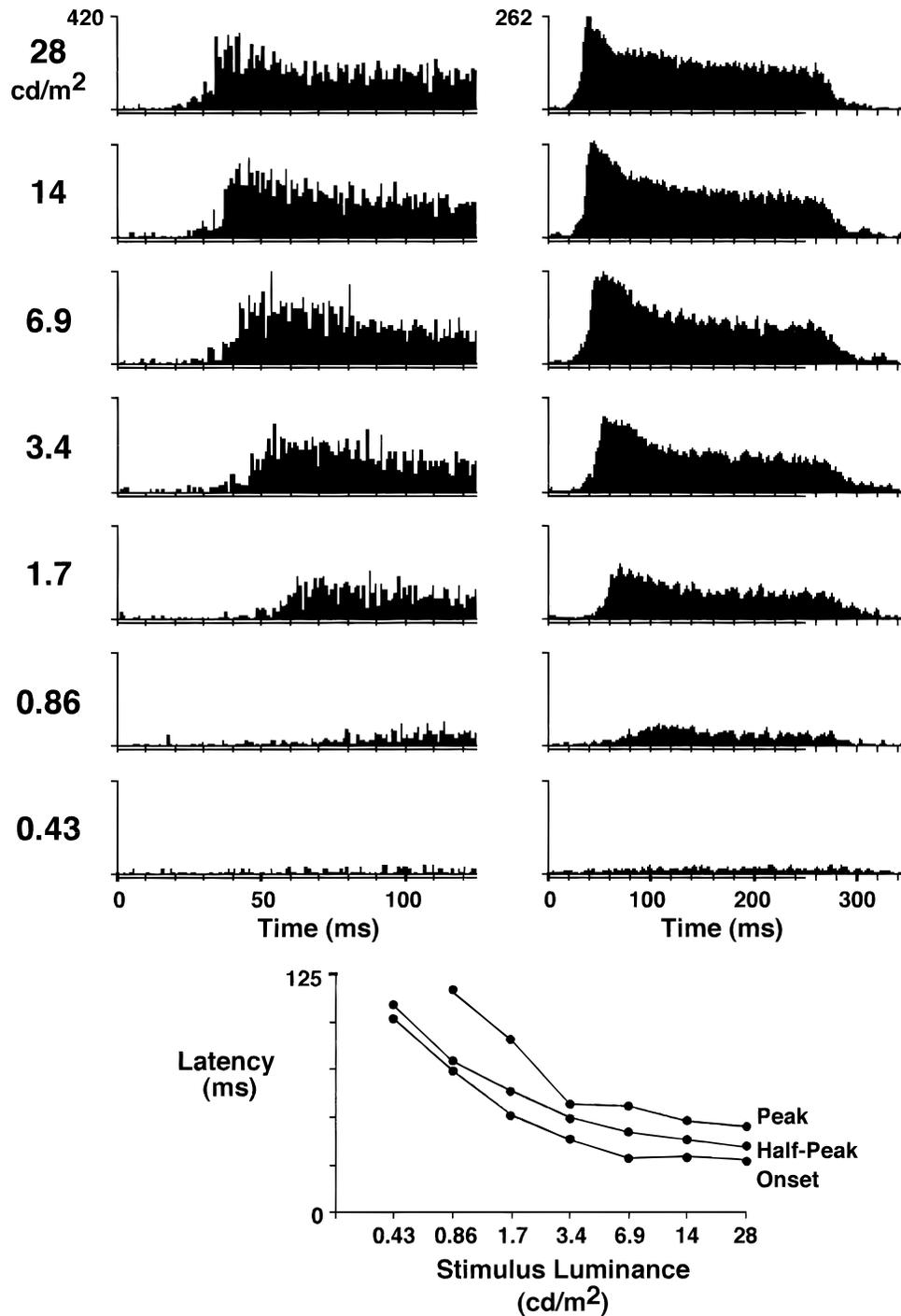
Fig. 5. Effects of stimulus luminance on visual responses. The responses are from a single parvocellular ON cell recorded in layer 6 of Animal 1. Seven different stimulus luminances were randomly interleaved, and each histogram is based on 100 stimulus presentations. The left and right columns plot the same data over different time scales, and stimulus luminance in cd/m^2 is indicated for each row. The vertical scaling is in units of spike/s, and is the same within each column. The plot at the bottom of the figure shows latency as a function of luminance. Each line represents a different measure of latency (see Methods). No value appears for the peak latency for the weakest stimulus because the peak in the histogram occurred long after the stimulus was removed, and was certainly a result of noise. Typical of neurons in our sample, stronger stimuli gave shorter latency responses.

Oversaturated responses

Not all LGN neurons responded most strongly to the highest luminance. For many, intermediate intensities produced the most

robust responses. The data in Fig. 7 illustrate this behavior. They were taken from a magnocellular neuron that gave its strongest response to stimuli in the range of 2–8 cd/m^2. The two lines in Fig. 7B plot the peak from the response histograms and the average
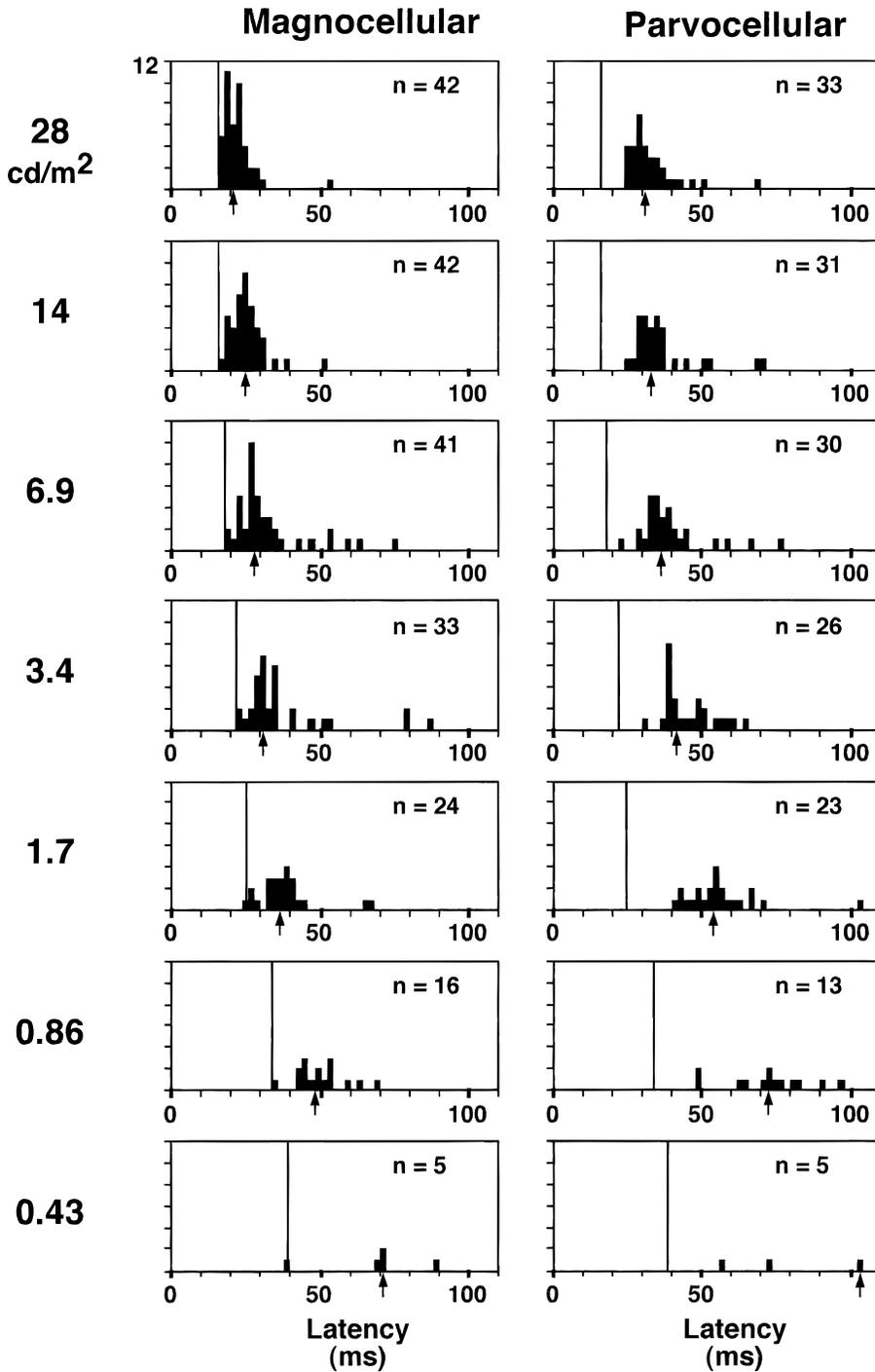
Fig. 6. Distribution of onset latencies for different stimulus luminances for Animal 1. Stimulus luminance (cd/m^2) is indicated to the left of each row. Arrows below the *x* axis on each plot mark the median latency. The vertical line in each plot marks the earliest *magnocellular* latency observed at that stimulus luminance. Some bins extend to the left of this line owing to the width and alignment of the bins used. Fewer points are included for weaker stimuli because many neurons did not have a detectable response to weak stimuli (see Methods). A few points with long latencies are not visible on these plots. Onset latencies became longer and more broadly distributed for weaker stimuli, but the difference between the shortest magnocellular and parvocellular responses did not change greatly.

rate of firing, both as a function of stimulus intensity. The decline in response probably depends on contributions from the surround of the receptive field. The center and surround of LGN receptive fields have different spatial and temporal contrast sensitivities (Derrington & Lennie, 1984), and inhibition from the surround may be proportionally greater at higher stimulus intensities for the spot stimuli that we used. The fixed spot size was probably larger than the center and surround for many neurons that we tested, especially for receptive fields close to the fovea (Derrington & Lennie, 1984). Consistent with this, 87% (13/15) of neurons with receptive fields at eccentricities beyond 20 deg responded best to the strongest

stimulus, compared with 66% (95/143) of neurons closer to the fovea.

Although response strength declined at stronger stimulus intensities for some cells, response latency typically continued to shorten. Fig. 7C shows that the response latencies computed for this neuron declined monotonically with stimulus intensity, whatever measure of latency was considered. This dissociation between response strength and latency was common.

The behavior of neurons with oversaturated responses is summarized in Fig. 8. We selected all magnocellular and parvocellular units that did not respond most strongly to the brightest stimulus,
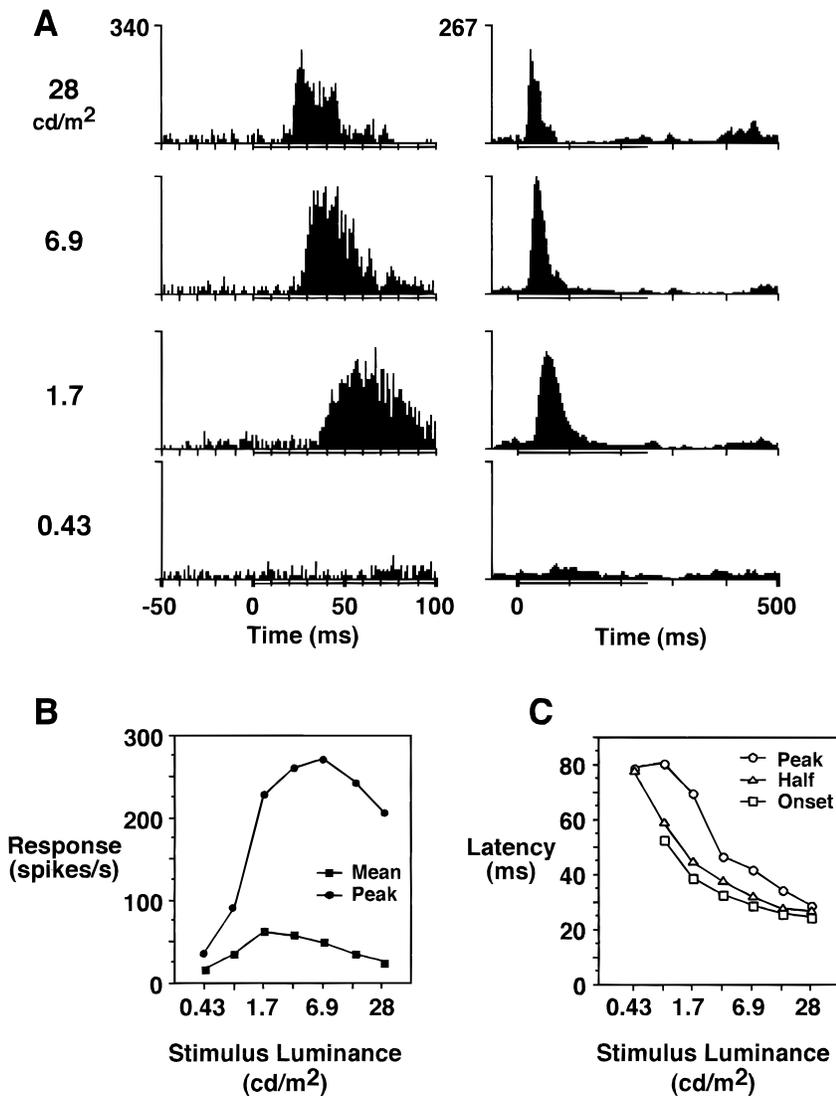
Fig. 7. Dissociation of latency and response strength. The histograms show the responses of a magnocellular neuron to selected stimulus luminances, which are indicated to the left of each row (cd/m^2). Each response is plotted twice at different time scales. Responses peaked at midrange luminances. Panel B plots the mean and peak rates of firing for this neuron during the stimulus presentation. Both measures show a clear roll-off in response at higher stimulus intensities. Panel C shows the latencies determined using three different measures. No onset latency is shown for the least intense stimulus because no response was detected. Latency continued to decline at higher stimulus intensities despite the reduced response.

and averaged their response strengths and latencies. Fig. 8A plots mean rate of firing for these oversaturated magnocellular and parvocellular responses. The decline in response strength was more pronounced for magnocellular neurons. Fig. 8B shows that latencies for both populations continued to decline at higher stimulus intensities. A dissociation of latency and response strength has also been reported in retinal ganglion cells of the cat (Bolz et al., 1982) and in monkey visual cortex (Oram & Perrett, 1992; Gawne et al., 1996).

Discussion

Latency differences between magnocellular and parvocellular neurons

Our results show that visual response latencies of magnocellular and parvocellular LGN neurons do not differ greatly. The earliest magnocellular responses preceded the earliest parvocellular responses by no more than about 10 ms across a broad range of stimulus intensities, and their distributions of latencies overlap extensively. At the highest stimulus luminances used here, the differences between the fastest magnocellular and parvocellular

responses were 7 and 8 ms in the two subjects examined. These values are consistent with a reported difference of 7–10 ms based on increases in visual latencies in V1 after ablating the magnocellular layers of the LGN (Maunsell & Gibson, 1992). They are also in agreement with the results of Schroeder and his colleagues (1989) who report a difference of about 5 to 6 ms in multiunit responses in the LGN to an intense strobe. Marrocco (1976) also reported a difference of about 8 ms between the earliest visual responses of transient, non-color-opponent (presumed magnocellular) and color-opponent (presumed parvocellular) LGN neurons. In the cat, the difference between the visual response latencies of X- and Y-cells in the LGN remains fairly constant at 5 to 10 ms across a broad range of contrasts (Sestokas & Lehmkuhle, 1986), consistent with an earlier report of a 10-ms difference in the latencies of transient and sustained cells in cat V1 (Ikeda & Wright, 1975).

Nowak et al. (1995) inferred a larger difference between macaque magnocellular and parvocellular visual responses latencies, based on recording in V1. They found a 20-ms difference between the earliest responses of isolated neurons encountered in layers 4Cα (magnocellular recipient) and 4Cβ (parvocellular recipient). This difference is appreciably larger than those presented here.
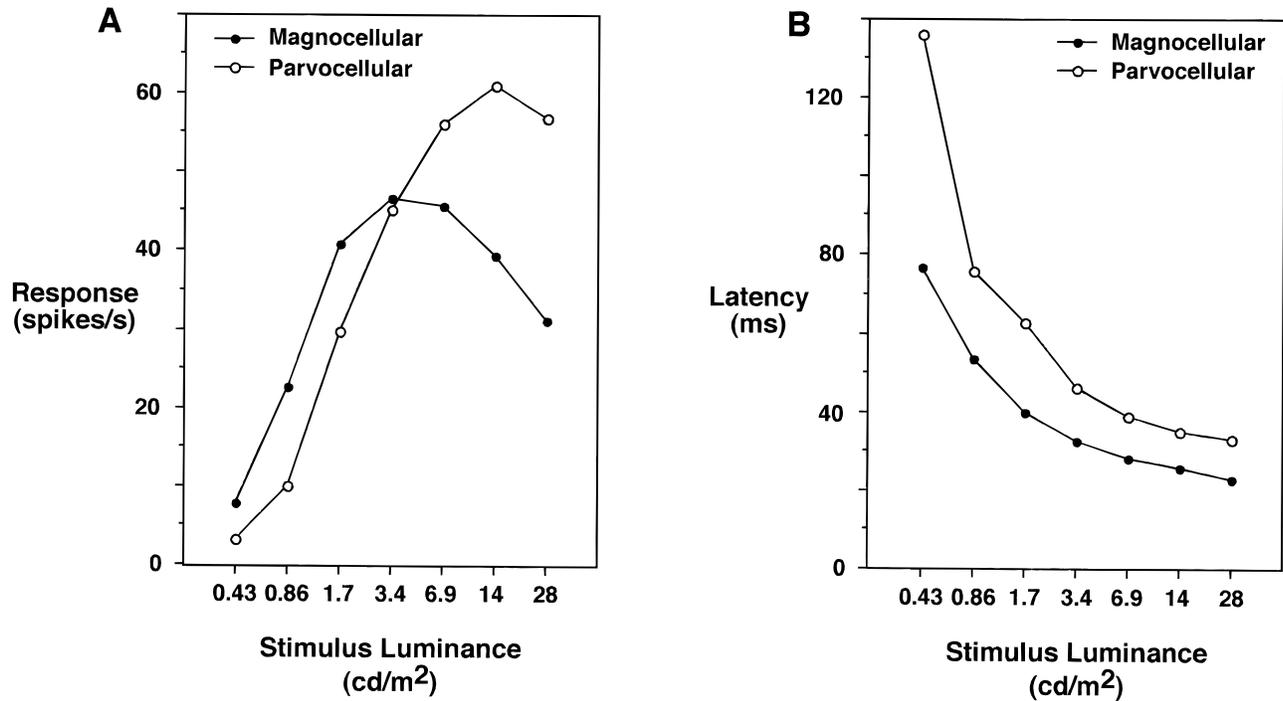
Fig. 8. Average behavior of oversaturated neurons. These plots are based on the responses of neurons from both animals that did not give their strongest response to the most intense stimulus (33 magnocellular and 17 parvocellular). Panel A is the average mean rate of firing as a function of stimulus intensity. Panel B shows the average latencies for the same data. Across the population the latency decreased monotonically while the response first grew and then declined.

While it is conceivable that the latency difference between magnocellular and parvocellular signal might double between the LGN and V1, other measurements of visual response latencies in layer 4C showed a difference consistent with the current LGN data (Maunsell & Gibson, 1992). Details of the analysis are unlikely to contribute to the difference, because the same method was used to estimate latency in the relevant studies. It is also unlikely that differences in stimulus configuration contribute, given that latency difference in the LGN does not change appreciably across a broad range of stimulus intensities.

Individual differences in latency

The two subjects in this study had different visual response latencies. The minimum and median latencies were longer for the larger animal. We selected animals that differed in age and size because an earlier study had noted inter-animal differences as large as 10 ms in the visual response latencies of V1 neurons, and suggested that they might be related to body size or age (Maunsell & Gibson, 1992).

The difference between the two animals cannot be explained by differences in axon length. Changes in axon length should produce a small, fixed offset in the distribution of latencies, whereas the observed difference is large and the distributions from the two animals differ in shape. The difference may reflect a change in the visual system with age. Age-related changes, such as loss of transmittance through the lens (see Pierscionek & Weale, 1995), could contribute to longer visual response latencies in older individuals. Spear and his colleagues (1994) did a comprehensive study of the effects of aging on spatial and temporal processing by neurons in monkey LGN, and found remarkably few differences. In particular,

their measurements of visual response latency did not differ between young and old animals. However, that study used a different measure of latency; they assessed latency using the lag of responses to drifting gratings of different temporal frequencies (Lee et al., 1981; Hamilton et al., 1989). To our knowledge, latencies based on response lag have not been compared directly with latencies in the responses to flashed stimuli. The two measures may not bear a close relationship. For example, latencies based on the lag of responses to drifting gratings do not differ between magnocellular and parvocellular neurons (77.1 *vs.* 76.5 ms; Spear et al., 1994), or between LGN neurons and simple cells in V1 (75 ms; Hamilton et al., 1989). It is possible that the latency to flashes might differ between old and young animals even though latencies based on the lag of responses to drifting gratings do not. More data will be needed to decide whether the individual differences in onset latency that we have seen are age related.

Koniocellular neurons

Magnocellular and parvocellular neurons are not the only cells in the LGN. Koniocellular (interlaminar) neurons make up a substantial fraction of the relay neuron population (Hendry & Yoshioka, 1994). They project primarily to the cytochrome oxidase rich regions (blobs) in the superficial layers (Blasdel et al., 1985; Fitzpatrick et al., 1985; Lachica et al., 1992). While the response properties of koniocellular neurons have not been extensively studied in the macaque, in the Galago they appear to get input from W-cells (Irvin et al., 1986).

Although we did not identify any koniocellular neurons in our recordings, it is possible that some cells in our population were koniocellular. It is unlikely, however, that incorrectly assigning

koniocellular neurons as magnocellular or parvocellular could affect our major conclusions. Visual response latencies of Galago koniocellular neurons are about 10 ms longer than those of parvocellular neurons (Irvin et al., 1986). If the responses of koniocellular neurons in the macaque are similarly slow, they would not interfere with estimates of the earliest magnocellular or parvocellular visual response latencies. The most likely contribution would be to add long latency values to the distributions.

*Are the latency differences between the parvocellular
and magnocellular pathways maintained in cortex?*

Some investigators have attributed shorter or longer response times in cortex to preferential magnocellular or parvocellular input. In addition to the substantial intermixing of magnocellular and parvocellular signals early in cortical processing (Malpeli et al., 1981; Nealey & Maunsell, 1994), there are several undetermined factors that could blur the distinction in visual response latencies for magnocellular and parvocellular pathways in cortex. First, the strength of magnocellular and parvocellular inputs could differ, such that a cortical cell would have to integrate weaker inputs from one pathway over a longer time before firing. Second, latency differences may be less evident for other types of stimuli that excite magnocellular and parvocellular neurons to different degrees. Third, most neurons in visual cortex have receptive fields that are larger than those in the LGN, indicating that they receive convergent input from many LGN neurons (usually indirectly). Because there are roughly ten times more parvocellular neurons than magnocellular neurons (Ahmad & Spear, 1993; Peters et al., 1994) a parvocellular-recipient cortical neuron has the potential to sum many times more inputs than a magnocellular-recipient neuron with a receptive field of similar size. A parvocellular-recipient neuron could thus have a better signal-to-noise ratio than individual parvocellular neurons in the LGN, which would make its visual responses detectable earlier. The improvement in signal-to-noise with averaging would of course depend on the degree to which the input signals are uncorrelated—which is yet another undetermined factor.

The issue of convergence is worth considering in more detail because it bears on the general issue of whether visual response latencies can be used to infer the serial connectivity of cortical areas. The effect of convergence on response latencies can be illustrated by analyzing latencies for summed spike trains. We performed such an analysis using spike trains taken from our set of LGN responses, and measured latency using a counting method similar to that used by others (Barlow & Levick, 1969; Lennie, 1981). This method assigns latency as the time when a counter (i.e. a cortical neuron) receives a number of spikes that exceeds, by a given statistical criterion, the number expected from spontaneous activity. Different degrees of convergence were examined by feeding the counter with summed spike trains that were created by adding together different numbers of LGN spike trains. This simple model is used only to illustrate a potential consequence of summing various numbers of inputs, and should not be taken as a hypothesis about the detailed anatomy or physiology of the circuits involved.

The method is illustrated in Fig. 9. For each test, a selected number of magnocellular or parvocellular spike trains were summed. Fig. 9A is a raster plot of responses from ten parvocellular neurons to a particular stimulus intensity. Each raster was drawn at random from the set of all parvocellular responses to this stimulus. This set of rasters was added, and converted into a cumulative plot of spike counts ("summed rasters" in Fig. 9B), starting from the time of stimulus onset (0 ms). A response latency was assigned by determining when the cumulative spike count exceeded the count expected from spontaneous activity by an amount corresponding to a probability of 0.0001. The number of spikes expected from spontaneous activity is marked in Fig. 9B by the dashed line that rises from the origin ("Spontaneous"). The slope of this line reflects the rate at which the ten input neurons fired spikes spontaneously during a 50-ms interval before stimulus onset. The number of spikes required to reach a criterion response was determined by assuming that the timing of spikes follows a Poisson distribution, and finding for each time after stimulus onset the number of spikes that exceeds the number of spontaneous spike with a probability of 0.0001. This number increases with time, and is plotted with a heavy line in Fig. 9B ("Criterion"). The time when the cumulative spike count crosses the criterion line is taken as a measure of response latency (32 ms in this example).

Because responses are selected at random, different samples drawn from the same set of responses will yield different latencies. Fig. 9C shows several cumulative spike counts superimposed. Each light trace is the sum of 20 parvocellular responses to a 28 cd/m^2 stimulus. The curves reach criterion between 30 and 40 ms. To find an average latency, we repeated the process for 500 sets of 20 parvocellular responses. This gave an average latency of 36.6 ms ± 0.13 S.E. Fig. 9D shows a corresponding analysis for sums of two magnocellular responses to the same stimulus. In this case the cumulative spike counts are noisier, because they average fewer inputs, and their intersections with the criterion line are widely dispersed. The response latency for 500 random samplings of two magnocellular responses averaged 42.6 ms ± 1.23 S.E. A 20:2 ratio of parvocellular and magnocellular approximates the ratio found in the LGN. Thus, for this stimulus condition a cortical cell monitoring parvocellular inputs might produce a detectable response earlier than a cell monitoring magnocellular inputs, if each used all available inputs within a small patch of retina.

We used this approach to examine the effects of input averaging over large ranges of stimulus luminances and numbers of inputs. The results are plotted in Fig. 10. The upper panel shows data for parvocellular inputs, and the lower panel plots magnocellular results. The *x* axis is the number of individual LGN responses averaged together before computing latency, and each line of points corresponds to a different stimulus intensity. Consistent with the results from individual neurons, response latencies are shorter for more intense stimuli. As expected from statistical considerations, responses latencies also become shorter as signals from more neurons are combined.

Because there are about ten times as many parvocellular neurons contributing inputs to cortex, we can compare the magnocellular and parvocellular performance by shifting one set of curves in Fig. 10 horizontally by an amount corresponding to a factor of ten. Fig. 11 shows the difference between calculated magnocellular and parvocellular latencies after making this adjustment. As before, each line corresponds to a different stimulus intensity, and values on the *x* axis are the number of responses averaged (differing by a factor of ten for magnocellular and parvocellular). Under the conditions of this simple first-pass model, the difference between magnocellular and parvocellular latencies is small and relatively constant (magnocellular leading by about 5 ms) over broad ranges of stimulus luminance (greater than ~2 cd/m^2) and numbers of neurons (greater than five magnocellular or 50 parvocellular neurons). Another striking feature of the plot in Fig. 11 is that when small numbers of LGN inputs are combined (fewer than five magnocellular or 50 parvocellular), parvocellular responses have shorter latencies. This result reflects the advantage of averaging ten parvocellular inputs for each magnocellular input. Thus, the effects of
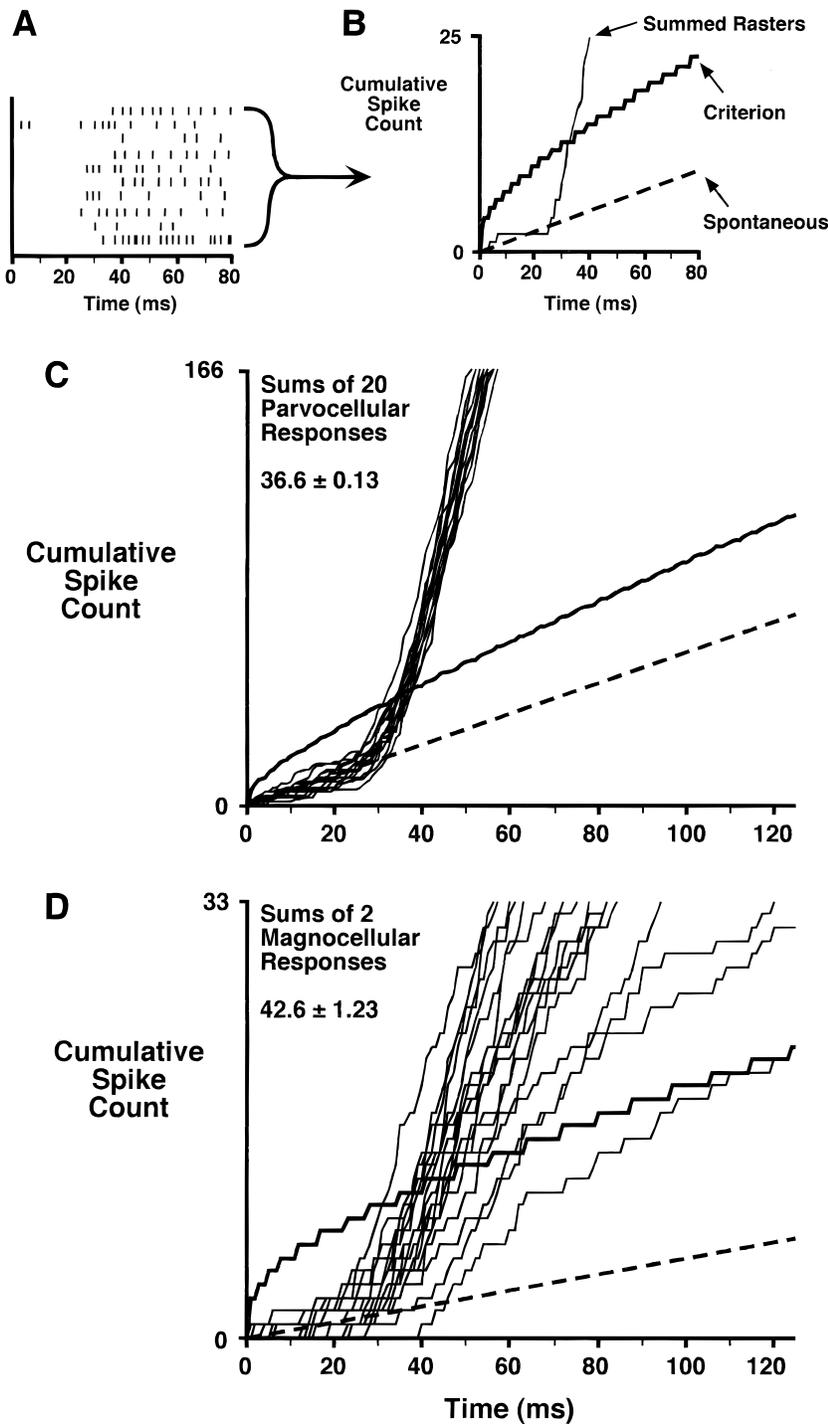
Fig. 9. Effects of combining LGN signals on response latency. A,B: Method for determining a response latency based on combining sets of spike trains drawn at random from the responses of all neurons of a given type. See text for details. The spike trains shown were taken from parvocellular responses to the 28 cd/m^2 stimulus. C,D: Latency determinations using different sets of randomly selected responses. See text for details. Panel C shows representative cumulative spike counts based on sets of 20 parvocellular responses to the 28 cd/m^2 stimulus. Panel D shows representative cumulative spike counts based on sets of two magnocellular responses to the same stimulus. Responses were drawn at random from all the data collected from both animals. In Panels B–D the dashed, straight line through the origin ("Spontaneous") corresponds to spontaneous activity, and the solid, heavy trace ("Criterion") is the number of spikes required to exceed spontaneous activity by a fixed criterion ($P = 0.0001$). Traces in Panel D are far more widely distributed than those in Panel C because fewer samples contributed to each.

pooling inputs can reduce or reverse differences in conduction speed.

It should be emphasized that this treatment of input summation is intended only as a demonstration of potential effects of cortical processing on visual response latencies, and not as a hypothesis about cortical circuitry. In that regard, several points are worth emphasizing. First, there is substantial intermixing of magnocellular and parvocellular signals early in cortical processing (Malpeli et al., 1981; Nealey & Maunsell, 1994), and other forms of processing may affect response latencies in unpredictable ways. Expectations based on the timing of pure magnocellular or pure parvocellular responses may have little bearing on actual cortical responses. Second, the data in Fig. 11 are based on a fixed 10:1 ratio of parvocellular to magnocellular inputs. While this is a good overall estimate, the ratio is actually higher for central representations, and lower for the periphery (Malpeli et al., 1996). For this reason latency differences would be expected to vary with eccentricity. Finally, the differences plotted in Fig. 11 assume that magnocellular- and parvocellular-recipient neurons would have receptive fields of similar sizes. The latency difference might be greater or smaller if, at a given level of cortical processing, one population summed over larger portions of the retina.
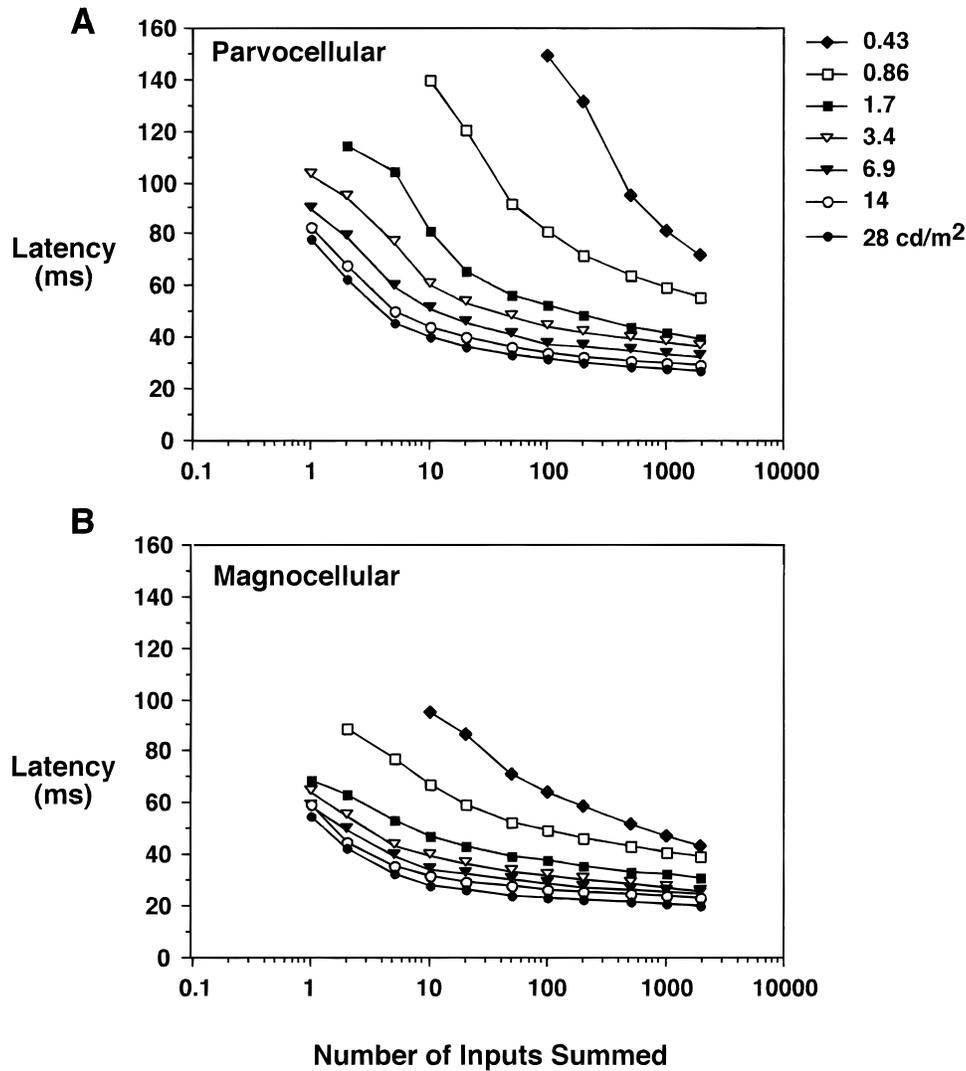
Fig. 10. Computed latency as a function of number of inputs averaged and stimulus intensity. Using the methods illustrated in Fig. 9, we computed an average latency for combined magnocellular and parvocellular inputs. Each point represents the average latency derived from 500 traces of the sort plotted in Fig. 9. Panel A shows data based on parvocellular responses, and panel B shows data based on magnocellular responses. The *x* axis is the number of inputs averaged before computing latency, and the *y* axis is the average latency. Different lines correspond to different stimulus intensities. Points for which fewer than 50% of the tests reached the criterion line are not plotted. The standard error of the mean for all points is less than 3 ms. For both magnocellular and parvocellular inputs responses are shorter for more intense stimuli or when more inputs are averaged.

The effects of summation are likely to apply to the visual response latencies of all neurons in cortex. Neurons in extrastriate cortex with large receptive fields receive, indirectly, signals from thousands of LGN neurons. This convergence may give these neurons unexpectedly short visual response latencies. This raises the intriguing possibility that neurons in later stages of the visual pathway could, at least in principle, have responses that are detectable earlier than the responses of the neurons that provide them with excitatory drive. This possibility is evident in Fig. 10. Values corresponding to one input represent the latencies for spike trains from individual LGN neurons. In every case these latencies are longer than those corresponding to the combination of the signals from multiple LGN neurons, as would occur in cortex. It should be emphasized that this behavior is not a peculiarity of a particular method of analysis, or specific to certain criteria for response. Any attempt to detect a change in the activity of a neuron, by either an

experimenter or another neuron, will be affected by the statistical effects of summation. Except in the case of no spontaneous activity, the signal-to-noise ratio will determine when a change in activity can be reliably detected, and this ratio will generally be improved by summing inputs.

The potential effect of input summation on response latencies makes it difficult to deduce neural circuitry based on the timing of responses. Short visual response latencies may not reflect an early position in the sequence of visual processing. This calls into question inferences from many studies. Response latency has also been used to infer length of anatomical pathways (Raiguel et al., 1989; Oram & Perrett, 1992; Givre et al., 1994; Beckers & Zeki, 1995), conduction times (Buchner et al., 1994), signal-processing time (Tovée et al., 1993; Wallis & Rolls, 1997), serial order of intra-cortical connections (Bullier et al., 1996), and the existence of input from alternative pathways (Ashford & Fuster, 1985; Coburn
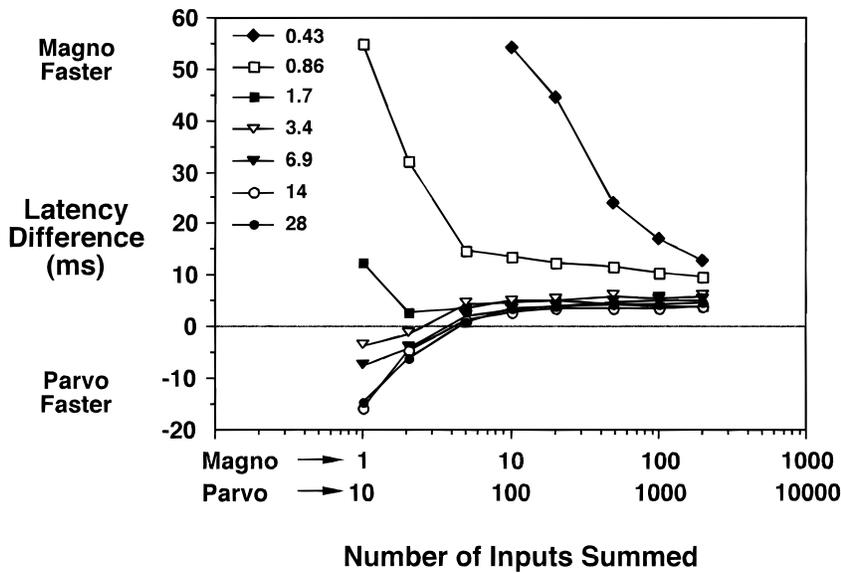
Fig. 11. Difference in latency between magnocellular and parvocellular mechanisms. Each point represents the calculated difference in latency for neurons that depended exclusively on either magnocellular or parvocellular inputs. Parvocellular latencies from Fig. 10 were subtracted from the magnocellular latency corresponding to one-tenth as many inputs. This ratio approximates the difference in the number of magnocellular and parvocellular LGN neurons. The number of parvocellular or magnocellular inputs averaged is given on the lower *x* axis. The difference between magnocellular and parvocellular latencies is small over most of the ranges examined, and parvocellular latencies are faster when small numbers of inputs are averaged.

et al., 1990). The potential shortening of response latency by input summation suggests that these conclusions are unjustified. Similarly, the suggestion that stimulus selectivity present in the earliest portion of a neuron's response cannot depend on feedback projections (Nowak & Bullier, 1997) is not safe. Patton et al. (1992) have described analogous problems in using the latency of responses to electrical stimulation to distinguish disynaptic connections from higher-order polysynaptic connections.

Because summation can make responses detectable earlier, serial anatomical relationships within visual cortex may not be evident in the latency of neural responses. The temporal pattern of activation across the visual system is difficult to predict without detailed information about patterns of convergence. The loci containing the earliest detectable responses could in principle be at any level in the visual system, and are likely to vary depending on what visual stimulus is presented.

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