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Adaptation to Visual Motion in Area MT

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Neuronal Adaptation to Visual Motion in Area MT of the Macaque

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Summary

The responsivity of primary sensory cortical neurons is reduced following prolonged adaptation, but such adaptation has been little studied in higher sensory areas. Adaptation to visual motion has strong perceptual effects, so we studied the effect of prolonged stimulation on neuronal responsivity in the macaque's area MT, a cortical area whose importance to visual motion perception is well established. We adapted MT neurons with sinusoidal gratings drifting in the preferred or null direction. Preferred adaptation reduced the responsiveness of MT cells, primarily by changing their contrast gain, and this effect was spatially specific within the receptive field. Null adaptation reduced the ability of null gratings to inhibit the response to a simultaneously presented preferred stimulus. While both preferred and null adaptation alter MT responses, these effects probably do not occur in MT neurons but are likely to reflect adaptation-induced changes in contrast gain earlier in the visual pathway.

Introduction

The responses of neurons can be influenced by their recent activity, on time scales ranging from milliseconds to minutes. Changes in responsiveness over short time scales are found in many neurons, but adaptation to prolonged stimuli—a term we will reserve for effects lasting many seconds or minutes—is not universal. The responses of neurons in primary visual (Maffei et al., 1973; Movshon and Lennie, 1979; Bonds, 1991; Muller et al., 1999; Dragoi et al., 2000), somatosensory (e.g., Lee and Whitsel, 1992), and auditory (e.g., Malone et al., 2002) cortex are altered by adaptation with stimuli that have no effect on the subsequent responsivity of subcortical neurons (Ohzawa et al., 1985; Bonds, 1991; but see Chander and Chichilnisky, 2001). In V1, adaptation is associated with a prolonged hyperpolarization that is not of synaptic origin, suggesting that the mechanism of adaptation lies largely within the adapted neuron (Carandini and Ferster, 1997; Sanchez-Vives et al., 2000). The adaptation properties of neurons in higher sensory areas are largely unknown. The activity of neurons in these areas has been linked to perception, making a thorough understanding of their adaptation properties desirable for understanding the neuronal basis of perceptual adaptation. Also, studying adaptation in higher sensory areas provides an opportunity to learn whether adaptation is a universal feature of cortical computation or whether it mostly occurs early in a sensory processing stream and is simply inherited as adapted signals pass to downstream cortical areas.

With this motivation in mind, we studied adaptation in neurons in cortical area MT (or V5), an extrastriate visual area that contains a high proportion of neurons that are selective for the direction of motion of visual stimuli (Zeki, 1974; Maunsell and Van Essen, 1983a). Adaptation in MT is of interest for several reasons. First, psychophysical studies suggest that visual motion processing is strongly affected by adaptation (for a review, see Mather et al, 1998). For instance, the prolonged viewing of a moving stimulus causes subsequently viewed static or motion-balanced stimuli to appear to move in the opposite direction (the well-known motion aftereffect, MAE). Second, neural activity in MT has been closely linked to the perception of motion (Newsome et al., 1989; Salzman et al., 1992; Thiele et al., 2000), so adaptation-induced changes in MT responses should have perceptual consequences. Third, functional imaging studies suggest that adaptation effects in MT may be profound. Adaptation causes a direction-specific reduction in activity in human area MT+ (Huk et al., 2001; Tolias et al., 2001), and static visual patterns evoke a substantial response in area MT+ after adaptation protocols which induce a perceptual MAE (Tootell et al., 1995; He et al., 1998; Culham et al., 1999; Taylor et al., 2000; but see also Huk et al., 2001).

While a few studies have evaluated the effect of brief adaptation on MT cells (Lisberger and Movshon, 1999; Priebe et al., 2002; van Wezel and Britten 2002), there is only a single report of the effects of prolonged adaptation in MT (Petersen et al., 1985). In that study, adaptation with a dot field moving in the null direction strongly enhanced the response to a subsequent test stimulus, whereas preferred adaptation reduced responsiveness. Other reports of adaptation in the visual motion-processing pathway have focused on the retina (Barlow and Hill 1963) and on primary visual cortex (V1) (Vautin and Berkley, 1977; von der Heydt et al., 1978; Hammond et al., 1988; Marlin et al., 1988; Saul and Cynader, 1989b; Giaschi et al., 1993). In all of these studies, the effect of adaptation was evaluated with stimuli of a single contrast, making it difficult to distinguish between effects involving changes in neuronal response gain and contrast gain. This distinction is important: a change in response gain involves a reduction in the cell's ability to fire at high rates and may simply reflect a deleterious fatigue; a change in contrast gain or sensitivity, on the other hand, involves a beneficial shift in the neuron's operating range, allowing the cell to encode large fluctuations in stimulus strength with a limited dynamic range (Movshon and Lennie, 1979; Albrecht et al., 1984; Ohzawa et al., 1982, 1985).

To determine how MT responses adapt to prolonged stimulation, and whether changes in response strength are caused by changes in response gain, contrast gain, or both, we measured the effect of adaptation on the subsequent response to stimuli of varying contrast. Ad-

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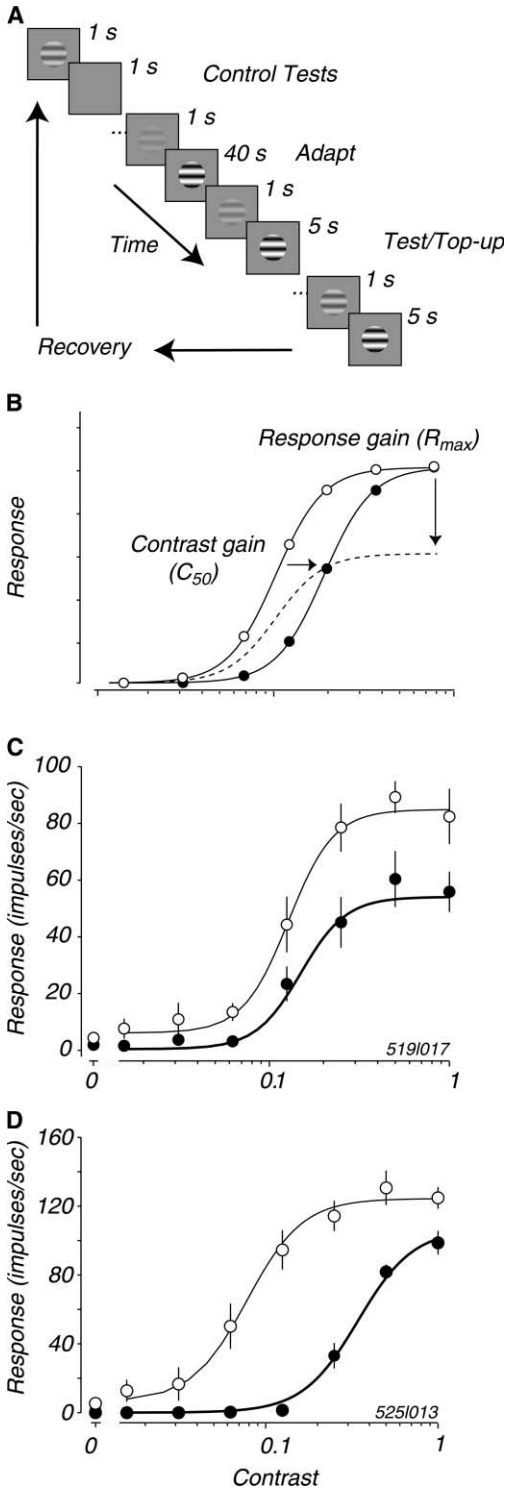

Figure 1. Motion Adaptation in Area MT

(A) Schematic diagram of the adaptation protocol. We measured responses to drifting gratings of variable contrast before and after adaptation to a grating of unit contrast presented for 40 s; adaptation level was maintained by 5 s "top-up" stimuli.

(B) Two potential effects of adaptation on the contrast response function. Changes in response gain compress the response range, whereas changes in contrast gain alter the range of contrasts over which the cell responds.

(C) Adaptation effects in an example MT cell. Contrast-response functions measured before (open symbols, thin line) and after (filled symbols, thick line) adaptation. The primary effect of adaptation is to reduce the maximum firing rate of the cell, rather than the range of contrasts evoking a response.

(D) Adaptation in a second example MT cell which caused a substantial change in contrast gain, and had little effect on response gain.

aptation strongly reduced the responsiveness of MT cells, primarily (though not exclusively) by changing contrast gain. Because similar adaptation effects have been described in V1, an area from which MT receives substantial direct and indirect input (Maunsell and Van Essen, 1983b), we wished to learn whether the effects we observed in MT were direct effects occurring in that area or could be explained by effects inherited from V1. We reasoned that in the latter case, adaptation would be limited in spatial extent by the size of receptive fields in V1. We found that the effect of adaptation was indeed spatially specific within the RF, consistent with contrast gain regulation occurring early in the visual stream, or at least prior to synaptic integration within MT cells. We also evaluated the effect of adapting MT cells with stimuli drifting in their null direction. Such stimuli often inhibit MT neurons (Snowden et al., 1991; Qian and Andersen, 1994; Heeger et al., 1999), but the effect of adaptation on this inhibition is unknown. We found that null adaptation weakens the suppressive effect of null motion, consistent with the prediction of models of the MAE (see review in Mather et al., 1998; Grunewald and Lankheet, 1996).

Our results provide information about the magnitude and characteristics of adaptation in MT, about how the visual system regulates contrast gain following prolonged stimulation, and about the cellular mechanisms responsible for adaptation.

Results

We recorded from 101 single MT units in 15 anesthetized, paralyzed macaque monkeys. All cells had RFs within 25° of the fovea, and most were within 15°.

Effect of Adaptation on Contrast Gain in MT

To probe for changes in contrast and response gain in MT, we recorded responses to drifting sine wave gratings (1 s duration) of varying contrast before and after presenting a 40 s, full-contrast grating drifting in the cell's preferred direction (Figure 1A). Top-up adaptation stimuli (5 s) were presented between each pair of post-adaptation test stimuli. The size, spatial frequency, and drift rate of the test, adaptation, and top-up gratings were identical and were optimized for each cell (see Experimental Procedures). To distinguish between changes in contrast gain and response gain, we fit the contrast response functions of our cells with the following equation:

$$R = R_{max} \frac{c^n}{(c^n + c_{50}^n)} + m$$

using a χ^2 minimization algorithm (STEPIT; see Experimental Procedures). A change in the parameter R_{max} captures a change in the response range of a cell or

an adjustment of response gain (Figure 1B), whereas a change in c_{50} indicates a horizontal shift of the contrast response function or an alteration in contrast gain (Figure 1B). A change in the spontaneous rate, m, shifts the entire response curve vertically. In preliminary analyses, we found that adaptation often caused statistically reliable changes in c_{50}, R_{max}, and/or m, but rarely affected n. We therefore fitted our contrast response data allowing c_{50}, R_{max}, and m to assume different values for the control and adapted data sets, but forcing n to assume a single value optimized jointly for both conditions. These fits described our data well, accounting for 93% of the variance on average.

An example of the effect of adaptation on the contrast response function of an MT cell is shown in Figure 1C. Before adaptation (open symbols; thin line shows fit to the data), this cell fired above spontaneous rate at contrasts greater than $\sim$0.03, and the response saturated at contrasts around 0.3. Adaptation shifted the contrast response function downward (closed symbols; thick line), due to a reduction in the spontaneous rate from 6.1 to 0.4 ips (leftmost open and closed symbols), and reduced the R_{max} value from 79 to 54 ips. The range of contrasts that evoked a response from the cell was unchanged (c_{50} increased from 0.13 to 0.15). However, adaptation that caused a substantial reduction in response gain without a change in contrast gain was atypical. Figure 1D shows data from a second, more representative cell, in which adaptation virtually eliminated the response at low contrasts ($<\sim$0.2) but had little effect on the response at full contrast. As a result, c_{50} increased from 0.08 to 0.34 while R_{max} decreased only slightly (from 118 to 106 ips). The main effect of adaptation in this case was thus a change in contrast gain.

As suggested by these examples, adaptation caused a change in both response and contrast gain in the population of MT cells studied with this paradigm ($n = 47$). The population distributions for the effect of adaptation on R_{max} and c_{50} are shown in Figures 2A and 2B, expressed as ratios of the values after adaptation compared to those before adaptation. The mean R_{max} ratio was 0.78 ($p = 0.011$), indicating that on average adaptation caused only a small change in the maximum firing rate of MT cells. The c_{50} ratio, on the other hand, was almost always greater than 1 (mean 3.28, $p < 0.001$), indicating that adaptation caused a substantial change in the contrast gain. Adaptation also consistently reduced the average spontaneous rate of MT cells, from 6.0 ± 0.5 to 2.4 ± 0.4 ips (Figure 2C; parameter m of the model; $p < 0.001$), which recovered on average with an exponential time course with a time constant of 14.5 s (measured in a subpopulation of MT cells, $n = 26$). We conclude that MT neuronal responsivity is affected significantly by adaptation, due primarily to a reduction in contrast gain.

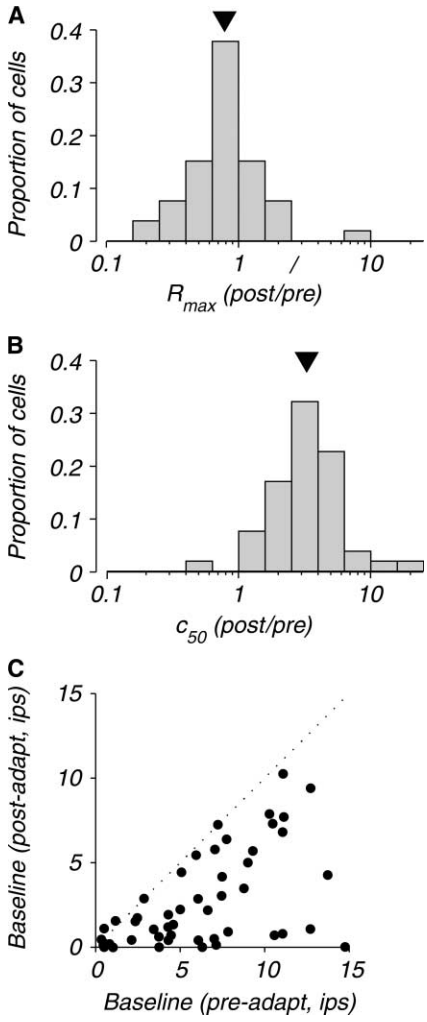

Figure 2. Distribution of Changes in Contrast Response Function Fits for a Population of MT Cells

(A) Histogram of R_{max} values before and after adaptation. Arrowhead indicates geometric mean (0.78, $p = 0.01$, $n = 47$).

(B) Histogram of c_{50} values before and after adaptation. c_{50} consistently increases after adaptation (geometric mean 3.28, $p < 0.001$).

(C) Spontaneous rate is reduced by adaptation. Dotted diagonal line indicates equal firing rate before and after adaptation.

Spatial Specificity of Adaptation

The change in MT contrast gain described in the preceding section could be a direct effect on MT or could be due to effects occurring earlier in the visual system (e.g., V1) (Ohzawa et al., 1982, 1985; Bonds, 1991). We distinguished between these possibilities by investigating the spatial specificity of adaptation in the MT receptive field. If the effect of adaptation was inherited from V1, or some other area with RFs much smaller than those in MT (Albright and Desimone, 1987), then adaptation should only affect colocalized test stimuli (i.e., those exciting the same population of V1 cells affected by the adaptation stimulus). If, on the other hand, adaptation has a direct effect on MT neurons, then the response of the cell would be reduced for all test stimuli, regardless of their position in the RF. We evaluated the spatial specificity of adaptation with stimuli half the diameter of the optimal size, which provided potent stimulus drive to MT cells (65% $\pm$ 4% of the response to the full RF stimulus; $n = 29$). We measured responses to various contrasts of these stimuli presented to each of two subregions before and after adapting one subregion with a 40 s full-contrast grating. The sequence and duration of the test, adapt, and top-up stimuli were the same as

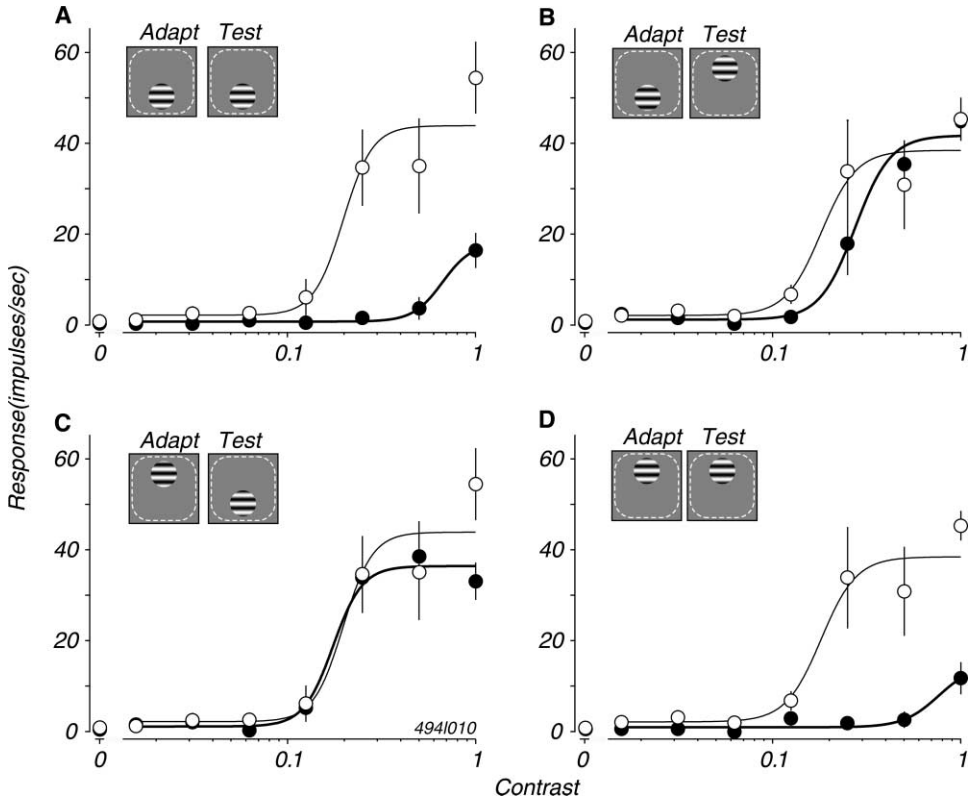

Figure 3. Adaptation Effects Are Spatially Specific in an MT Receptive Field

Each panel compares contrast-response functions for a single neuron, measured before (open symbols, thin line) and after (closed symbols, thick line) adaptation. The spatial arrangement of the adapting and test gratings is indicated above each panel.

(A and D) When the adapting and test stimuli were colocalized, the response of the cell was strongly reduced.

(B and C) Responses were largely unaffected when the adapting and test stimuli were presented in different patches.

those shown in Figure 1A. After we had verified that the neuron had recovered from adaptation, we repeated the measurements with the adapting stimulus in the other subregion of the receptive field, to give four adapt-test combinations in all.

The response of an example cell studied with this adaptation paradigm is shown in Figure 3. The icons in each panel indicate the relative placement of the adaptation and test stimuli. In Figure 3A responses before (open symbols; thin lines) and after (closed symbols; thick lines) adaptation are shown for adaptation and test stimuli presented to the same location in the RF. The effect of adaptation in this case is similar to that observed with full RF adaptation: responses were considerably weaker after adaptation, due to a change in both response (by a factor of 0.48) and contrast (by 3.8) gain. The effect of adapting one subregion of the RF and testing in another is shown in Figure 3B: the contrast response functions before and after adaptation look nearly identical. The data shown in Figures 3C and 3D show the same spatial specificity for adaptation in the second region of the RF.

We characterized the adaptation effect for each subregion of our population of cells in the same manner used for the full RF data (on average the fits captured 94% of the variance in the data). The R_{max} and c_{50} values obtained for colocalized adaptation and test stimuli are shown in Figures 4A and 4B, respectively; those from different adaptation and test locations are shown in Figures 4C and 4D. Each cell is counted twice in each histogram: once for each subregion tested. When the adaptation and test stimuli are presented to the same subregion of the RF, the effect is similar to that observed following full RF adaptation. The R_{max} value decreased by a factor of 0.67 on average (Figure 4A, $p < 0.001$) and c_{50} increased 3-fold (Figure 4B, $p < 0.001$). The adaptation had little effect on the response to stimuli placed in another location in the RF (Figures 4C and 4D): the average R_{max} and c_{50} ratios were 0.88 ($p = 0.002$) and 0.94 ($p = 0.38$), respectively, when the test and adapting stimuli were not colocalized.

Since adaptation stimuli presented to a subregion of the RF were only capable of reducing the response to colocalized test stimuli, the contrast gain effects we observe in MT are likely to reflect a change in the strength of feedforward inputs rather than a direct effect on the MT cell. The spatial specificity of adaptation thus suggests that the regulation of contrast gain occurs early in the visual system and is inherited by subsequent areas, rather than occurring at multiple levels of the system.

Null Adaptation

Models of visual motion processing suggest the need for a stage of opponent processing in which the response to stimuli moving in one direction is subtracted from those

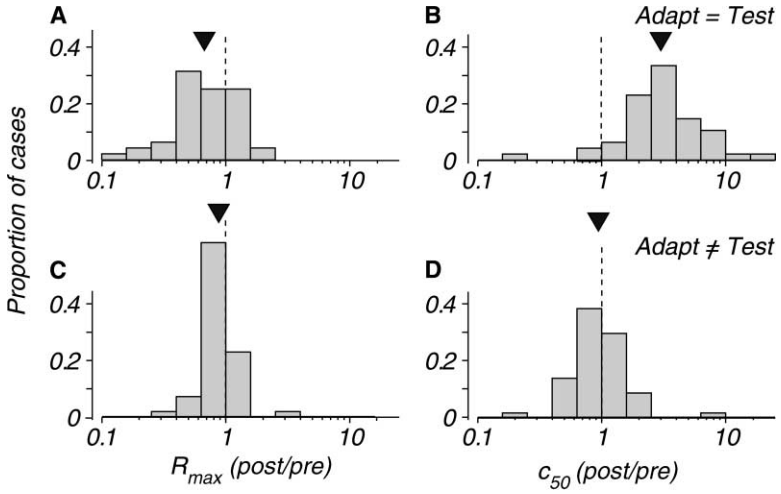

Figure 4. Distribution of Changes in R_{max} and c_{50} for a Population of MT Cells

Adaptation causes a slight reduction in R_{max} (A) and a substantial increase in c_{50} (B) when the adaptation and test stimuli are presented in the same location in the RF ($n = 50$ cases in 29 cells). R_{max} (C) and c_{50} (D) change little when the adaptation and test stimuli are presented to different locations in the RF ($n = 58$ cases). Arrowhead indicates geometric mean.

moving in the opposite (Adelson and Bergen, 1985; Qian et al., 1994; Simoncelli and Heeger, 1998). Experimental results suggest that MT cells might implement this subtraction, as they are inhibited by motion opposite to their preferred direction ("motion opponency") (Snowden et al., 1991; Qian and Andersen, 1994; Heeger et al., 1999). Models of the motion aftereffect propose that the strength of inhibition from null stimuli should be reduced by adaptation (see review in Mather et al., 1998; Grunewald and Lankheet, 1996), while other studies have suggested that adaptation should lead to a strengthening of inhibitory input (Dealy and Tolhurst, 1974; Ohzawa et al., 1985; Barlow, 1990; Wainwright et al., 2002).

To measure the effect of null adaptation on MT neurons, we recorded the response of neurons to the combination of a fixed contrast (0.25), full RF grating drifting in the preferred direction combined with a grating of varying contrast (0–0.75) drifting in the null direction. We compared responses to these compound stimuli before and after null adaptation using our standard adaptation protocol. The response of an example cell to a 0.25 contrast preferred grating, as a function of increasing null grating contrast, is shown in Figure 5A. The response to the preferred grating, when presented alone, was 43 ips (leftmost open symbol). Superimposing a null grating had little effect on the response of the cell (open symbols, thin line), until the contrast of the null grating exceeded 12.5%, at which point the response of the cell was strongly reduced. At the highest null contrast (0.75; rightmost open symbol), the response of the cell was suppressed below the spontaneous firing rate (dashed line). Null adaptation at full contrast had little effect on the response of the cell to the preferred grating alone (leftmost closed symbol) or to the preferred grating combined with low contrast null gratings (closed symbols, thick line), or on the spontaneous firing rate (dotted line). The suppression observed at null contrasts of 0.25 and above, however, was strongly reduced after adaptation. For instance, the evoked response to a 0.5 contrast counterphase grating (0.25 null grating and 0.25 preferred grating; arrow in Figure 5A) increased markedly from 2 ips above the spontaneous rate to 20 ips. Moreover, the response of the cell was no longer suppressed below the spontaneous rate by even the highest null contrast (rightmost closed symbol).

We fit the data from each cell in our data set ($n = 22$) with the following model:

$$R = m + R_{max}c_{pref} - b\frac{c_{null}^n}{(c_{null}^n + c_{50}^n)}$$

where c_{pref} and c_{null} are the contrast of the preferred and null gratings; negative responses in the model were set to zero. The model consists of three terms: the spontaneous activity, m; the response to a preferred grating scaled by R_{max}; and a subtractive inhibitory term for the null stimulus. This final term is identical to that used to describe the contrast-response functions in the previous sections, and its strength is determined by the contrast sensitivity parameter, c_{50}, and a scaling factor, b, which sets the response gain of the subtractive term. We found that the best fits were obtained by allowing the parameters R_{max} and c_{50} to vary between the pre- and postadaptation sets, while using a single value, optimized by the fitting routine, for the pre- and postadaptation values of the other parameters (see Experimental Procedures). The fits accounted for 88% of the variance in the data on average.

The primary effect of null adaptation was to increase c_{50} (Figure 5B; geometric mean ratio 1.43; $p = 0.015$), which reduces the sensitivity of the subtractive, inhibitory term in the model. The increase in c_{50} can be viewed as a change in contrast gain of neurons tuned to the null motion, with a consequent reduction in their ability to suppress the recorded cell's response to its preferred stimulus. Although allowing the R_{max} to vary improved the quality of fit, null adaptation had essentially no effect on the response to low contrast, preferred stimuli presented alone—R_{max} was unchanged by adaptation (geometric mean of 1.09, $p = 0.32$; Figure 5C). Combined with our finding that preferred adaptation strongly reduces the response to the same low-contrast preferred stimulus (by 68% on average; $p < 0.001$), these results suggest that changes in contrast gain are direction dependent in the primate visual system (see Harris et al., 2000 for opposite finding in the fly). Finally, null adaptation had little effect on the spontaneous firing rate of the cells, which increased from 8.8 ± 1.5 to 10.6 ± 2.4 ($p = 0.24$).

The reduced efficacy of opponent, inhibitory input

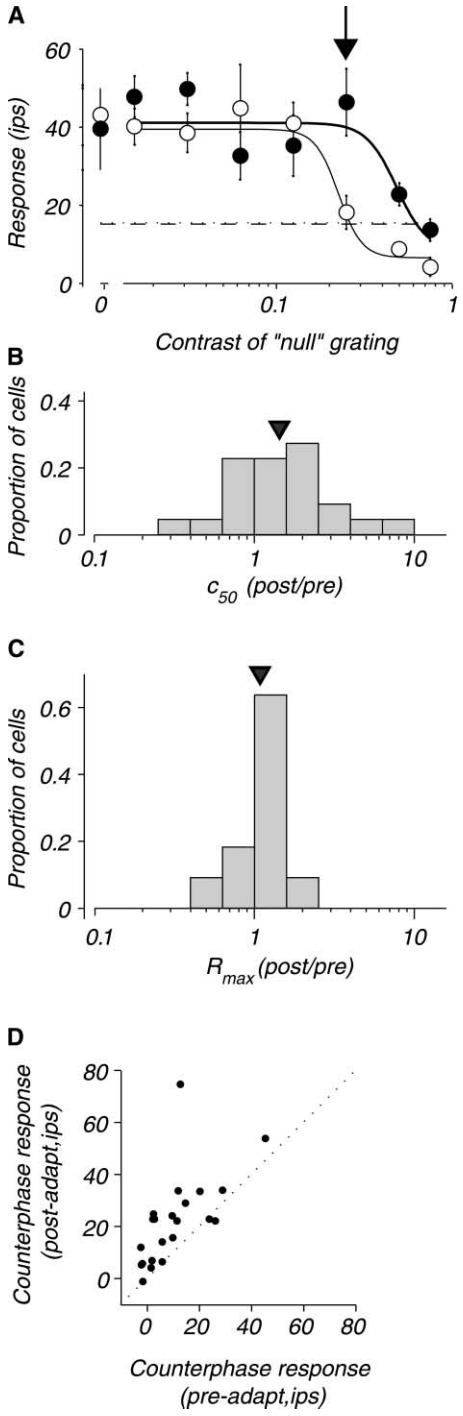

Figure 5. Null Adaptation Weakens Opponent Input

(A) Responses of an MT neuron to a low-contrast, preferred stimulus and a superimposed null grating of varying contrast before (open symbols, thin line) and after (closed symbols, thick line) null adaptation. Dashed and dotted line (overlying) indicate spontaneous activity before and after adaptation, respectively.

(B and C) Histograms of the effect of null adaptation on the c_{50} (B) and R_{max} (C) parameters of the model (see text; n = 22). Adaptation causes an increase in c_{50}, but has little consistent effect on R_{max}. Arrowhead indicates geometric mean.

(D) Effect of null adaptation on the response to a counterphase test stimulus. Dotted line indicates equal responses before and after null adaptation. Negative responses indicate that the response was below the spontaneous firing rate.

caused the response to a counterphase grating to be strongly enhanced after null adaptation (Figure 5D), increasing on average from 10 to 22 ips ($p = 0.013$). The enhanced counterphase response is a direct correlate of the flicker MAE (Mather et al., 1998) as the neurons' increased response rate signals the presence of motion in their preferred direction, opposite to that of the adaptation direction. As a result, we wished to determine whether the decay of the enhancement after the end of adaptation was similar to the decay of the MAE percept reported in human psychophysical studies. To this end, we recorded the response of a subpopulation of MT neurons ($n = 5$) to a counterphase test stimulus before and after 40s of null adaptation. The test stimuli were 1s in duration and separated by 2–3s periods in which a blank screen was shown; no top-up adaptation was provided. We found that the response to the counterphase grating returned to its preadaptation level after an average of 18 $\pm$ 4s, similar in duration to the MAE percept in human subjects measured with the continuous presentation of a counterphase grating test stimulus (up to 14s) (Ashida and Osaka, 1994).

We conclude that null adaptation weakens the strength of opponent input to MT neurons, and that this effect can be explained by a change in the contrast gain of neurons tuned to the adaptation direction. Weakened inhibition, in turn, causes an enhanced response to motion-balanced stimuli such as counterphase gratings. Null adaptation has little effect on spontaneous firing or on the response to preferred stimuli.

Discussion

We find that MT neurons undergo substantial changes in responsiveness after adaptation, due primarily to a reduction in contrast gain with response gain being reduced to a lesser degree. Adaptation effects are specific for position in the RF, indicating that contrast gain can be regulated independently in different subregions of the RF and that contrast gain effects in MT are likely to reflect a change in the strength of feedforward input. Null adaptation has little effect on the response to preferred stimuli or on spontaneous firing, but reduces the ability of null motion to inhibit the response to a simultaneously presented preferred grating. As a result, the response to a counterphase grating increased substantially after null adaptation, apparently a direct correlate of the MAE.

Regulation of Contrast Gain in MT

Preferred adaptation has been shown to reduce the subsequent responsiveness of direction-selective units in the rabbit retina (Barlow and Hill, 1963), in cat primary visual cortex (Vautin and Berkley, 1977; Hammond et al., 1988; Saul and Cynader, 1989b; Giaschi et al., 1993), and in macaque area MT (Petersen et al., 1985), but the interpretation of these results was complicated by a number of factors. First, different stimuli were often used to adapt and test (e.g., testing with bars after adapting with texture patterns by Petersen et al. [1985]), which could confound differences between stimuli with the susceptibility of the cells to adaptation. Second, many of the cells studied in primary visual cortex were not strongly direction selective. Finally, the effect of pro-

longed stimulation was evaluated using a test stimulus of fixed contrast, making it unclear whether adaptation caused a change in response gain or a functionally beneficial change in the cells' contrast gain.

Our finding is in broad agreement with these previous studies in that preferred adaptation reduces the responsiveness of MT cells. This is due primarily to a change in contrast gain, although adaptation also reduces response gain. In a number of cells, the substantial change in contrast gain resulted in a lack of response saturation after adaptation (e.g., Figures 3A and 3D). As a result, the R_{max} fits for these cells were not well constrained by the data. This was evident when we examined the fit error surfaces and found that a range of c_{50} and R_{max} combinations provided reasonable fits to the data. However, we believe that our estimate of the change in R_{max} for our population of cells is meaningful. First, we found that small manipulations of the fitted R_{max} resulted in significantly worse fits. For instance, increasing the fitted R_{max} value for each cell by 20% caused the variance accounted for by the fits to drop from 93.5% to 89.9% ($p = 0.03$), even when new values of the other parameters were chosen by the fitting routine. Second, we estimated the changes in the maximum response rate in a second, model-independent manner—we calculated the ratio of the response at full contrast after adaptation to the response before adaptation. The mean value of this response ratio was 0.65 for the full receptive field data (compared to 0.78 for the mean fitted R_{max} value) and 0.61 for the colocalized condition in the spatial specificity experiments (compared to the mean R_{max} value of 0.67). This concordance suggests that our estimates of changes in R_{max} accurately represent the modest decrease in firing rate observed at full contrast, and that changes in c_{50} are therefore of much greater importance.

The contrast gain change we observed in MT is similar to that observed in previous studies in cat (Ohzawa et al., 1982, 1985; Albrecht et al., 1984) and monkey primary visual cortex (Sclar et al., 1989). The effects we observed are inconsistent with the suggestion that contrast gain in the magnocellular pathway is unaffected by adaptation (Sclar et al., 1990). Since MT neurons are extremely sensitive to contrast and have responses that saturate at relatively low contrasts, modifying contrast gain may allow MT neurons to signal small changes in the contrast of moving stimuli over a wide range of absolute contrasts, a task in which MT neurons may play an important role (Thiele et al., 2000).

The change in MT contrast sensitivity we observed could explain a number of perceptual effects. Figure 6 represents the effect of adaptation for our entire population by normalizing and averaging the responses of all cells. As suggested by data from representative cells (e.g., Figure 1D), adaptation shifts the aggregate MT contrast-response function to the right, reducing contrast gain. This shift predicts an increase in the detection threshold for low-contrast drifting targets (as described by Tolhurst, 1973), since higher contrasts are needed to evoke a response distinguishable from baseline. Moreover, the change in contrast gain would be expected to reduce the apparent contrast of suprathreshold gratings, consistent with the psychophysical findings of Snowden and Hammett (1996). The curves fit to the aggregate data in Figure 6 are separated by a factor of about three along the contrast axis, so that after adaptation, roughly three times as much contrast is required to elicit a given preadaptation response—thus adaptation reduces "apparent contrast" by a factor of three. Finally, the inability of null adaptation to affect the response to low-contrast preferred stimuli suggests that the changes in contrast gain are direction tuned, a perceptual effect first described by Sekuler and Ganz (1963).

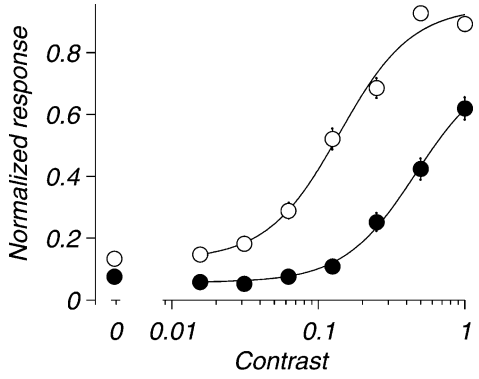

Figure 6. The Effect of Preferred Adaptation on the Aggregate Contrast-Response Function of Area MT

The data for the 47 cells forming the population analyzed in Figure 2 were independently normalized to their peak preadapted firing rates and then averaged to produce the two curves, which are well described by the smooth curves fit from the equation in the text. The shift in c_{50} for the population computed in this way was 3.31, and the shift in R_{max} was 0.86.

Spatial Specificity of Adaptation

Spatially specific adaptation has previously been reported for both simple and complex cells in cat striate cortex (Marlin et al., 1991, 1993), although the effects were measured with flashed bars which evoked weak responses and caused little change in subsequent responsivity. Our finding that adaptation is spatially specific is consistent with similar adaptation specificity for orientation (Muller et al., 1999; Dragoi et al., 2000) and spatial and temporal frequency (Saul and Cynader, 1989a, 1989b; Movshon and Lennie, 1979; Maffei et al., 1973) in V1.

Because adaptation has been shown to cause a change in the contrast gain of V1 neurons, the spatial specificity we observe in MT is likely due to effects inherited from V1, both directly and indirectly through intermediate cortical areas. Synaptic depression of feedforward inputs to MT (Abbott et al., 1997; Tsodyks and Markram, 1997; Chance et al., 1998) may also contribute to the spatial specificity we observe. The spatial specificity of adaptation is not easily reconcilable with a primary role for the activation of a postsynaptic hyperpolarizing conductance in MT neurons, as observed in V1 cells following full RF adaptation with a high-contrast stimulus (Carandini and Ferster, 1997b; Sanchez-Vives et al., 2000). Postsynaptic hyperpolarization would be expected to reduce a cell's response to all test stimuli equally. The spatial specificity in MT is particularly striking given the high firing rates evoked by the adapting stimuli, which should be capable of recruiting activity-

dependent postsynaptic mechanisms such as the hyperpolarizing conductance.

Using a similar spatial specificity paradigm to study short-term adaptation in MT, Priebe et al. (2002) found that the vigorous transient response (lasting less than 100 ms) of MT cells to motion onset is reduced when it is preceded by a brief (64 or 256 ms) conditioning stimulus, even when the test and conditioning stimulus were presented to different locations in the RF. The authors conclude that short-term adaptation is not due to a change in the strength of feedforward inputs. The differing spatial specificity of our results suggest that adaptation effects that follow prolonged (tens of seconds) visual stimulation involve cellular and network mechanisms that are distinct from those recruited by briefer conditioning paradigms.

Inhibition and Adaptation

In addition to the proposed role of synaptic depression and postsynaptic hyperpolarization in mediating adaptation effects, a number of psychophysical and modeling studies have suggested that adaptation may cause a transitory strengthening of inhibition (Dealy and Tolhurst, 1974; Ohzawa et al., 1985; Barlow, 1990). Our results suggest that, at least for inhibitory input provided by null motion, this is not the case: the suppressive effect of null gratings on the response to preferred stimuli is reduced, not strengthened, after null adaptation, due presumably to a change in the contrast gain of cells tuned to the null direction. In a recent study using dynamic random dot stimuli, van Wezel and Britten (2002) reported that short periods (3 s) of null adaptation had little effect on the response to zero coherence random dots. The difference between our results may be due to the shorter adaptation period used in that study.

While inhibition between neurons tuned to opposite directions is weakened, it remains possible that adaptation could strengthen inhibition between neurons tuned to similar directions (Barlow, 1990). One form of this inhibition may be the divisive, inhibitory input MT cells are believed to receive from a population of other MT cells tuned to a wide range of directions (a "normalization" signal similar to that found in V1) (Heeger, 1992; Simoncelli and Heeger, 1998). Could it be that adaptation weakens opponent input, but strengthens this form of inhibitory input (Heeger, 1992; Wainwright et al., 2002)? We feel this is unlikely. Our laboratory (N. Majaj, personal communication) and others (Heuer and Britten, 2002) have found that the response of MT neurons to two simultaneously presented small stimuli is less than the sum of the responses to each presented alone. This sublinear summation is consistent with an inhibitory interaction between stimuli due to the activation of a normalization circuit in MT. Since this interaction occurs for stimuli presented to the same or to different parts of the RF, normalization appears to be a global property of the RF (N. Majaj, personal communication). We find, however, that adaptation remains spatially localized within the RF. Since normalization and adaptation have different spatial specificity, it seems unlikely that adaptation involves a strengthening of inhibitory connections within the normalization circuit. Our conclusion that adaptation does not cause a potentiation of inhibition—of either the opponent or normalizing type—is consistent with the inability of pharmacological agents that block (DeBruyn and Bonds, 1986; Vidyasagar, 1990; McLean and Palmer, 1996) or activate (Vidyasagar, 1990) inhibition to affect the strength of adaptation in V1.

Our null adaptation experiments revealed an apparent correlate of the MAE in MT—an enhanced response to counterphase gratings after adaptation in the null direction. Since the MAE is believed to result from a temporary imbalance in the excitability of motion detectors tuned to different directions (Sutherland 1961; Mather et al., 1998), our finding that adaptation creates such an imbalance by reducing the activity of neurons tuned to the adaptation direction lends further support to the idea that MT is involved in the MAE. A role for MT in the MAE has been suggested by a number of functional imaging studies showing that unidirectional adaptation causes an enhanced response to a stationary visual stimulus (Tootell et al., 1995; He et al., 1998; Culham et al., 1999; Taylor et al., 2000). Although we observed a correlate of the MAE, the enhanced fMRI signal in MT after adaptation is surprising given our finding that preferred adaptation strongly reduces the excitability of MT neurons, whereas null adaptation has little effect on spontaneous rate and a relatively weak effect on response strength in general. Thus, we would expect adaptation to reduce the *overall* level of activity in MT. The difference between this prediction and the increased fMRI signal cited above may be due to a change in the attentional state of the subjects when experiencing the MAE (Huk et al., 2001).

Does Extrastriate Cortex Adapt?

Our finding that changes in contrast gain in MT are likely inherited from an earlier cortical area suggests that the visual system uses an information processing strategy in which adaptation to a particular stimulus attribute occurs early in the processing stream, rather than at multiple levels of the system. Thus, just as adaptation to luminance levels occurs in the retina (Shapley and Enroth-Cugell, 1984), adaptation to contrast may occur only in primary visual cortex and then be encoded in the output that V1 sends to other cortical areas. While contrast adaptation in MT may be explained by effects occurring early in the visual system, it remains possible that extrastriate neurons adapt to stimuli which drive them strongly while activating cells in earlier cortical areas only weakly. Such stimuli might consist of features that only weakly drive neurons in V1, but combine to provide potent input to extrastriate neurons. Moreover, extrastriate neurons may adapt in natural viewing conditions because their large spatial receptive fields will make the sensory drive they receive relatively insensitive to eye movements and, thus, steadier over time than that provided to neurons early in the visual system. It remains to be seen whether extrastriate neurons adapt to stimuli that fail to cause substantial effects earlier in the visual pathway.

Experimental Procedures

We made recordings in 13 cynomolgus macaques (*Macaca fascicularis*), 1 bonnet macaque (*M. radiata*), and 1 pig-tailed macaque (*M. nemestrina*). All animals were adult males.

The procedures used in our laboratory for single-unit recording in anesthetized, paralyzed macaque monkeys have been described in detail elsewhere (Cavanaugh et al., 2002). Briefly, animals were premedicated with atropine (0.05 mg/kg) and diazepam (1.5 mg/kg) and initially anesthetized with ketamine HCl (10 mg/kg). Anesthesia was maintained during recording by intravenous infusion of the opiate anesthetic sufentanil citrate (Sufenta, 4–8 μg/kg/hr). To minimize eye movements, the animal was paralyzed with intravenous infusion of vecuronium bromide (Norcuron, 0.1 mg/kg/hr). Vital signs (EEG, ECG, end-tidal PCO_2, temperature, and lung pressure) were monitored continuously. The pupils were dilated with topical atropine and the corneas protected with gas-permeable hard contact lenses. External supplementary lenses were chosen by direct ophthalmoscopy to make the retinas conjugate with a screen 80–100 cm distant; the lenses were adjusted as necessary to optimize the response of recorded units. All experimental procedures were approved by the New York University Animal Welfare Committee.

Recordings were made either with platinum/tungsten (Thomas Recording; Giessen, Germany) or tungsten-in-glass microelectrodes (Merrill and Ainsworth, 1972). Electrode penetrations were made in a parasaggital plane at an angle of 20° degrees from horizontal, through a craniotomy centered 16 mm lateral to the midline and 4 mm posterior to the lunate sulcus. Signals from the microelectrode were amplified, bandpass filtered (typically 300 Hz to 10 kHz), and fed into a hardware dual time-amplitude window discriminator (Bak Electronics) and audio monitor. Spike times were saved with a temporal resolution of 0.25 ms. The receptive field location and minimum response field were determined by hand using hand-held stimuli projected onto a tangent screen.

To allow histological confirmation of the recording sites, we made small electrolytic lesions at the end of each track by passing DC current (2 μA for 5 s, tip negative) through the recording electrode. At the end of the experiment, the monkeys were killed with an overdose of Nembutal and perfused through the heart with 0.1 M PBS followed by 4% paraformaldehyde in 0.1 M PBS. Sections (40 μm) were stained for Nissl substance with cresyl violet or for myelin using the method of Gallyas (1979). Most recording locations could be confirmed directly. In the remaining cases, we relied on the proximity to histologically confirmed recording sites and the high proportion of directional cells with relatively small RFs as evidence that the recordings were made in MT (Desimone and Ungerleider, 1986).

Visual Stimuli

Stimuli were luminance modulated, drifting sine-wave gratings presented at a frame rate of 100 Hz and a resolution of 1024 × 731 pixels. The monitor (Eizo T550) subtended ~22° of visual angle and had a mean luminance of approximately 33 cd/m^2. Stimulus contrast is defined as the difference between the maximum and minimum luminance divided by their sum. For each cell, we determined, in order, the optimal direction, spatial and temporal frequency, position, and size of a drifting sine wave grating. Gratings were presented to the dominant eye in one or two circular apertures, surrounded by a gray field of average luminance.

Adaptation Protocol

We measured the effects of adaptation on the contrast-response function using preferred gratings whose contrast ranged in equal logarithmic steps between 0.016 and 1.0. Spontaneous activity was measured either using a blank stimulus intermixed with the test stimuli, or during a brief epoch immediately preceding and following the stimulus sequence. We used two adaptation protocols. In the first, a trial consisted of a single randomized sequence of 1 s test stimuli, followed by a 40 s adapting stimulus, and a second sequence of test stimuli, each proceeded by a 5 s top-up stimulus. Each test, adapt, top-up/test trial was followed by at least 3 min of recovery. We recorded three to five trials for each adaptation condition. The test, adapt, and top-up durations in our second adaptation protocol (similar to that described in Movshon and Lennie, 1979) were the same as those described above, but we ran multiple sequences of test stimuli before and after adaptation, with a single recovery period (~15 min) between adaptation conditions. We obtained similar results with the two protocols and pooled the results.

Data Analysis

We fit models to the data using the STEPIT algorithm (Chandler, 1969) to minimize the combined χ^2 error between the model predictions and the recorded responses. We fit the control and adapted data for each cell simultaneously. We considered several variants of each model by allowing different combinations of parameters to vary between the control and adapted data sets; parameters that did not so vary were forced to assume a value that was jointly optimal for both data sets (see Results). We assessed the goodness of fit of each variant by calculating the χ^2 error between the data and the predicted response, and normalizing by the degrees of freedom in the model (for more details, see Cavanaugh et al., 2002). We removed cells from the data set if the fit of the best-fitting model failed to capture at least 60% of the variance for both the pre- and postadaptation data (9 cells of 101). In addition, we removed 6 cells from the preferred adaptation data set because the responses were best described by a model in which c_{50} exceeded unit contrast. All indications of variation in graphs and text are standard errors of the mean. The statistical significance of differences was evaluated with a t test.

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