The impact of brief exposure to high contrast on the contrast response of neurons in primate lateral geniculate nucleus

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The impact of brief exposure to high contrast on the contrast response of neurons in primate lateral geniculate nucleus. J. Neurophysiol. 106: 1310–1321, 2011. First published June 8, 2011; doi:10.1152/jn.00943.2010.—Prolonged exposure to an effective stimulus generally reduces the sensitivity of neurons early in the visual pathway. Yet eye and head movements bring about frequent changes in the retinal image, and it is less clear that exposure to brief presentations will produce similar desensitization. To address this, we made extracellular recordings from single neurons in the lateral geniculate nucleus of anesthetized marmosets, a New World primate. We measured the contrast response for drifting gratings before and after 0.5-s exposure to a high-contrast drifting grating, a stationary grating, or a blank screen. Prior exposure to the drifting grating reduced the contrast sensitivity of cells in the magnocellular pathway, on average by 23%; this reduction remained strong when the adapting and test stimuli were separated by 0.4 s. Exposure to a stationary grating of the preferred spatial phase did not change the contrast response; exposure to the opposite spatial phase did. None of the brief adaptors reduced the sensitivity of parvocellular cells. We conclude that brief periods of high contrast, such as those that would be expected to occur during a normal visual fixation, are sufficient to reduce the sensitivity of magnocellular-pathway cells. The effect of contrast adaptation has generally been characterized during or following long exposure to a particular level of image contrast. At least perceptually, such long exposures are not required: brief exposure to a high-contrast pattern can induce perceptual aftereffects (Kanai and Verstraten 2005; Sekuler and Littlejohn 1974) that are similar to those that follow longer exposures (Blakemore and Campbell 1969; Graham 1989). Contrast adaptation may, therefore, alter perceptual contrast sensitivity following adapting durations on the order of a single fixation, and changes in sensitivity occurring during one fixation may carry over to stimuli viewed on subsequent fixations (Gallant et al. 1998; Yarbus 1967).

This suggests that both contrast adaptation and the contrast gain control adjust neuronal sensitivity over short time scales. Regardless, we know little about the impact of brief exposures on the response of neurons in the visual pathway, particularly the subcortical components. In cortex, physiological aftereffects have been reported following brief exposure to high contrast (Chance et al. 1998; Dragoi et al. 2002; Muller et al. 1999; Nelson 1991a). One study has shown in lateral geniculate nucleus (LGN) of cat that presentation of a large stationary pattern can lead to a transient reduction, or a transient facilitation, of responses to a subsequently presented probe (Nelson 1991b). Here we are interested in how the contrast sensitivity of subcortical neurons depends on the very recent history of stimulation. To establish this, we measure the responses of P and M neurons in the LGN before and after 0.5 s of exposure to an effective stimulus. We show that brief exposure to high contrast reduces the contrast sensitivity of neurons in the M pathway.

METHODS

Surgery

Experiments were undertaken as part of a larger series on 10 adult male common marmosets (Callithrix jacchus), weighing 320–400 g. All procedures conformed to the guidelines approved by Animal Ethics Committee of The University of Sydney. Each animal was initially sedated with an intramuscular injection of 12 mg/kg Alfaxan (Jurox) and 3 mg/kg diazepam (Roche). We then gave preoperative intramuscular injections of 0.2 mg/kg atropine (Pfizer), to reduce lung secretions, and dexamethasone (0.3 mg/kg; Maine Pharmaceuticals) to reduce inflammation. Subsequent surgery was performed under supplemental local anesthesia (Lignocaine 2%; Astra Zaneca). A femoral vein was cannulated, the trachea exposed, and an endotracheal tube inserted. The head was placed in a stereotaxic frame, and a craniotomy made over the right LGN. A small incision was made in the dura, and a guide tube containing the electrodes (tetrodes, 2–5 MΩ, Thomas Recordings, or paralyne-coated tungsten electrodes, 9–12 MΩ, Frederick Haere) was placed above this.
Postoperative anesthesia was maintained by continuous intravenous infusion of sufentanil citrate (4–12 μg·kg⁻¹·h⁻¹; Sufenta Forte, Jansen Cilag, Beerse, Belgium) in physiological solution (sodium lactate, Baxter International) with added dexamethasone (0.4 mg·kg⁻¹·h⁻¹; Mayne Pharma) and Synthamin 17 (225 mg·kg⁻¹·h⁻¹; Baxter International). The ECG and EEG were monitored continuously to ensure adequate depth of anesthesia. Muscular paralysis was induced and maintained by continuous infusion of pancuronium bromide (0.3 mg·kg⁻¹·h⁻¹; Astra Zeneca). The animal was artificially ventilated so as to keep end-tidal CO₂ near 33 mmHg. At any sign of the anesthesia becoming less effective, the dose of sufentanil citrate was increased. Rectal temperature was kept near 38°C with the use of a heating blanket. Additional antibiotic and anti-inflammatory cover were given daily by intramuscular injection of 25 mg Noricillin and 0.1 mg dexamethasone. The pupils were dilated with topical atropine sulfate, and the corneas were protected with high-permeability contact lenses that remained in place for the duration of the experiment. No artificial pupils were used. Supplementary lenses (with power determined by ophthalmoscopy, and subsequently adjusted to maximize the spatial resolution of P-cells) were used to focus the eyes at a distance of 114 cm. At the end of the experiment, the animal was euthanized by intravenous injection of sodium pentobarbitone (500 mg/kg; Lethobarb; Verbac).

Visual Stimuli and Recording

A front-silvered mirror was used to bring the receptive field onto the center of a cathode-ray-tube monitor (ViewSonic G810, 100-Hz refresh rate; or Sony G520, refresh rate 120 Hz), viewed at a distance of 114 cm. Visual stimuli were generated by a G5 Power Macintosh computer using custom software (EXPO; P. Lennie); they were drawn with 8-bit resolution using commands to OpenGL. For each phosphor, we determined the relationship between the output of the video card and the photopic luminance; the inverse of this relationship was applied to the image that was sent to the video-card. The stimulus was a drifting sinusoidal grating, or a stationary one whose contrast was modulated in time; all stimuli modulated around the mean luminance (45–55 cd/m²) and were presented within a circular window with hard edges, outside of which the screen (20° × 15°) was held at the mean luminance. The analog signal from the electrodes were amplified, filtered, and sampled at 48 kHz by the same computer that generated the visual stimulus. Putative spikes were displayed on a monitor, and templates for discriminating spikes were constructed by analyzing multiple traces. The timing of waveforms that cohered to the template was recorded with an accuracy of 0.1 ms. Offline analysis was performed using Microsoft Excel and Matlab (MathWorks, Natick, MA).

Cell Identification

For all cells encountered, we determined the sign of response (On, Off), the tuning for temporal frequency, spatial frequency, size, and contrast. Along with the pattern of transitions between eye representations and in some cases subsequent histological reconstructions, these measures were used to classify cells as part of the P or M pathway (Derrington and Lennie 1984; Dreher et al. 1976; White et al. 2001). Cells that could not be reliably classified as P or M, including those where the receptive field received strong input from the short-wavelength-sensitive ("blue") cones, are not included in the following analyses. Receptive fields were on average 11.3° from the fovea (SD 8.7, n = 67); 50 neurons had receptive fields within 15° of the fovea. We cannot rule out the possibility that the neurons recorded here include a small proportion of interneurons (Wang et al. 2011). Interneurons comprise ~25% of the cell population in marmoset LGN (Solomon 2002), but the soma of these neurons is small compared with P and M relay cells, making it unlikely that they account for a significant proportion of our sample.

Adaptation Protocol

For each neuron, we first established the spatial location of the receptive field. This was done by finding the preferred location of a small (0.1°) modulated spot under manual control, or by reverse correlation of the spiking response to pseudorandom modulation of a 256-pixel checkerboard. The size of the checkerboard was set to encompass the receptive field of the neuron under study; every 0.03 s the luminance of each pixel was drawn independently from a Gaussian distribution centered on the mean luminance. We then found the preferred spatial frequency, temporal frequency, spatial phase, and size of a patch of drifting grating [examples of the relevant tuning curves can be found in Camp et al. (2009)]; the average stimulus used for the measurements here was a spatial frequency of 1.5 cycles/° (SD 1.3), a temporal frequency of 9.3 Hz (SD 4.4), and a diameter of 0.9° (SD 0.7). We then determined how brief exposure to a high-contrast grating changed the contrast response. Each trial started with a blank screen held at the mean luminance; after 1.2 s, this was replaced with the adapting stimulus, which lasted for 0.5 s before being replaced with the blank screen for an interval of 0.1–0.4 s; the test stimulus was then presented for 0.2 s and the next trial was initiated. The adaptor was a maximum-contrast grating of the optimum spatial configuration and drifting at the preferred rate (always greater than 5 Hz), or was a blank screen of the mean luminance; the test was of the same spatial and temporal configuration but of variable contrast. For each of the two adaptors, we measured response to each of seven test contrasts (one of which was always a blank screen of the mean luminance). The set of trials was interleaved such that full-contrast adaptors and blank screen adaptors were presented on alternate trials; the test contrast presented on each trial was selected pseudorandomly.

In other experiments, we measured the contrast response before and after brief exposure to stationary patterns. The temporal sequence was the same as above, except that there were three adaptation conditions: a stationary grating of optimal spatial configuration and the optimal spatial phase; the same grating at the opposite spatial phase (180° different); and a blank screen of the mean luminance. To enable direct comparison, the test was always a drifting grating of the optimal spatial and temporal configuration, as above.

Analysis

For each adapting stimulus (0.5-s duration) and each test stimulus (0.2-s duration), we made peristimulus time histograms (PSTHs) of the discharge rate, averaged across all presentations of the same stimulus. There were seven test contrasts, each of which was presented after either a blank screen (control condition), or after an adapting stimulus (adapted condition). The number of presentations of each test contrast in each condition was on average 16 (range 5–40). PSTHs of response to the adapting stimulus were generated from on average 111 presentations (range 35–280).

Each PSTH extended from 0.3 s before the onset of the relevant stimulus to 0.3 s after its offset, was sampled at a resolution of 0.005 s, and was smoothed by convolving with a Gaussian filter of standard deviation 0.01 s. We accepted a neuron for analysis if the highest contrast stimulus under study raised the discharge above the maintained rate by at least 25 impulses/s.

Response to the adapting stimulus. For presentation of stationary gratings, we fit the PSTH with a descriptive model of the response, based on an exponential decay \( E_{o,r} \)

\[
E_{o,r} = S + (T - S) \cdot e^{\left(-t - t_0\right)/\tau}
\]  

where \( t \) is a time constant, \( t_0 \) is the visual latency, \( T \) is the amplitude of the response transient, and \( S \) is the amplitude of the sustained response. We evaluated Eq. 1 at a resolution of 0.005 s, including a term for the maintained discharge, and half-wave rectified the predictions before fitting.
For drifting adapting gratings, we used the same equation, but added another term to describe the modulation of the rate $R_{(\omega)}$, 

$$R_{(\omega)} = [M + \sin(2 \pi \omega t + \theta) \cdot E_{(\omega)}]^{+}$$  

(2)

where $\omega$ is the temporal modulation frequency, $\theta$ is the response phase, $M$ is the maintained discharge rate, and $[\cdot]^+$ denotes half-wave rectification. For both Eqs. 1 and 2, values of the free parameters were found that minimized the mean-square error between the prediction and the observed rate using the Solver routine in Excel.

Response to test stimulus. The response of P-cells can be broadly explained by supposing that the cell computes a weighted linear sum of local contrast over its receptive field. The response of M-cells can be broadly explained by supposing that a similar weighted linear sum is normalized by a separate neural measure of stimulus energy. For a stimulus of fixed spatiotemporal configuration, this model predicts response amplitude

$$R_{(c)} = R_{\text{max}} \sqrt{\frac{c}{\sigma^2 + c^2}}$$  

(3)

where $c$ is contrast, $\sigma$ is the semi-saturation constant, and $R_{\text{max}}$ is a scale factor. One biophysical implementation of this normalization model (Carandini and Heeger 1994; Carandini et al. 1997; Solomon and Lennie 2005) derives linked changes in response amplitude and phase from changes in membrane conductance. The semi-saturation constant ($\sigma$) in Eq. 3 is calculated as

$$\sigma = \frac{1}{(\tau_{\text{f}}/\tau_{\text{i}})^2 - 1}$$  

(4)

$\sigma$ is thus determined by the temporal frequency ($\omega$) and two time constants ($\tau_{\text{i}}$ and $\tau_{\text{f}}$). Here we simply use the time constants to link response amplitude to response phase, which is given by

$$\theta_{(c)} = P_0 - \arctan \left\{ \frac{2 \pi \omega \tau_{\text{i}}}{\sqrt{1 + c^2 \cdot ((\tau_{\text{i}}/\tau_{\text{f}})^2 - 1)}} \right\}$$  

(5)

where $P_0$ allows the overall response phase to be adjusted (as might be brought about, for example, from the phototransduction and conduction delays). To provide a time-varying discharge rate at the same resolution as the PSTH we used,

$$R_{(c)} = [M + \sin(2 \pi \omega t + \theta_{(c)}) \cdot R_{(c)}]^{+}$$  

(6)

The fitting procedure (the function lsqnonlin provided by Matlab) found the five parameters ($M$, $P_0$, $\tau_{\text{i}}$, $\tau_{\text{f}}$, and $R_{\text{max}}$) that minimized the mean square error between the prediction and the PSTH. The fitting procedure and the equations above defined phase in units of radians; for clarity throughout the paper, we plot and describe phase in units of degrees. To allow easier comparison of the responses and model predictions, we obtained their modulation amplitude and phase. Because there were usually a noninteger number of cycles within the analysis window, and to avoid any windowing artifacts from Fourier analysis, we fit the PSTHs or predictions to a half-rectified sinusoid of the same frequency as the test stimulus, allowing free parameters for the modulation amplitude and phase. The mean of the sinusoid was, respectively, always the measured or predicted rate for a test contrast of zero. Unless otherwise noted we used a two-tailed, paired Students $t$-test to evaluate adaptation-induced changes in response.

RESULTS

We made extracellular recordings from neurons in the LGN of the common marmoset, a New World primate. In each neuron, we measured contrast response for a patch of drifting grating whose size, spatial frequency, and temporal frequency were optimized for the neuron under study. The test measurements were made shortly after 0.5-s presentation of an adapting stimulus of the same spatial configuration, or after presentation of a blank screen held at the mean luminance. In what follows, we will describe the response of P- and M-cells to each of the adaptors we used and then show how these adaptors change the contrast sensitivity of these neurons.

Response of P- and M-cells to Stationary and Drifting Gratings

Figure 1A shows the response of one P-cell during presentation of a stationary high-contrast grating that was presented in the preferred spatial phase (black lines) or the anti-preferred phase (gray lines). The response of the P-cell to a grating of the preferred phase is highest at the onset of the grating and remains substantially elevated (sustained) throughout the presentation. During presentation of a grating at the anti-preferred phase, the response is always suppressed to response floor (0 imp/s); at stimulus offset there is a reliable but smaller transient discharge above the maintained rate. The response of the M-cell (Fig. 1B) is quite different: the large responses at the onset of the preferred grating decay rapidly back to the maintained rate. The offset of a grating of anti-preferred phase also produces a transient discharge, which is similar in shape to the response at the onset of a grating of preferred phase and larger than that found in the P-cell.

Over a population of 13 P-cells (8 Off-cells), the response to a preferred stimulus decayed by 71.5% (SD 8.0) of its initial amplitude within 0.5 s; in 28 M-cells (11 Off-cells), the decay was significantly greater and averaged 98.2% (SD 4.4; $P < 0.001$, one-tailed Students $t$-test). The time taken to reach a

![Fig. 1. Discharge rate of parvocellular (P-) and magnocellular (M-)cells during presentation of stationary and drifting patterns. A and B: peristimulus time histograms (PSTHs) showing the response of an example P-cell (A) and M-cell (B) during presentation of a high-contrast stationary grating presented in either the preferred (black lines) or anti-preferred (gray lines) spatial phase. Dashed lines show best-fitting predictions of Eq. 1 in METHODS. C and D: PSTHs showing the response of the same two cells during presentation of high-contrast drifting sinusoidal gratings of optimal temporal frequency. Dashed lines show best-fitting predictions of Eq. 2 in METHODS. P-cell: stimulus diameter 1°, spatial frequency 1.5 cycles/°, temporal frequency 12 Hz in C. M-cell: 1°, 1 cycle/°, 10 Hz. Number of trials used to generate the PSTH: 74 (A), 140 (B), 88 (C), 166 (D). For clarity, error bars are omitted.](http://jn.physiology.org/10.1152/jn.00907.2010)
stable amplitude was captured by fitting an exponential decay to the response (Eq. 1; dotted lines in Fig. 1, A and B): for a preferred phase grating in M-cells, the mean time constant ($\tau$ in Eq. 1) was 0.039 s (SD 0.019), and for P-cells it was 0.072 s (SD 0.014). The different response of M- and P-cells to stationary patterns is consistent with the idea that different postreceptive mechanisms provide adaptation in the two pathways (Dreher et al. 1976; Hawken et al. 1996; McLelland et al. 2009; Purpura et al. 1990; Yeh et al. 1996). The offset of an anti-preferred grating produced discharges with a shorter time constant of the decay, 0.033 s (SD 0.012) in M-cells and 0.056 s (SD 0.012) in P-cells, and for both onset and offset responses the time constants of the M-cells was significantly less than that of P-cells ($P < 0.01$; one-tailed Student’s $t$-tests). On- and Off-center cells within each cell class were not distinguished by the parameters above.

Figure 1, C and D, show how P- and M-cells respond during presentation of a high-contrast grating drifting at the preferred spatial and temporal frequency: the cycle-by-cycle response amplitude of the P-cell is nearly constant throughout the 0.5-s presentation. The response of the M-cell, which is initially higher, decays slightly over time. An exponential was fit to the response to capture the amplitude of this decay (Eq. 2). Over the population of P-cells, the response to a preferred stimulus decayed by a median 16.7% ($\mu$ 31.1; SD 37.5; $n = 26$) of its initial amplitude within 0.5 s; for M-cells this was 20.1% ($\mu$ 27.5; SD 25.0; $n = 35$), both significantly different from zero ($P < 0.001$, Student’s $t$-test) and not significantly different to each other ($P = 0.56$). The decaying response during presentation of a moving grating may reflect the fact that the temporal frequency spectrum of the stimulus is broader at its onset than during it, the action of a contrast gain control, or the presence of slower forms of contrast adaptation (Baccus and Meister, 2002). To characterize the changes brought about by the brief adaptors, we, therefore, examined responses to subsequent tests.

**Response Before and After Brief Exposure to Adapting Patterns**

We measured contrast sensitivity for drifting test gratings of preferred spatial and temporal frequency, either after presentation of a blank screen, or after the offset of an adapting stimulus that was presented for 0.5 s. The test was always very brief (0.2-s duration) and was separated from the adaptor by a short period (0.1–0.4 s), during which the screen was held at the mean luminance. Unless otherwise stated, the interval between the offset of the adaptor and the onset of the test was 0.2 s.

The filled histograms in Fig. 2, A and B, show PSTHs, constructed from 12 (Fig. 2A) or 10 (Fig. 2B) presentations at each test contrast, of the response of one Off-center P-cell and one On-center M-cell. Response was obtained either after a period of exposure to a blank screen (left panels) or after the presentation of a high-contrast drifting grating (right panels). Following an adapting grating, the M-cell, but not the P-cell, is less responsive, and this is most apparent in the responses to high contrast. The test was sufficiently long after the offset of the adaptor that any response to the adaptor (e.g., Fig. 1D) should have disappeared. Consistent with this, there was no overall impact of the adaptor on the maintained discharge.

![Fig. 2](http://jn.physiology.org/)

**Changes in Contrast Response Brought About by Brief Exposures**

To quantify the change in sensitivity brought about by the adaptor, we used a simple model of the light response (Carandini et al. 1997; Solomon and Lennie 2005). The model, based on a resistor-capacitor circuit, captures how the response phase and amplitude depends on the contrast of a test grating and is described by Eqs. 3–6 in METHODS. Briefly, the model predictions are a function of time and stimulus contrast. Two time
constants allow the model to predict the amplitude (Eqs. 3 and 4) and phase (Eq. 5) of response at every contrast; additional parameters scale the response and provide a maintained rate. To find the set of five parameters that provided the best predictions, we compared those predictions to the PSTHs at all of the seven test contrasts, only three of which are shown in Fig. 2, A and B. To compensate for fixed temporal delays in the light response of LGN neurons, we fit the model to the PSTH extending from 0.05 s after onset of the test to 0.05 s after its offset.

The smooth lines in Fig. 2, A and B, show the predictions of the model over the relevant time period. These predictions were calculated independently for the unadapted and adapted conditions. In these neurons and in most others, the quality of the predictions was good: for the neurons in Fig. 3 the model captured 65% (Fig. 2A, P-cell) and 79% (Fig. 2B, M-cell) of the variance present in the PSTHs (Carandini et al. 1997); across the population of 22 P-cells the average was 72% (SD 20) and for 34 M-cells was 75% (SD 16). The model’s capacity to predict adapted and unadapted responses, that is, the proportion of variance the model explained, was not significantly different (P > 0.05), and for further analysis we accepted those neurons in which the model captured at least 50% of the response variance in each condition, leaving 16 P-cells (10 Off-center) and 33 M-cells (13 Off-center). Among these neurons, the model accounted for, on average, 79.2% (SD 10.4, n = 49) of the variance in the PSTHs. The remaining variance not accounted for arises in part because the shape of the PSTH in these neurons is not quite predicted by any rectified sinusoid. To estimate the upper limit of performance of any model based on rectified sinusoids, we conducted a separate analysis where the mean, amplitude, and phase were optimized for each PSTH. Across the neurons included here, these accounted for an average 83.2% (SD 10.1, n = 49) of the variance in the PSTHs.

In the following, we will describe the changes in response brought about by adaptation, using the parameters returned by the model. In parallel analyses, we fit two variants of the model to the adapted and unadapted responses: one where we found the best predictions of the model when none of its parameters were allowed to change with adaptation, and a second when all parameters when they are allowed to change. Allowing all parameters to change with adaptation improved model performance, increasing the percent variance explained by 5.7% in the 33 M-cells, and by 5.4% in the 16 P-cells. There are more parameters when they are allowed to vary with adaptation, so we expect some improvement in the performance of the model. We used the Akaike Information Criterion to assess the level of complexity of model required (Motulsky and Christopoulos 2004): by this criteria, in all cells fits were worse when the model parameters were not allowed to vary with adaptation, indicating that brief adaptation does alter the shape of the contrast response.

Figure 2, C and D, compares the modulation amplitude and phase of the best-fitting prediction of the model to that of the underlying data (see METHODS). The responses and the model predictions show that 1) there is little change in the response of the P-cell, and 2) for the M-cell, the major impact of the adaptor is to reduce the response at intermediate and high contrasts, with less effect on the response to low contrasts, or on response phase. This was not always the case, in some

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**Fig. 3.** Impact of brief exposure to a drifting grating on the contrast response of a population of neurons in lateral geniculate nucleus (LGN). A: comparison of contrast sensitivity (imp s⁻¹ unit contrast⁻¹) for drifting gratings of optimal spatiotemporal configuration, during the control condition and after 0.2 s after a 0.5-s exposure to a high-contrast drifting grating of the same configuration. Points below the diagonal indicate neurons in which the adaptor reduced contrast sensitivity. Inset histograms compare contrast sensitivity before and after adaptation. Values >1 represent neurons where sensitivity is reduced by adaptation. B: comparison of the response phase advance (the reduction in response latency that accompanies an increase in contrast from 0 to 1.0) during control measurements and after adaptation. Points below the diagonal indicate neurons where adaptation led to a reduction in phase advance. One P- and one M-cell showed phase “advance” less than the limits of the plot and are not shown. Inset histograms compare phase advance before and after adaptation. Values >1 represent neurons where the phase advance is reduced by adaptation. C and D: comparison of the change in semi-saturation constant (C) and maximum response (R_max) for M-cells, which is brought about by adaptation. For the semi-saturation constant, values <1 represent neurons where adaptation increased the contrast required to reach one-half the saturating response rate. For R_max, values >1 indicate neurons where adaptation reduced the saturating response rate.
M-cells the adaptor did have an effect on the response at low contrasts and on the response phase.

To illustrate how adaptation changed response across the population, we found for each neuron the maximum response ($R_{max}$), and the semi-saturation constant ($\sigma$). For P-cells, the response amplitude is still increasing at high contrast and, consequently, the estimate of maximum response and that of the semi-saturation constant are poorly constrained. Figure 3A instead plots the contrast sensitivity of P- and M-cells (the slope of the contrast-response, $\text{Sensitivity} = R_{max}/\sigma$, with units of impulses·s$^{-1}$·contrast$^{-1}$), which is more constrained. The majority of M-cells in Fig. 3A plot below the diagonal, indicating that they are less sensitive after exposure to the brief adaptor than after a gray screen; sensitivity was, on average, 22.5% less (SD 22.6; $P < 0.0001$) after the adapting grating than before it. For P-cells, there was a smaller, and nonsignificant, reduction in sensitivity (9.1%, SD 24.9; $P = 0.28$).

To characterize the response dynamics, we obtained from the model fits the change in response phase as the stimulus increased from zero contrast to full contrast. In all but two cells, response phase advanced (latency was reduced) as contrast increased. This is the behavior expected in cells that express contrast gain controls (Shapley and Victor 1979). Figure 3B plots the magnitude of the phase advance in the adapted state against that in the control state. The M-cells plots further from the origin, confirming that phase advances are much more prominent in M-cells than in P-cells (Benardete et al. 1992; Lee et al. 1994). In M-cells, the average phase advance in the control state was 44.9° (SD 36.9), and in P-cells it was 6.5° (SD 12.6). The phase advance in M-cells is reduced slightly but consistently by adaptation: on average, it was 4.8° less (SD 11.7; $P = 0.03$) during adaptation. This was because adaptation reduced the response latency at low contrasts, but not at high contrasts (not shown). Phase advances seen in P-cells were not changed by adaptation, and there was no difference between M-On- and M-Off-cells.

Figure 3, C and D, plots for M-cells the values of $\sigma$ (Fig. 3C) and $R_{max}$ (Fig. 3D) obtained from the best-fitting predictions of the model. These plots show that, for M-cells, adaptation generally increased the semi-saturation constant (on average by 5.3%, SD 31.2, $P = 0.064$) and reduced $R_{max}$ (on average by 11.4%, SD 24.3; $P = 0.014$). The reduction in sensitivity seen in Fig. 3A reflects a combination of changes in both of these. The sample of M-cells comprised 20 On-cells and 13 Off-cells. Adaptation reliably reduced the sensitivity of both On-cells (average 13.6%, SD 17.2; $P < 0.01$) and Off-cells (average 38.2%, SD 23.5; $P < 0.0001$). The desensitization seen in Off-cells was significantly greater than that in On-cells ($P < 0.01$) and was largely because adaptation produced a stronger reduction in $R_{max}$ (not shown). In sum, brief adaptors reliably desensitize M-cells, particularly Off-cells, but have little impact on the sensitivity of P-cells.

Our test stimuli always included a blank screen of the mean luminance. Comparison of the maintained discharge rate in the adapted and unadapted states, during the same time period used to characterize responses to the test stimuli, show adaptation has inconsistent effects on the maintained rate. For M-On-cells, the maintained rate was slightly reduced by adaptation, from 9.8 to 7.9 imp/s ($P = 0.03$), but in M-Off-cells, where the maintained rate was lower, there was no change (5.6 vs. 6.1; $P = 0.56$). Adaptation did not change the maintained discharge of Off- or On-cells.

**Increasing Duration of Exposure to the Adapting Stimulus**

To see if longer exposures increased the impact of adaptation, in five M-cells (three Off-center), we increased the duration of the adaptor to either 1 or 2 s, with correspondingly greater duration of exposure to a blank screen in the control condition. Exposure to the longer adaptors reduced contrast sensitivity by 25.9% (SD 20.7, $P = 0.042$); this was brought about by a combination of a decrease in $R_{max}$ in all neurons and in four neurons an increase in the semi-saturation constant. The longer adaptors also brought about a reduction in phase advance (sped up responses to low-contrast stimuli) and a reduction in spontaneous discharge. All of these changes were slightly greater than those induced by 0.5-s adaptors, and we expect that extending the duration of the adaptor further would bring about a monotonic increase in the desensitization that it causes (Manookin and Demb, 2006).

**Extended Impact of Brief Exposure to Adaptor**

Above, we presented results for an adaptor-test interval [inter-stimulus interval (ISI)] of 0.2 s, which is at or beyond the integration time of retinal and LGN neurons (Benardete and Kaplan 1999; Benardete and Kaplan 1997; Chander and Chichilnisky 2001; Solomon et al. 2010). To make sure that changes brought about by the adaptor did not simply reflect a direct interaction between the response to the adaptor and that to the test stimuli, we measured response at other ISIs. Figures 4, A and B, shows the average contrast response functions for the P- and M-cells in our sample when the ISI is extended to 0.4 s (in each case, the response of each neuron was normalized to the unadapted response at maximum contrast). Figure 4 shows that the adaptor still has substantial impact at this longer interval.

To quantify this, we returned to the model and examined the adaptation-induced changes in sensitivity and dynamics. We were able to measure the changes brought about by adaptation for one or more of three ISIs: 0.1, 0.2, and 0.4 s. Measurements at ISIs of 0.1 and 0.4 s were more likely to be made on neurons where adaptation brought about a change in response at an ISI of 0.2 s, and the measurements at these ISIs may, therefore, be biased. For an ISI of 0.1 s, the sensitivity ($R_{max}/\sigma$) of M-cells was, on average, 22.2% less (SD 19.4; $n = 10$; $P = 0.003$) after adaptation; at 0.4-s ISI sensitivity was 18.1% (SD 18.0; $n = 7$; $P = 0.03$) less than in the unadapted state. These are very similar to that obtained for an ISI of 0.2 s above (22.5%). ISI had somewhat more of an effect on response dynamics: at an ISI of 0.1 s, phase advance was substantially attenuated by adaptation in 6 of 10 M-cells (and on average by 26.6°, SD 38.5; $P = 0.06$); at 0.4 s ISI this was only 1.6° (SD 19.6). For P-cells, the sample is smaller, but ISI might have more of an effect; adaptation reduced sensitivity by 21.2% (SD 21.5; $n = 5$; $P = 0.08$) at an ISI of 0.1 s and by 11.6% (SD 6.2; $n = 4$; $P = 0.03$) at 0.4 s.

In seven M-cells (5 On-center) and four P-cells, where an ISI of 0.2 s appeared to suggest that the adaptor changed the contrast response, we investigated ISIs of 0.1, 0.2, and 0.4 s. Figure 4, C and D, shows for these neurons how sensitivity and response phase advance depends on ISI. Figure 4C plots the...
ratio of sensitivity in the unadapted condition to that in the adapted (values >1 indicate that adaptation reduced sensitivity): for the seven M-cells, most points are >1, indicating that sensitivity is reduced at all ISIs; for the P-cells, sensitivity was reduced only at ISIs of 0.1 and 0.2 s. Figure 4D shows that the change in phase advance that is brought about by adaptation is greatest at short ISIs, but persists at longer intervals (here values >0 indicate points where adaptation reduced phase advance). Repeated-measures ANOVA conducted on the data in Fig. 4, C and D, did not reveal a significant change in the magnitude of the adaptor’s effect on gain and phase over the range of ISIs that we tested (P > 0.05).

**Sensitivity Following Adaptation to Stationary Gratings**

Within an individual fixation, the image on the retina is dominated by low temporal frequencies, and so an eye movement will generally bring the receptive field onto a stationary pattern. Our laboratory has shown previously that adaptors of low temporal frequency have little effect on the contrast response, even when presented for long periods (Camp et al. 2009; Solomon et al. 2004). It might, therefore, be expected that stationary gratings are not effective adaptors for M-cells, but this has not been tested. Additionally, the general lack of adaptation in P-cells might simply reflect the fact that they are generally less responsive than M-cells to a drifting grating (compare Fig. 1, C and D); a stationary grating of the preferred spatial phase brings about a sustained increase in action potential rate in P-cells (Fig. 1A) and may, therefore, induce more adaptation.

We, therefore, measured the contrast sensitivity of P- and M-cells following exposure to a stationary grating, in the same way as above, presenting brief tests 0.1–0.2 s after the offset of the stationary grating, which was presented for 0.5 s. In what follows, we combine measurements obtained (in different neurons) at ISIs of 0.1 and 0.2 s, because we found no difference. We again used the model to explore how adaptation changed responses to the test. Figure 5 shows, in a similar format to Fig. 2, the response of one On-center M-cell after adaptation to a grating in the preferred phase, a blank screen of the mean luminance, or a grating in the anti-preferred phase. Responses were largely unaffected by prior exposure to the preferred grating; in this and some other M-cells, we found that exposure to the anti-preferred grating caused greater changes in the response to the test. In these cases, the response was reduced at low or mid-contrasts and often increased at high contrast. The response of P-cells was unaffected by adaptation to either the preferred phase or the anti-preferred phase.

Figure 6 characterizes adaptation to stationary gratings on our sample of 25 M-cells (12 Off-center) and 11 P-cells (9 Off-center) that met criterion. Figure 6, A and C, characterizes the responses after adaptation for 0.5 s to a grating of the preferred spatial phase. For both P- and M-cells, adaptation had no effect on the contrast sensitivity, on response dynamics, or on the maintained rate (not shown). Figure 6, B and D, shows equivalent measurements after adaptation to a spatial phase 180° away from the preferred phase. There was no consistent impact of adaptation on the contrast sensitivity of P-cells and M-cells, but for M-cells there were significant changes in the maintained rate and response dynamics. The adaptor reduced the maintained rate of On-cells (by 4.3 imp/s, P < 0.05), but not that of Off-cells. Phase advance was reduced in On- and Off M-cells: within each class there was no significant effect, but, including all cells, the phase advance was reduced (by 18.0°, SD 41.3; P = 0.04).

The changes in maintained rate and response dynamics shows that adaptation to anti-preferred gratings has an impact on the response of M-cells, even though there was no overall change in contrast sensitivity. We, therefore, asked whether adaptation to anti-preferred gratings was reflected in changes to individual parameters of the contrast response curve. Figure 6, E and F, shows for M-cells the influence of the two adaptors on the parameters returned by the model. As expected from Fig. 6, A and C, adaptation to the preferred spatial phase had no overall effect on either σ or $R_{max}$ (Fig. 6E). Adaptation to the anti-preferred grating increased σ (by 33.5%, SD 18.2; P < 0.0001), but the effect on $R_{max}$ was variable (overall it in-
increased by 8.0%, SD 18.5, \( P = 0.07 \). This was also the case if we examined On- and Off-center cells separately.

We, therefore, compared the fractional change in \( \sigma \) that is brought about by adaptation to the anti-preferred stimulus to the fractional change in \( R_{\text{max}} \) (not shown). There was a significant positive correlation (\( r^2 = 0.66; P < 0.0001 \); linear correlation on the logarithms of the ratios) between the two. The lack of an overall change in sensitivity after adaptation to the anti-preferred stimulus is, therefore, likely due to the fact that, in some cells, there are simultaneous increases in the maximum response and the contrast at half-maximal value, which have opposing effects on the contrast sensitivity.

DISCUSSION

Brief (0.5 s) presentation of a high-contrast grating led to a reduction in the contrast sensitivity of M-cells, but not P-cells, in the LGN of marmoset. Figure 7 summarizes the impact of the brief adaptors: Fig. 7, \( A-D \), confirms that a drifting grating desensitizes Off-M-cells more than On-M-cells, and that a stationary grating has similar effect on the two cell types; Fig. 7, \( E-G \), confirms that the sensitivity of P-cells is largely unaffected by prior presentation of either drifting or stationary gratings.

Impact of Brief and Prolonged Exposure to High Contrast

Brief exposure to high contrast drifting gratings reduced the sensitivity of M-cells, but the effect was less than is seen after prolonged exposure. For comparison, 30-s exposure to a high-contrast adaptor brings about an 81% reduction in the contrast sensitivity of M-cells in LGN of marmoset and a 38% reduction in that of P-cells (Camp et al. 2009), considerably more than the brief exposures here, where this reduction was, respectively, 23 and 9%.

Our experimental design was to measure responses to brief test pulses (duration 0.2 s), so the tests themselves will have minimal influence on the adaptation state of the neuron under study. We expected the brief adaptors to have only a small effect, and that we would, therefore, need to average over many repetitions of the test stimuli; so to obviate any slow fluctuations in neuronal sensitivity, the adaptation and control trials were interleaved. For an ISI of 0.2 s, there was 1.9 s between the offset of the brief adaptor and the presentation of a test stimulus in the control condition. It is, therefore, possible that the brief adaptors exert an impact on responses nominally obtained in the “unadapted” state, in other words, that our control measurements may underestimate the underlying sensitivity of the neurons, and that our measurements of the impact of adaptation are likely to be lower bounds.

Role of Contrast Gain Controls and Contrast Adaptation

An unresolved question is whether the change in response that is brought about by brief exposure reflects mechanisms of “contrast gain control” or “contrast adaptation”. Baccus and Meister (2002) distinguish contrast gain control as the essentially instantaneous (active within 0.1 s) mechanisms that reduce sensitivity and sharpen the temporal response of visual neurons, whereas contrast adaptation is a slower activity-dependent process that reduces sensitivity, but does not change the temporal response.

Previous work suggests that following a transition from low to high contrast response rate adjusts over 2–10 s (Chander and Chichilnisky, 2001; Baccus and Meister, 2002). This reflects both recruitment of contrast gain controls and contrast adaptation. Following transition from high to low contrast, the maintained rate recovers slowly, so at least one of these mechanisms of sensitivity regulation, usually thought to be contrast adaptation, has a slow time constant of recovery (Solomon et al., 2004; Baccus and Meister, 2002, Manookin and Demb, 2006). The time course of recovery from contrast gain control is less clear.

Here, brief exposure to drifting gratings changed slightly the temporal response to subsequent tests: if temporal re-
response properties depend only on contrast gain control, then, once engaged by the adaptor, they remain active over the time windows (up to 0.4 s) we studied. There is evidence for inhibitory mechanisms with appropriate time constants (Eggers and Lukasiewicz 2011). However, if the contrast gain controls accumulate signals over long time periods, we would expect them to be engaged by stationary patterns. Instead, stationary adapting gratings of the preferred spatial phase had no effect on contrast sensitivity.

A parsimonious explanation for our observations is that the desensitization reflects an activity-dependent mechanism, contrast adaptation, which reduces sensitivity through somatic hyperpolarization (Carandini and Ferster 1997; Manookin and Demb 2006; Sanchez-Vives et al. 2000a; Sanchez-Vives et al. 2000b), or synaptic depression (Carandini et al. 2002; Chance et al. 1998; Chung et al. 2002; Manookin and Demb 2006). The impact of contrast adaptation increases with time of exposure to the adapting stimulus, but it is robust after 2 s of exposure to high contrast (Manookin and Demb 2006) and is greatest for stimuli that cause large responses (Solomon et al. 2004; Camp et al. 2009). An activity-dependent

Fig. 6. Impact of brief exposure to a stationary grating on the contrast response of a population of neurons in LGN. A and B: comparison of contrast sensitivity (imp s⁻¹ unit contrast⁻¹) for drifting gratings of optimal spatiotemporal configuration, during the control condition and after a 0.5-s exposure to a high-contrast stationary grating presented in the preferred spatial phase (A) or the anti-preferred phase (B). Conventions are as in Fig. 3A. C and D: comparison of the response phase advance during control measurements and after adaptation to the preferred phase (C) or anti-preferred phase (D). Conventions are as in Fig. 3B. E and F: comparison of the change in $\sigma$ (top) and $R_{max}$ (bottom) for M-cells, which is brought about by adaptation to the preferred phase (E) or anti-preferred phase (F). Conventions are as in Fig. 3C.

Fig. 7. Summary of the impact of brief exposures on the contrast response. A: average contrast-response function for 20 On-center M-cells, where the offset of a drifting adapting grating preceded the tests by 0.2 s. Filled circles show responses after exposure to a blank screen; open circles show responses after exposure to the adapting grating. B: average contrast response for 13 On-center M-cells obtained after the offset of a stationary adapting grating, which was separated from the tests by 0.1 or 0.2 s. Black circles show responses after exposure to a blank screen, open circles show responses after exposure to a grating of the preferred spatial phase, and gray circles show responses after exposure to a grating of the anti-preferred spatial phase. C and D: average contrast-response of 13 (C) and 12 (D) Off-centre M-cells. Conventions are same as in A and B, respectively. E: average contrast-response of 6 On-center P-cells. Conventions are same as in A, F and G: average contrast-response of 10 (F) and 9 (G) Off-centre P-cells. Conventions are same as in A and B, respectively. In each panel, response modulation amplitude was obtained for each cell by fitting to the PSTH a half-wave-rectified sinusoid at the fundamental frequency. These were then normalized to the response to full contrast in the control condition and then averaged across cells. Error bars show ±1 SE.
mechanism would also allow stationary adaptors of the anti-preferred spatial phase to have a greater impact than those of the preferred phase, because the neuronal activity brought about by the adaptor (the response that occurs at the offset of the anti-preferred stimulus) is closer in time to the tests.

The aftereffect of contrast adaptation is not expressed equally in all preparations and cell classes: in guinea pig, it seems more prominent in Off-cells than On-cells (Manookin and Demb 2006), in primate retina it seems more prominent in On-cells than Off-cells (Chander and Chichilnisky 2001). Here we found greater effect of brief exposures on Off-M-cells than in On-M-cells. The asymmetry is consistent with functional asymmetries in the two types of cells, which include receptive field size, kinetics, and the weights applied to different cone inputs (Chichilnisky and Kalmar 2002; Field et al. 2010; Tailby et al. 2008). While Off-M-cells show a greater reduction in sensitivity after presentation of a drifting adaptor, On-M-cells showed a greater reduction in the maintained rate. The maintained discharge of Off-cells was less than that of On-cells, probably reflecting similar asymmetries in the retina (Chichilnisky and Kalmar 2002; Kremers et al. 1993; Troy and Lee 1994), and so reductions in it may be harder to identify.

Potential Contribution of Thalamic Mechanisms

In these experiments, we did not observe the S-potentials that reflect the activity of the retinal afferents (Bishop et al. 1962; Solomon et al. 2004). We, therefore, do not know if the impact of brief exposures reflects mechanisms in the LGN, or is inherited from the retinal ganglion cells. Other work suggests a potential role of thalamic mechanisms. In cat, LGN presentation of a stationary high-contrast stimulus for 0.2 s leads to a brief period (<0.2 s) of visual desensitization, often followed by a longer period of facilitation (Nelson 1991b). The effect is less when stimuli are configured to stimulate only the receptive field center, and it is thought that intrageniculate inhibition is important in this mechanism (Hirsch and Burmod 1987; McIlwain and Creutzfeldt 1974; Singer and Phillips 1974).

Additionally, there is substantial cortical feedback to LGN neurons, and it is possible that the impact of contrast adaptation involves changes in this (Przybyszewski et al. 2000; Webb et al. 2002). Were feedback important, then the impact of adaptation should reflect the properties of cortical neurons and depend on the relative configuration of the adapting and test stimuli. Our laboratory has previously shown that, at least during prolonged exposure to an adapting stimulus, adaptation transfers completely across orientation and spatiotemporal frequency (Solomon et al. 2004; Camp et al. 2009). This suggests that cortical feedback does not contribute substantially to contrast adaptation in the LGN. Nevertheless, in our previous work and here, both adaptor and test were the size preferred by the LGN neuron under study and therefore smaller than that preferred by most cortical neurons; enlarging the stimulus (but not so much that it engages surround suppression) may make it more effective for cortical neurons and reveal a greater cortical contribution to adaptation in the LGN.

Our measurements were made from anaesthetized animals, in the absence of eye movements. Visual perception is altered during saccadic eye movements, primarily through suppression. Both sensory and nonsensory mechanisms contribute to saccadic suppression, and it is strongest in tasks thought to rely on M-cells (Burr et al. 1994; Mackay 1970). Rapid adaptation in M-cells may, therefore, alter the visual components of suppression, which probably first arise in the retina (Breitmeyer and Valberg 1979; Derrington 1984; Solomon et al. 2006). How these interact with extra-retinal signals, which can be identified as early as the LGN (Reppas et al. 2002; Sylvester et al. 2005), remains unclear.

Relationship to Visual Cortical Responses and Natural Viewing

Prolonged exposure to high-contrast flickering white noise leads to a prolonged desensitization of retinal ganglion cells and neurons in the LGN (Baccus and Meister 2002; Chander and Chichilnisky 2001; Solomon et al. 2004), but adaptation to movies of natural scenes does not (Mante et al. 2008). Unlike white noise, movies of natural scenes are dominated by low spatial and temporal frequencies (Bex et al. 2009; Dong and Atick 1995; Field 1987; van Hateren 1997), which visual neurons are generally insensitive to, and which therefore may not continually engage mechanisms responsible for contrast adaptation. It follows that a lack of aftereffect for natural movies would be expected, if the impact of a brief, effective segment of the movie were dispersed by less effective segments. Nevertheless, the results here suggest that sensitivity during the presentation of an adapting movie will depend on the recent temporal context (Gallant et al. 1998).

The impact of a brief adaptor on LGN neurons appears to be less than its impact on visual cortical neurons. Muller and colleagues (Muller et al. 1999) show substantial desensitization in primary visual cortex of macaque following 0.5-s presentation of a high-contrast stationary grating, or the same grating modulated in counterphase; the impact of the adaptor was greatest for test stimuli of similar orientation to the adaptor and lasted for 1–5 s. Most neurons in LGN respond well to all orientations, so we expect that there will be no dependence of adaptation on the relative orientation of the adaptor and test. In macaque, the time constant of adaptation to stationary patterns is much shorter in visual cortex than in LGN (McLelland et al. 2009; McLelland et al. 2010), and cortical neurons are less sensitive to low temporal frequencies than subcortical neurons (Hawken et al. 1996). In cat, adaptation to brief exposures of a stationary stimulus has a larger and longer impact in V1 than LGN (Nelson 1991a; Nelson 1991b). Combined, these observations suggest that visual cortical neurons possess rapidly adapting mechanisms that are not expressed, or are less effective, in subcortical neurons.

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GRANTS

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