nature neuroscience

Task difficulty modulates the activity of specific neuronal populations in primary visual cortex

Yao Chen[1], Susana Martinez-Conde[2], Stephen L Macknik[2], Yulia Bereshpolova[3], Harvey A Swadlow[3] & Jose-Manuel Alonso[1]

Spatial attention enhances our ability to detect stimuli at restricted regions of the visual field. This enhancement is thought to depend on the difficulty of the task being performed, but the underlying neuronal mechanisms for this dependency remain largely unknown. We found that task difficulty modulates neuronal firing rate at the earliest stages of cortical visual processing (area V1) in monkey (*Macaca mulatta*). These modulations were spatially specific: increasing task difficulty enhanced V1 neuronal firing rate at the focus of attention and suppressed it in regions surrounding the focus. Moreover, we found that response enhancement and suppression are mediated by distinct populations of neurons that differ in direction selectivity, spike width, interspike-interval distribution and contrast sensitivity. Our results provide strong support for center-surround models of spatial attention and suggest that task difficulty modulates the activity of specific populations of neurons in the primary visual cortex.

One function of our visual system is the detection of rapid changes in the visual environment that could have behavioral importance. The speed[1,2] and sensitivity[3,4] of detection are improved by allocating selective attention to the region of the visual field where the stimulus change is likely to occur. Moreover, increased task difficulty reduces the interference caused by peripheral distracters[5,6], decreasing the likelihood that distracters will deviate the focus of attention[7].

Although the behavioral benefits of spatial attention are well documented and its neuronal mechanisms are increasingly better understood[8–12], the effect of task difficulty on attentional gain is still unclear. Task difficulty modulates functional magnetic resonance imaging (fMRI) blood oxygen level–dependent signals at multiple stages of the visual pathway, including area V1 (refs. 13–15). However, electrophysiological recordings have only found task difficulty–modulated responses in higher cortical areas such as area V4 (refs. 16,17), inferior temporal cortex[18] and the prefrontal cortex[19,20]. Moreover, although previous electrophysiological studies in area V4 indicated that the main effect of increasing task difficulty was an enhancement in visual responses[16], a more recent study found evidence for suppression of visual responses as well[17].

Precise measurements of task-difficulty modulations throughout the cortical visual hierarchy are important for understanding the relative contribution of each area to attentional gain[21]. Although it is now widely accepted that spatial attention modulates the activity of neurons in area V1 (refs. 11,22–27), the extent that V1 activity is modulated by task difficulty remains unclear[28]. Moreover, it is unknown which cell types are most strongly modulated as a function of task difficulty. For example, a recent study in area V4 indicates that both putative inhibitory and excitatory neurons are modulated by spatial attention[29], but it is not known whether both cell types are modulated in earlier cortical areas such as area V1. We used a technique that allowed us to study the visual responses of well-isolated V1 neurons with a great level of detail and to vary the difficulty of an attention task that was spatially localized either inside or outside of the neuronal receptive fields. We found that task difficulty strongly modulated V1 activity and that these modulations could enhance or suppress V1 neuronal responses. Moreover, we observed that the amount of suppression and enhancement depended on the receptive field location (relative to the focus of attention) and the functional properties of the V1 neurons. Some of these results have already been published in abstract form (Chen *et al.*, *Soc. Neurosci. Abstr.* **286.14**, 2005).

RESULTS

We recorded well-isolated V1 neurons from two rhesus monkeys as they carried out a task that required fast detection of a visual stimulus. The recordings were obtained by using an implantable, multi-electrode/microdrive array with ultra-thin electrodes[30] that allowed us to study each neuron for several hours. The combination of the recording stability and the excellent spike isolation allowed us to measure the response properties from each neuron with a great level of detail (**Supplementary Fig. 1** online). In addition to quantifying response modulations to spatial attention and task difficulty, we also measured orientation tuning, direction selectivity, spatial frequency tuning, receptive-field structure (by reverse correlation analysis), response latency, color selectivity, contrast sensitivity, spike width, interspike-interval distribution, response linearity (F1/F0) and the

[1]Department of Biological Sciences, State University of New York, 33 West 42nd Street, New York, New York 10036, USA. [2]Barrow Neurological Institute, 350 West Thomas Road, Phoenix, Arizona 85013, USA. [3]Department of Psychology, University of Connecticut, 406 Babbidge Road, Storrs, Connecticut 06269, USA. Correspondence should be addressed to J.-M.A. (jalonso@sunyopt.edu).

Received 27 January; accepted 22 May; published online 6 July 2008; doi:10.1038/nn.2147

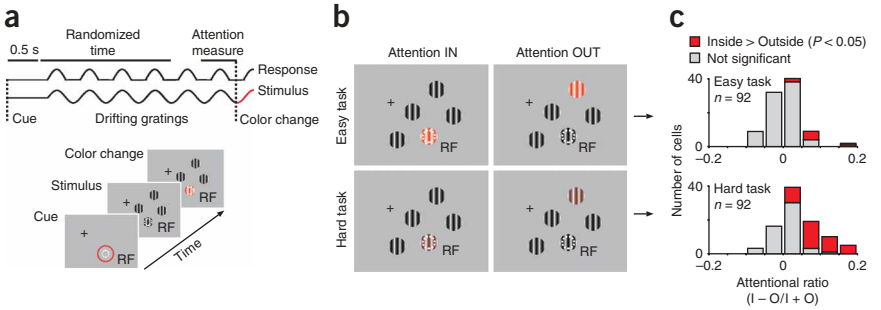

Figure 1 Behavioral task and attentional response ratios measured in V1 single cells during hard and easy tasks. (**a**) Temporal structure of a trial. Two rhesus monkeys were trained to fixate a small cross while covertly attending to a spatial location that was cued at the beginning of each trial. The cue was a thin red ring with a diameter that was threefold larger than the diameter of the neuronal receptive field (RF). Following the cue, drifting gratings were presented simultaneously at five different spatial locations for 1.5–3 s. Following a randomized period of time, one of the gratings changed color/luminance and the animal was tasked with detecting the change by releasing a bar within 0.5 s. The attentional modulations were measured at the last cycle of the drifting grating before the color change. (**b**) The color change could be easy or hard to detect and could occur inside or outside of the receptive field. (**c**) The number of cells that were significantly modulated by attention (red) was much lower during the easy task (top) than during the hard task (bottom). Eight cells were significantly modulated by attention during both the easy and the hard task ($P < 0.05$).

spontaneous firing rate for each neuron. We sought to characterize the functional properties of neurons that are modulated by spatial attention and task difficulty, so as to identify the specific types of neurons that mediate attentional effects.

Effects of spatial attention and task difficulty

During the recordings, monkeys held a bar and fixated a small cross while attending to one of five peripheral drifting gratings, which was cued at the beginning of each trial (**Fig. 1a**). The five gratings had different spatial locations, but they were all identical in terms of orientation and direction of movement, spatial frequency, temporal frequency and size (matching the response properties of the neuron studied). After a randomized period of time that lasted 1.5–3 s, the cued grating changed color and the monkey indicated the color change by releasing the bar as fast as possible (shorter reaction times resulted in larger rewards; reaction times longer than 500 ms were not rewarded). Response modulations to spatial attention and task difficulty were measured in the 500 ms preceding the color change (1–2.5 s after the cue was turned off; **Fig. 1a**). The color change could be either easy or hard to detect (as a result of the change in its color/luminance contrast) and it could take place either inside or outside of the neuron's receptive field (**Fig. 1b**, see Methods). The level of task difficulty was adjusted in each recording session to obtain reaction times that were significantly longer during the hard task than during the easy task ($P < 0.05$, Wilcoxon test). The cue was blocked for both spatial location and difficulty for 20 or more consecutive trials so that the monkeys could maximize their effort in a trial block (that is, if the first trial was difficult to detect, the monkeys knew that the following trials would be also difficult and would need to increase their effort to maximize reward). We studied visual responses from 92 neurons at two or more different levels of task difficulty and two spatial locations of attention. We also measured the response properties of each neuron in detail (average recording duration, 1.6 h; **Supplementary Fig. 1**).

During the easy task, the monkeys detected the color change rapidly (average reaction time, 337 ± 47 ms) and made few mistakes (percentage of rewarded bar releases, 98%), but only 8 out of 92 V1 neurons (8%) were modulated by spatial attention (see Methods for data on each monkey; **Fig. 1c**). During the hard task, the reaction times were significantly higher (394 ± 61 ms, $P < 0.0001$, Wilcoxon test), errors were more frequent (percentage of rewarded bar releases, 86%) and 39 out of 92 neurons in V1 (42%) were modulated by spatial attention (all cells modulated by attention during the easy task were also modulated during the hard task; **Fig. 1c**). We selected the cells that were significantly modulated by attention for further analysis ($n = 39$, $P < 0.05$, Wilcoxon test, see Methods for measurements of significance; **Fig. 1c**). Throughout the text, visual responses measured in the four different conditions of task difficulty and spatial attention will be referred to as Easy (responses during the easy task), Hard (responses during the hard task), Inside (responses while the focus of attention was inside the receptive field) and Outside (responses while the focus of attention was outside the receptive field).

We examined the modulation of V1 visual responses by spatial attention and task difficulty at the last drifting cycle preceding the color change (**Fig. 1a**). Two representative cell examples are shown (cell A and cell B; **Fig. 2**). The most pronounced effect of increasing task difficulty in cell A (from an easy to a hard task; **Fig. 2a**) was response enhancement when spatial attention was located inside the receptive field. In contrast, the most pronounced effect of increasing task difficulty in cell B was response suppression when attention was located outside the receptive field (**Fig. 2b**). Cell A and cell B differed in several other response properties. Cell B had wider spike waveforms and a tighter interspike-interval distribution than cell A. Moreover, unlike cell A, cell B was direction selective, color selective (data not shown) and could not be visually driven with sparse noise stimuli (light and dark spots presented for 40 ms in the receptive field). Other properties, such as spatial frequency tuning and Fourier harmonic F1/F0 ratio, were similar in both cells.

On average, the attentional ratio, (Inside – Outside)/(Inside + Outside), of attention-modulated V1 cells was 0.09 during the hard task, which corresponds to a mean response enhancement of 22% when spatial attention was located inside versus outside the receptive field $\left(100 \cdot \frac{(\text{Inside} - \text{Outside})}{\text{Inside}}\right)$. In contrast, the average attentional ratio during the easy task was significantly lower (0.03, $P < 0.0001$, Wilcoxon test), which corresponds to a modest enhancement of just 7% when attention was inside versus outside of the receptive field (**Fig. 3a**). Clearly, increasing task difficulty made the attentional modulations much stronger in area V1, from a 7% modulation, which matches some V1 measurements in previous studies[21], to a 22% modulation, which approaches the modulations measured in higher cortical areas[8,10,21].

The effect of task difficulty on visual responses was spatially specific. Increasing task difficulty (from an easy to a hard task) enhanced the visual responses of cells with receptive fields at the focus of attention and suppressed the responses of cells with receptive fields outside of the focus. We measured the difficulty ratio, (Hard – Easy)/(Hard + Easy), of the responses from the attention-modulated cells at two spatial locations of attention (**Fig. 3b**). When spatial attention was inside the receptive field, most difficulty ratios were positive (30 out of 39, $P = 0.0008$, χ^2 test), indicating a stronger response from V1 neurons

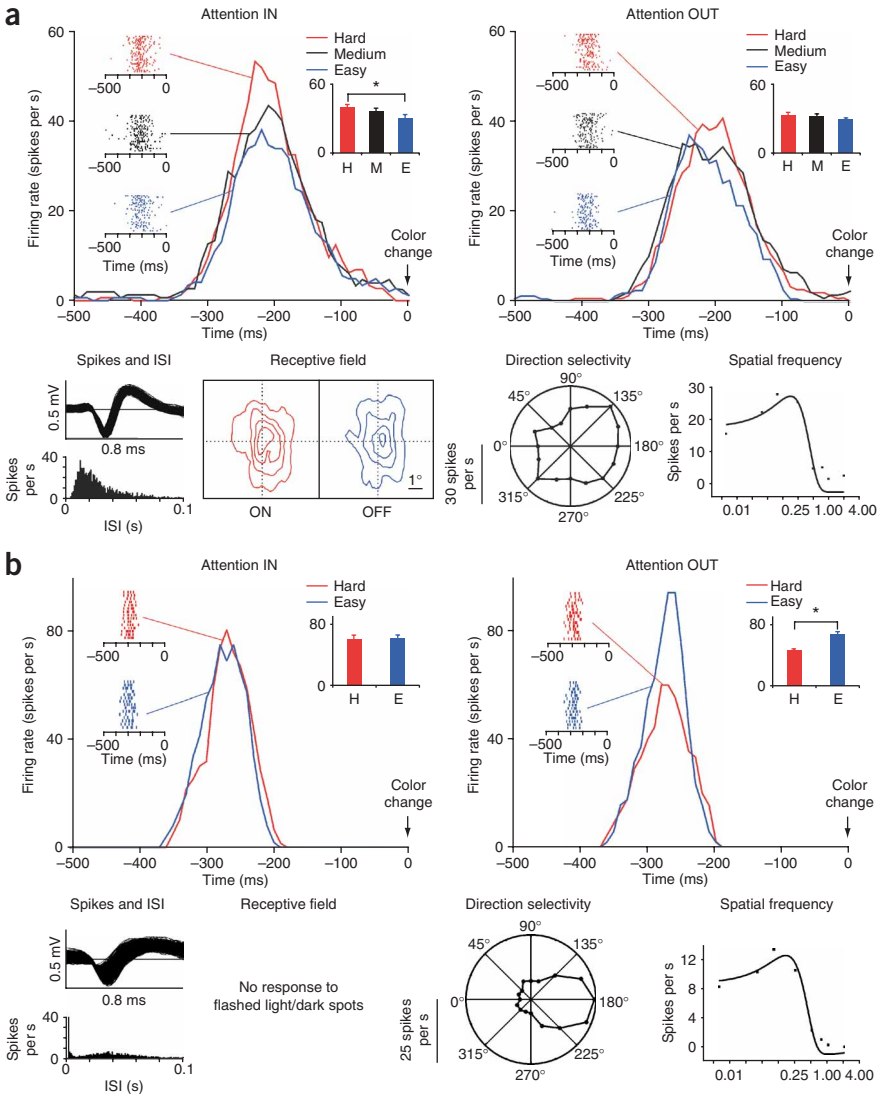

Figure 2 Examples of two V1 cells whose responses were modulated by task difficulty and spatial attention. (**a**) Cell showing response enhancement with increasing task difficulty. The response enhancement was stronger when spatial attention was located inside the receptive field (left) as opposed to outside (right). The PSTHs show visual responses 500 ms before the grating changed color (the last cycle of the drifting grating). The bar graphs on the top right corner of the PSTHs show the average firing rate and s.e.m. measured from the PSTHs. The s.e.m. is defined as one s.d. divided by the square root of the sample size. The star indicates $P < 0.05$, Wilcoxon test. This cell was tested with three different levels of difficulty. The region below the PSTHs shows the spike waveforms, ISI distributions, receptive field measured with reverse correlation, orientation tuning and spatial frequency tuning. (**b**) Cell showing strong response suppression with increasing task difficulty. When spatial attention was outside the receptive field, the cell response was significantly stronger during the easy task than during the hard task (66 versus 45 spikes per s, $P = 0.009$, Wilcoxon test). Notice that, during the easy task, this cell seemed to respond more strongly when attention was outside versus inside the receptive field; however, the difference was not significant (61 versus 66 spikes per s, $P = 0.57$, Wilcoxon test).

during the hard task than during the easy task (response enhancement). In contrast, when spatial attention was located outside of the receptive field, most difficulty ratios were negative (28 out of 39, $P = 0.006$, χ^2 test), indicating a weaker response from V1 neurons during the hard task than during the easy task (response suppression). The magnitudes of the response enhancement and response suppression were significantly correlated to each other ($r = 0.56$, $P < 0.001$; **Fig. 3c**). That is, neurons that showed the strongest response suppression when spatial attention was outside of the receptive field showed the weakest response enhancement when spatial attention was inside of the receptive field. Conversely, neurons that showed the strongest response enhancement when attention was inside of the receptive field showed no response suppression when attention was outside of the receptive field. This suggests that the response suppression and response enhancement driven by an increase in task difficulty could be mediated by different populations of neurons. We investigated this idea further by carrying out a detailed study of the functional properties of neurons modulated by attention.

Functional properties of V1 neurons

Intrigued by the differences in the response properties of cell A and cell B, we divided our population of attention–modulated cells into two groups, difficulty-enhanced and difficulty-suppressed neurons. Difficulty-enhanced neurons were those cells that showed a net enhancement in visual response with task difficulty, such as cell A ($n = 20$), and difficulty-suppressed neurons those that showed a net suppression of visual responses, such as cell B ($n = 19$). By definition, difficulty-enhanced neurons generate the strongest visual responses when the task is hard (**Fig. 4a**) and difficulty-suppressed neurons generate the strongest visual responses when the task is easy (**Fig. 4b**). We noticed that difficulty-enhanced neurons, such as cell A, were usually not directional selective, and had narrow spike-widths and broad interspike-interval distributions (illustrated by four cell examples; **Fig. 4a**). In contrast, difficulty-suppressed neurons, such as cell B, were directional selective, and had broader spike-widths and tighter interspike-interval distributions (**Fig. 4b**).

To quantify the relation between task-difficulty modulations and neuronal functional properties, we calculated a summed difficulty ratio for each cell, $(Hard_s - Easy_s) / (Hard_s + Easy_s)$, where $Hard_s$ = Inside Hard + Outside Hard and $Easy_s$ = Inside Easy + Outside Easy. A positive ratio indicates that the cell responded more strongly during the hard task than during the easy task (independent of attention location) and a negative ratio indicates that the cell responded more strongly during the easy task. Consistent with the examples shown above, the summed difficulty ratio was correlated with the cell direction selectivity in both the sample of cells modulated by spatial attention ($r = –0.58$, $P < 0.001$, $n = 39$; **Fig. 5a**) and the entire sample ($r = –0.25$, $P < 0.02$, $n = 92$, data not shown). Moreover, the summed difficulty ratio was correlated with the cell's spike width ($r = –0.58$, $P < 0.001$; **Fig. 5b**) and the peak of the interspike-interval distribution ($r = 0.45$, $P < 0.004$; **Fig. 5c**). We also found a correlation between the summed difficulty

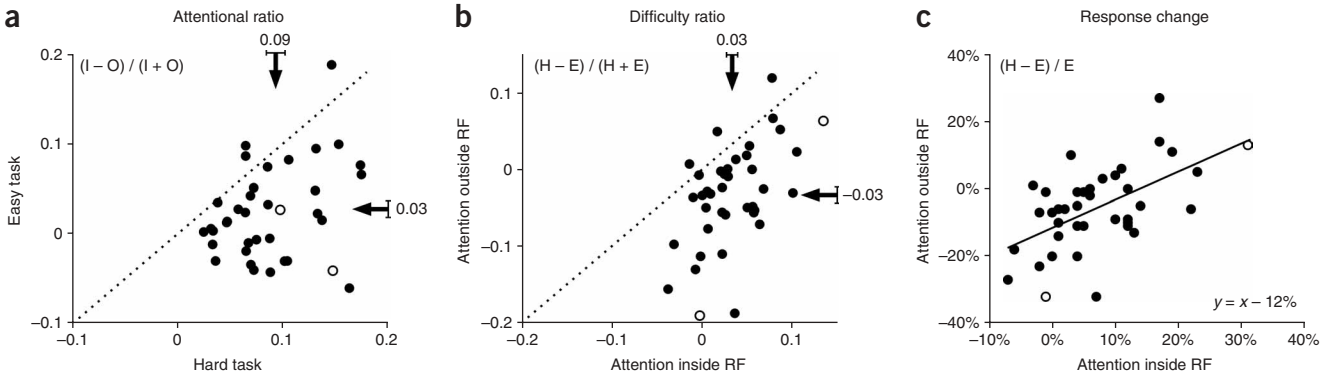

Figure 3 Spatial attention and task difficulty modulations of V1 visual responses. (**a**) The attentional ratio was independently calculated for the hard task (*x* axis) and easy task (*y* axis) as (I – O) / (I + O), where I is the visual response when spatial attention was inside the receptive field (Inside) and O is the visual response when spatial attention was outside the receptive field (Outside). During the easy task, some cells (including cell in **Fig. 2b**) had negative attentional ratios, indicating stronger responses when attention was located outside versus inside the receptive field; however, all attentional ratios were positive during the hard task. The arrows indicate the average ratio and s.e.m. for each condition. (**b**) The difficulty ratio was calculated independently when spatial attention was inside or outside of the receptive field, as difficulty ratio = (H – E) / (H + E), where H is the visual response during the hard task and E is the visual response during the easy task. (**c**) Response change with increasing task difficulty, calculated independently when spatial attention was inside and outside of the receptive field as response change = (H – E) / E. There was a positive correlation between the response change measured when spatial attention was inside and outside the receptive field. Open circles in the three plots (**a**, **b** and **c**) mark the cells illustrated in **Figure 2** (the neuron illustrated in **Fig. 2b** has the lower *y* axis values in the three plots).

ratio and contrast sensitivity ($r = 0.51$, $P < 0.03$), although the sample of cells that we tested for contrast was smaller ($n = 19$; **Fig. 5d**). Notably, the regression lines from some of these correlations seemed to link two separate clusters of cells rather than appear as a continuum (**Fig. 5a**).

To estimate the significance of this observation, we tested all of the scatter plots (**Fig. 5**) for bimodality[31] (Hartigan tests were run in histograms with the *x* axes parallel to the regression lines). These tests revealed a significant bimodal distribution in the projection defined by direction selectivity and the summed difficulty ratio ($P = 0.018$; **Fig. 5a**), supporting the notion that difficulty-enhanced and difficulty-suppressed neurons form two separate clusters. Neurons whose responses were not modulated by spatial attention had intermediate properties between these two clusters (**Fig. 6** and **Table 1**). Other response properties were also compared between clusters but were not significantly different. These included mean firing rate (suppressed with nonmodulated, $P = 0.51$; suppressed with enhanced, $P = 0.89$; nonmodulated with enhanced, $P = 0.67$), response linearity measured as F1/F0 ratio ($P = 0.05$, $P = 0.05$, $P = 0.5$), color sensitivity ($P = 0.81$,

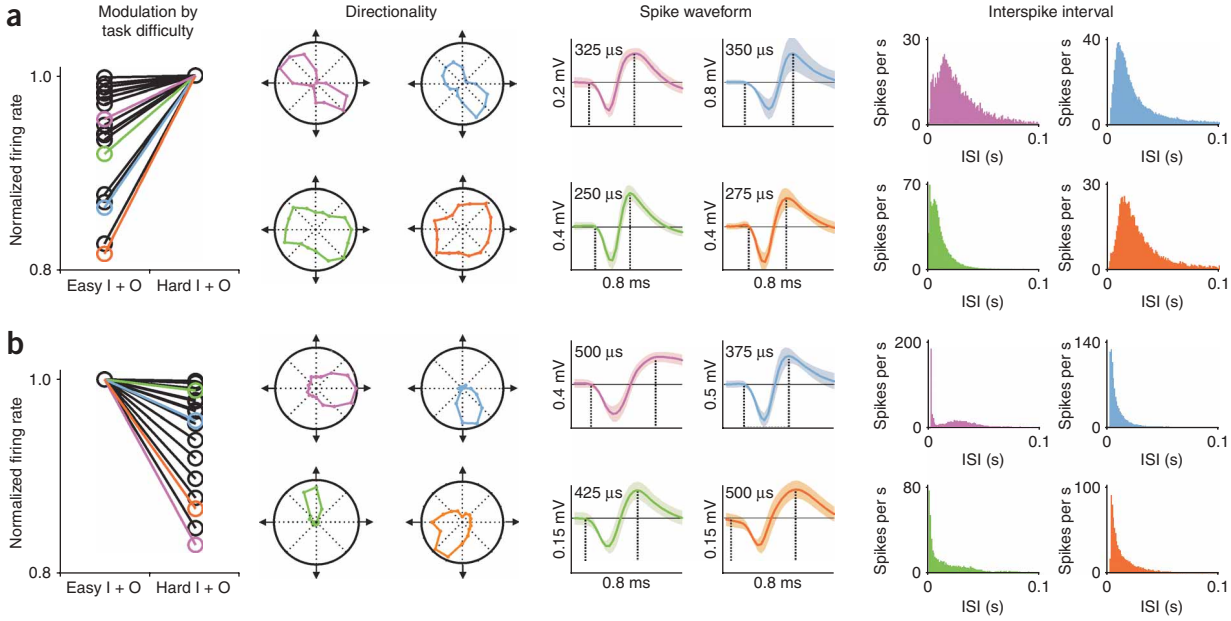

Figure 4 Modulation by task difficulty in V1 cells. The graphs on the left show normalized visual responses summed across the two spatial locations of attention for the easy task (Inside + Outside) and the hard task (Inside + Outside). This graph includes all cells that were significantly modulated ($P < 0.05$, Wilcoxon test) by spatial attention (as defined in **Fig. 1c**). The graphs on the middle and right show the direction selectivity, spike width and interspike-interval distribution of eight cells chosen as representative examples (including the cells illustrated in **Fig. 2**). (**a**) Cells that enhanced visual responses when task difficulty was increased. (**b**) Cells that suppressed visual responses when task difficulty was increased.

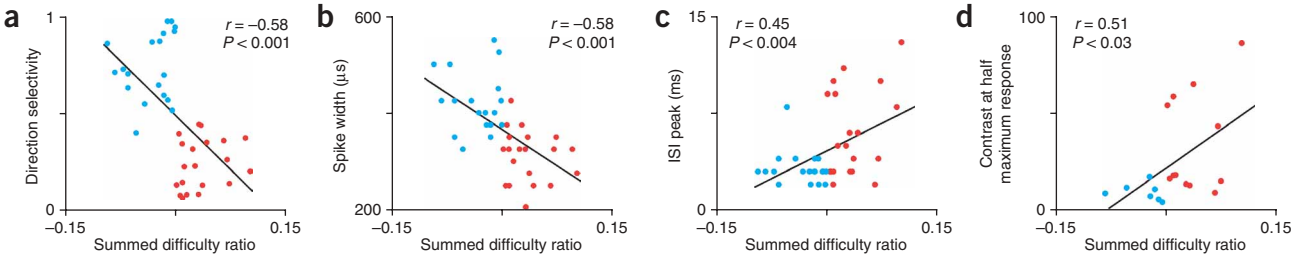

Figure 5 Response modulations to spatial attention and task difficulty are correlated with the direction selectivity, spike width, interspike interval and contrast sensitivity of the cell. A summed difficulty ratio was calculated as $(H_s - E_s) / (H_s + E_s)$, where H_s is the visual response during the hard task and E_s is the visual response during the easy task (summed across Inside and Outside conditions). (**a**) Negative correlation between summed difficulty ratio and direction selectivity. (**b**) Negative correlation between summed difficulty ratio and spike width. (**c**) Positive correlation between summed difficulty ratio and the peak of the interspike-interval distribution (ISI peak). (**d**) Positive correlation between summed difficulty ratio and the stimulus contrast that generated 50% of the maximum response. The spike width was measured from the beginning of the first phase of the spike waveform to the peak of the second phase. The ISI peak was measured as the ISI at the peak of ISI distribution obtained with drifting gratings (with a bin width of 1 ms). Blue and red circles indicate difficulty-suppressed neurons and difficulty-enhanced neurons, respectively.

$P = 0.9$, $P = 0.85$), spatial frequency tuning peak ($P = 0.64$, $P = 0.28$, $P = 0.13$) and bandwidth ($P = 0.62$, $P = 0.46$, $P = 0.77$), orientation tuning measured as circular variance[32] ($P = 0.05$, $P = 0.07$, $P = 0.86$), receptive field size ($P = 0.66$, $P = 0.54$, $P = 0.25$), response latency ($P = 0.32$, $P = 0.87$, $P = 0.32$) and visual responses to brief dark/light spots ($P = 0.48$, $P = 0.1$, $P = 0.17$) (see **Supplementary Fig. 2** online).

Ideally, attentional modulations should be measured at multiple levels of task difficulty to quantify the correlation between task difficulty and response magnitude. However, it was not technically possible to measure multiple levels of task difficulty and acquire detailed quantification of the response properties from each cell, primarily because of the amount of time that the animals were willing to work. To address this limitation, we gave priority in a group of cells ($n = 59$) to the measurement of attentional modulations over response properties and studied three or more levels of difficulty at two spatial locations. Of 22 attention-modulated cells in the group, seven were classified as difficulty enhanced (summed difficulty ratio > 0) and six as difficulty suppressed (summed difficulty ratio < 0). We calculated separate correlation coefficients for difficulty-enhanced and difficulty-suppressed neurons by measuring the mean firing rate at three different levels of difficulty (hard, medium and easy) and then normalizing the mean firing rate after dividing by the maximum mean rate obtained under the three conditions. Consistent with the results reported above, the mean firing rate of the difficulty-enhanced neurons was positively correlated with task difficulty only when the spatial attention was inside of the receptive field (attention inside the receptive field: $r = 0.66$, $P < 0.0001$; attention outside the receptive field: $r = 0.07$, $P = 0.69$). In contrast, the mean firing rate of the difficulty-suppressed neurons was correlated with attention difficulty only when attention was outside of the receptive field (attention inside the receptive field: $r = 0.12$, $P = 0.55$; attention outside the receptive field: $r = -0.77$, $P < 0.0001$; **Fig. 7**).

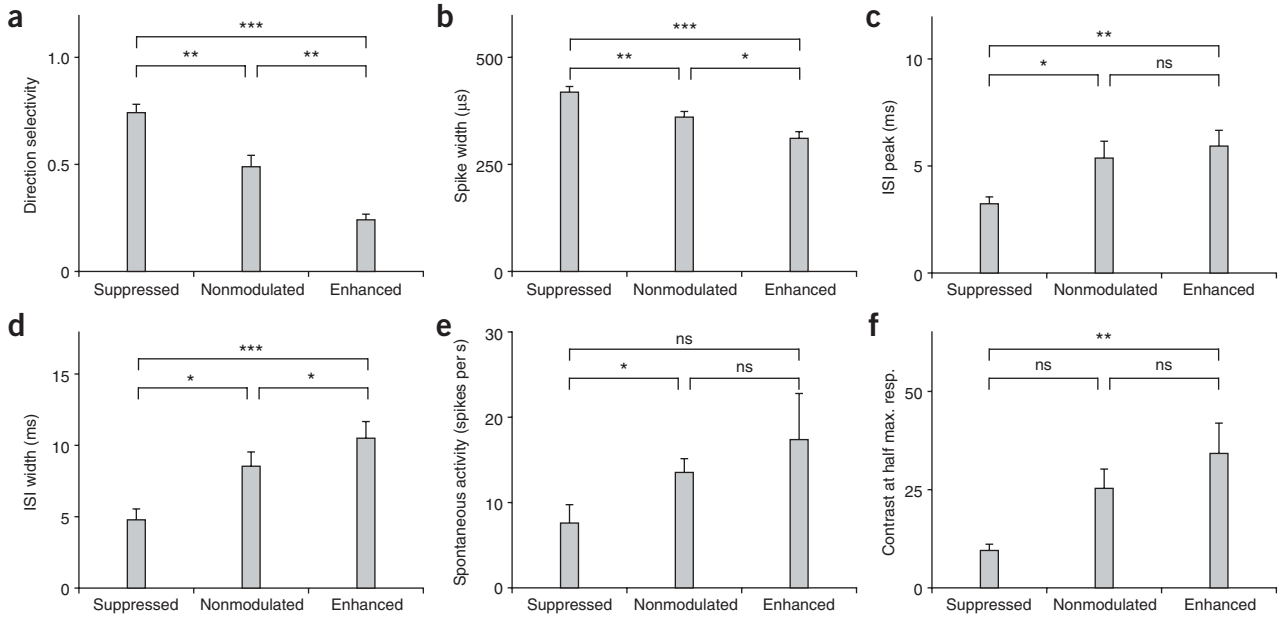

Figure 6 Response properties that distinguish V1 cells classified as difficulty suppressed (summed difficulty ratio < 0), difficulty enhanced (summed difficulty ratio > 0) and nonmodulated (no significant modulation by spatial attention as defined in **Fig. 1c**). (**a**–**f**) Bar graphs represent the average direction selectivity (**a**), spike width (**b**), ISI peak (**c**), ISI width (**d**), spontaneous activity (**e**) and contrast at half-maximum response (**f**) for each cell group. Standard errors are defined as in **Figure 2**. *** $P < 0.001$; ** $P < 0.005$; * $P < 0.05$; ns, not significant (Mann-Whitney test).

Table 1 Two types of V1 neurons modulated by spatial attention

	Suppressed	Enhanced	Significance
$(H_{I+O} - E_{I+O})/(H_{I+O}+E_{I+O})$	–0.03	0.03	$P < 0.0001$
$\|IH - IE\|/\|OH - OE\|$	0.42	5.48	$P < 0.0001$
Directional index	0.74	0.24	$P < 0.0001$
Spike width (μs)	418	313	$P < 0.0001$
ISI peak (ms)	3.3	6	$P < 0.005$
ISI width (ms)	4.8	10.6	$P < 0.0001$
Contrast at half max. response	9.6	34.3	$P = 0.003$

Functional differences between two populations of V1 neurons, difficulty suppressed and difficulty enhanced. The width of the interspike-interval (ISI) distribution was measured at half of its amplitude and the peak as the time with the maximum value in the distribution (measured with a bin width = 1 ms). The contrast sensitivity was measured from the contrast response function as the contrast that generated half-maximum response. Significance was measured with a Mann-Whitney test. E, Easy; H, Hard; I, Inside; O, Outside.

DISCUSSION

Our results demonstrate that task difficulty modulates the activity of single neurons in the primary visual cortex and that attentional gain can be enhanced by a factor of about 3 when task difficulty is increased (**Fig. 3a**). We show that the increase in V1 attentional gain is obtained through a center-surround mechanism that enhances visual responses at the focus of attention and suppresses visual responses outside of the focus (**Fig. 3b**). We also demonstrate that the amount of response enhancement and suppression are correlated across neurons; neurons that show the strongest suppression when attention is outside of the receptive field show the weakest response enhancement when attention is inside of the receptive field and vice versa (**Fig. 3c**).

Finally, we show that response enhancements and suppressions are mediated by two distinct populations of neurons with different response properties (**Fig. 5** and **Table 1**). The difficulty-suppressed neurons are more directionally selective, and have tighter interspike-interval distributions, wider spikes and higher contrast sensitivity than the difficulty-enhanced neurons. These two populations of neurons may work together to increase sensitivity at the focus of attention while suppressing distractions caused by peripheral transient movement[7]. Also, there may be laminar differences corresponding to the two populations of neurons modulated by attention. We found it interesting that some functional properties of difficulty-suppressed neurons (that is, high directional selectivity and high contrast sensitivity) match the functional properties of V1 neurons projecting to area MT[33], as area MT is involved in detecting fast transient movement that could lead to shifts in the spatial focus of attention[34,35].

Task-difficulty modulations in visual cortex

Human psychophysical studies have demonstrated that visual detection is strongly dependent on the location of spatial attention[1,3] and that increasing task difficulty substantially reduces the amount of interference caused by peripheral distracters[5,6]. However, the neuronal mechanisms responsible for the reduction in peripheral interference are not well understood. The first measurements of task-difficulty modulations at the level of single neurons were performed in area V4 and revealed an increase in visual responses with task difficulty[16]. More recent measurements in the same area have also found evidence of response suppression[17]. The response suppression described in area V4 provided a neuronal mechanism for a reduction of peripheral interference during high attentional load. However, it remained unclear as to whether this suppressive mechanism (at the level of single cells) was restricted to high cortical areas or could be found at earlier stages of cortical processing.

Previous electrophysiological measurements using chronically implanted microwires and recordings from multi-unit activity found no evidence for task-difficulty modulations in area V1 (ref. 28). However, although recordings from multi-unit activity[36] (and local field potentials[37]) are a powerful approach for measuring the average attentional modulation across clusters of neurons, they could easily miss modulations restricted to specific cell types. On the other hand, there is evidence from fMRI in humans that V1 signals are modulated by task difficulty[13–15,38,39], and our findings provide a correlate at the level of primate single neurons for these fMRI measurements.

Potential contribution of small eye movements

Although our results clearly demonstrate the existence of task-difficulty modulations in area V1, a potential contribution from small microsaccade movements to these modulations must be carefully evaluated. Microsaccades increase the firing rate of V1 neurons during fixation[40,41]; therefore, differences in microsaccade frequency could potentially generate different firing rates in the various conditions tested here.

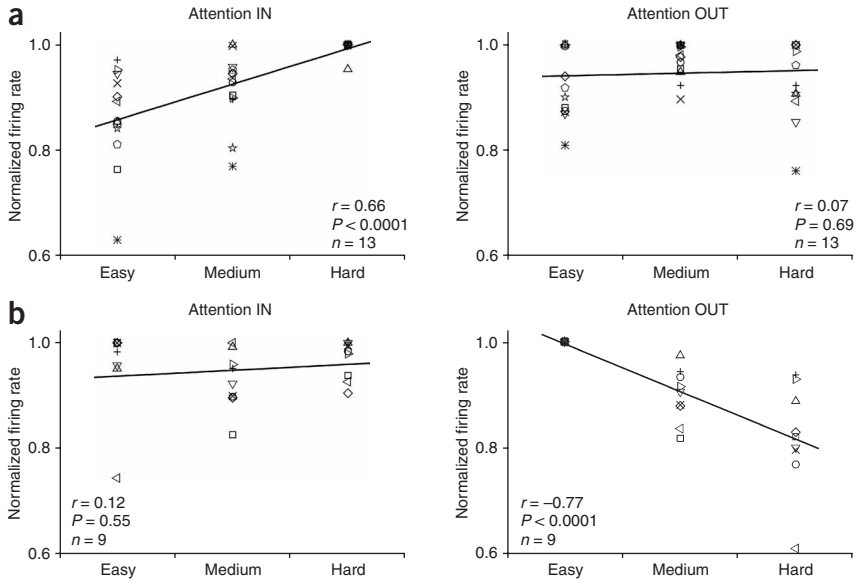

Figure 7 The magnitude of the visual responses was correlated with the level of task difficulty. (**a**) Normalized firing rate of difficulty-enhanced neurons measured at different levels of difficulty when attention was inside (left) of and outside (right) of the receptive field. The visual responses of the difficulty-enhanced neurons were positively correlated with task difficulty only when attention was located inside of the receptive field ($r = 0.69$, $P < 0.0001$). (**b**) Normalized firing rate of difficulty-suppressed neurons. The visual responses of difficulty-suppressed neurons were negatively correlated with task difficulty only when spatial attention was located outside of the receptive field ($r = –0.82$, $P < 0.0001$).

There are several reasons why microsaccades are unlikely to affect our measurements. First, microsaccade frequency was not significantly different between the easy and hard tasks (0.40 ± 0.02 Hz versus 0.45 ± 0.02 Hz, $P = 0.087$, Wilcoxon test). Second, the average eye position and fixation stability were similar across conditions and were not correlated with either the location of attention or the task difficulty (**Supplementary Fig. 3** online). Third, our results could be replicated when we selected trials without microsaccades (see Methods). And finally, it would be difficult to explain how a small change in microsaccade frequency or eye position could generate the correlations reported here between the magnitude of the visual response and the cell's response properties (**Fig. 5**). For the eye movements to generate these correlations, the monkeys would have to be aware of both the direction selectivity of the cell recorded and the location of the neuronal receptive field, and use this information to generate patterns of eye movements that consistently suppressed the response of directional cells only when paying attention outside of the receptive field.

Selective spatial attention during the easy task

It is important to emphasize that the monkeys had to attend selectively even when performing the easy task. For example, it could be argued that if the color change was very noticeable, the monkeys could detect it as a bottom-up, pre-attentional 'pop-out' effect instead of as a result of top-down selective spatial attention. This scenario is improbable for several reasons. First, the color change was subtle (see Methods), and monkeys reacted significantly faster when the spatial location of the change was cued at the beginning of the trial ($P < 0.0001$, see Methods). Second, at the end of most trials, the monkeys made saccades aimed at the cued spatial location, indicating that they were paying attention to this region of visual space (**Supplementary Fig. 4** online). Third, we found strong spatially selective correlations between the level of task difficulty and the magnitude of the visual response (as these correlations required the use of at least three levels of difficulty, it is clear that the monkeys used spatial attention to perform tasks that differed in difficulty; **Fig. 7**). Fourth, a main result of this study (the correlation between difficulty-modulations and direction selectivity) could be replicated in a foveal task, in which the monkey must always pay attention, independent of task difficulty (**Supplementary Fig. 5** online). Finally, the task was designed to highly reward increased effort: the faster the detection, the larger the reward. As monkeys are primarily motivated to perform for the reward, it is unlikely that they would increase the attentional effort during the hard task and fail to pay attention during the easy task, which is when they could best hope to achieve maximal reward.

Neuronal circuitry of visual attention

Our results suggest that the neuronal network of visual spatial attention involves not only specific brain areas[8,12,21] but also specific neuronal populations in each area. It can be speculated that the attention-enhanced neurons with short-duration spikes may have been fast-spiking GABAergic interneurons. This conclusion is consistent with a recent study in area V4 that found strong attentional modulations in neurons with different spike widths[29] (the distribution of spike widths in our sample of V1 neurons resembles the distribution reported previously in area V4; **Supplementary Fig. 6** online).

The finding that task difficulty can enhance or suppress visual responses in area V1 has important implications for current models of spatial attention. Although response enhancement could be explained by a spotlight that 'increases in intensity' with attentional load, response suppression is better explained by models that emphasize the role of response-suppression and center-surround interactions in spatial attention[8,10,22,24,42–47]. Most mathematical models of visual attention assume that response suppression is mediated by intracortical inhibition[10,44]. Our results support these models by showing that neurons with the thinnest spikes (putative inhibitory neurons) enhanced their visual responses with increased task difficulty, whereas neurons with the broadest spikes (unlikely to be inhibitory neurons) suppressed their responses (**Supplementary Fig. 6**). Consistent with these models[10,44], our results also indicate that the strongest inhibition should be found inside the focus of attention, as the difficulty-enhanced neurons increased their responses more strongly when the focus of attention was inside the receptive field (**Fig. 3c**). It should be noted, however, that not all inhibitory populations have short-duration spikes and, conversely, that some cortical spiny neurons have very brief spikes[48].

An important finding of this study is that difficulty-suppressed neurons are more directional selective and have tighter interspike-interval distributions than difficulty-enhanced neurons. Moreover, although neurons with the thinnest spikes are all difficulty enhanced, neurons with broad spikes (presumably excitatory neurons) can be either difficulty enhanced or difficulty suppressed (**Supplementary Fig. 6**). On the basis of this finding, we would like to propose a conceptual model for the V1 neuronal circuitry involved in visual attention (**Supplementary Fig. 7** online). According to this model, an increase in attentional load has two different effects on V1 neuronal responses. First, it increases the visual responses of nondirectional/sustained neurons at the focus of attention to improve detection. Second, it reduces the neuronal responses of directional/transient cells outside of the focus of attention to suppress distraction. We speculate that neurons with enhanced responses are part of a neuronal network involved in making detection more reliable at the focus of attention. And neurons with suppressed responses are part of a neuronal network involved in detecting transient movements in the visual periphery, which need to be suppressed to avoid attentional shifts during difficult detection tasks. As part of this conceptual model, we predict that, unlike V4 cells[16,17], most V1 neurons projecting to area MT (and perhaps most MT neurons) should be difficulty suppressed.

Taken together with results from previous studies[16,17], our findings suggest that the mechanisms driving task difficulty modulations of neuronal responses are probably similar in both early and late cortical stages of visual processing. Moreover, our study provides further evidence that area V1 is important in the neural network of visual attention[11,22–24,49,50].

METHODS

Surgical procedures. Experiments were carried out in two adult rhesus monkeys. Surgery was performed under general anesthesia and sterile conditions in a surgical suite (**Supplementary Methods** online). Each macaque was implanted with a head post for head stabilization, a scleral eye coil to monitor visual fixation and a recording chamber. The recording chamber contained arrays of 3–5 independently movable electrodes[30] that remained implanted in the brain for 6 months to >1 year (some of the electrodes were changed without removing the implant). During this time, the interior of the recording chamber remained sealed. The electrodes were made of a platinum-alloy core (90% platinum and 10% tungsten) with a quartz coating, both of which are very durable and stable materials when chronically implanted in the brain[30] (see also Chen *et al.*, *Soc. Neurosci. Abstr.* **286.14**, 2005). They had a maximum shaft diameter of 40 μm and were pulled to a taper and sharpened to a fine tip. The short length of the electrodes and their attachment to the skull resulted in excellent recording stability, allowing us to study well-isolated neurons for long periods of time (**Supplementary Fig. 1**). During the electrophysiological recordings, the animals had controlled water access and obtained most of their fluid intake (water or juice) by performing the behavioral tasks during the experiment. All the animal procedures were approved by the Institutional

Animal Care and Use Committee at the State University of New York College of Optometry and followed the recommendations of the US National Institutes of Health Guide for the Care and Use of Laboratory Animals and the Animal Welfare Act of 1986 and its revisions.

Behavioral task. Response modulations by spatial attention and task difficulty were measured while the macaques carried out a behavioral task. A small fixation cross and a thin red ring were presented after the animal grabbed a bar. The ring had a diameter threefold larger than the diameter of the neuronal receptive field; it was presented for 500 ms and served as a cue to indicate the spatial location to be attended. This thin ring was separated by 1–2.5 s from the time window used to measure response modulations by attention and difficulty. After the ring disappeared, five gratings were presented at five different locations. Following a randomized period of time (1.5–3 s), the grating at the cued spatial location changed color and the animal was tasked with releasing the bar as fast as possible to obtain a reward.

The cued grating could be the one located inside the receptive field or one of the other four gratings located outside of the receptive field. The color change could be either very noticeable (easy task) or difficult to detect (hard task). The cued grating was kept at the same spatial location for at least 20 trials so that the monkeys could adjust their effort to maximize reward. The two spatial locations of the cued grating (inside or outside of the receptive field) were equidistant from the point of fixation and were separated from each other by 14–22°. Once the grating changed color, the primate had 500 ms to release the bar and receive a reward.

The amount of reward was determined by the reaction time according to the following linear equation:

$$R = -0.02RT + 12$$

where R is the reward (number of juice drops) and RT is the reaction time in ms. Because reaction times longer than 500 ms were not rewarded, the animal had to make a greater effort during the hard task than during the easy task to obtain large rewards. The color and luminance change was adjusted at each recording session until the reaction times during the hard task and easy task were significantly different ($P < 0.05$, Wilcoxon test).

The color and luminance was always changed at the trough of the grating (the luminance at the peak of the grating remained constant at 109 cd m^{-2}). The changes in color at the trough of the grating were very subtle and the amount of change depended on eccentricity, grating size, training experience and day-to-day variability. The value of the red gun ranged between 20–52% for the hard task and 25–67% for the easy task, which corresponds to a change in luminance of 1–24% for the hard task and 8–38% for the easy task.

Behavioral performance. The reaction times were significantly faster during the easy task (mean = 337 ms, median = 329 ms, range = 231–464 ms) than during the hard task (mean = 376 ms, median = 394 ms, range = 278–500 ms; $P < 0.0001$, Wilcoxon test). In some experiments, we cued a spatial location that was different from the location where the grating changed color (10% of wrongly cued trials). In these experiments, the reaction times were 34 ms slower in the wrongly cued trials than in the trials that were cued correctly ($P < 0.0001$, Wilcoxon test), indicating that the animals were paying attention to the cued spatial location, where the color change had to be detected.

The reaction times for each monkey were as follows. For monkey Smitty, the average reaction time was 328 ms during the easy task and 348 ms during the hard task ($P < 0.0001$, Wilcoxon test). For monkey Red, the average reaction time was 338 ms during the easy task and 403 ms during the hard task ($P < 0.0001$, Wilcoxon test). These reaction times were very short and the animals were highly motivated to obtain the largest reward possible during both the easy and hard tasks. Three naive human subjects performing the easy task all had longer reaction times (J.J. = 404 ms, C.W. = 421 ms, Y.W. = 429 ms) than Smitty (328 ms) and Red (338 ms) even after being given specific instructions to pay attention to the location of the target and to make all possible efforts to be faster than the monkeys. The reaction times of two of the authors from this paper were also measured. One of us was faster than either monkey (Y.C. = 318 ms) and the other slower (J.M.A. = 434 ms).

Errors resulting from slow reaction time (the animal released the bar too late) were less frequent during the easy task (2%) than during the hard task (average, 14%). The error rates for each monkey were as follows. Monkey Smitty made 1% of errors during the easy task and 8% during the hard task. Monkey Red made 2% of errors during the easy task and 14% during the hard task. Increasing the task difficulty also led to an increase in other types of errors that were not directly related to the color change, as if the animals were becoming more impatient with the difficult task. For example, both monkeys broke fixation more frequently during the hard task than during the easy task (note that these breaks in fixation are probably a consequence of impatience and not fixation stability, as the fixation stability was similar across conditions in non-aborted trials; **Supplementary Fig. 4**). Monkey Red made significantly more early-release errors (that is, the bar was released before the color change) during the hard task than during the easy task ($P < 0.0001$, Wilcoxon test).

In total, we recorded from 214 V1 cells (108 in Smitty and 106 in Red). From this sample, 114 cells were studied with enough detail to be included in this paper. We studied 92 cells under different conditions of attention and task difficulty (15 in Smitty and 77 in Red) and studied 34 cells foveally under different levels of detection difficulty (all in Smitty). The two monkeys (Smitty versus Red) did not differ in the percentage of attentionally modulated cells (40% versus 43%), difficulty ratios when attention was inside (0.0376 versus 0.0316, $P = 0.4835$, Mann-Whitney test) or outside of the receptive field (–0.101 versus –0.0211, $P = 0.0114$, Mann-Whitney test), and attentional ratios during the easy task (–0.0037 versus 0.0334, $P = 0.1391$, Mann-Whitney test). There was a significant difference in the attention ratios during the hard task (0.1349 versus 0.0858, $P = 0.0091$, Mann-Whitney test), probably because task difficulty was increased more aggressively in the second monkey (Red). In the second monkey, we learned that we could make the task harder if we intercalated the easy task when the monkey started failing too frequently.

Data and statistical analysis. The effects of spatial attention and task difficulty on visual responses were quantified as follows. First, we calculated the peristimulus time histogram (PSTH) of the visual response preceding the color change (500-ms time window, 10-ms bin, the last cycle of the drifting grating; **Fig. 1**). Then, we fit this PSTH with a Gaussian function and obtained the time values (t_1 and t_2) at which the Gaussian was at half of its maximum amplitude. The average of the PSTH bins contained in this time window (t_1 and t_2) was used as a measurement of the visual response obtained under each level of task difficulty and spatial attention.

On average, we used 20 10-ms bins around the PSTH peak to measure the attentional modulations (median, 18 bins). This statistical criterion was quite strict and considerably reduced the number of cells that were significantly modulated by attention ($P < 0.05$, Wilcoxon test), particularly during the easy task. However, the mean attentional and difficulty ratios were relatively independent of the time window used for the measurements (**Supplementary Fig. 8** online). Only when the time window was narrowed down to one 10-ms bin, the measurements became very variable and the average differences lost statistical significance. We believe that the time window used here (half width and half height of the PSTH) is the most appropriate measurement for this study, as the PSTH width varied across cells.

All of the time windows selected for measurements of response modulation were separated by at least 1 s from the cue. The magnitude of the attentional ratios did not seem to depend on the duration of the time interval between cue and target. In the hard task, the strongest attentional ratio was obtained with delays of 2 s and the weakest with delays of 3 s; however, the difference was not significant (0.1 versus 0.07, $P = 0.18$, Mann-Whitney test). It should be noted that the monkeys made more errors in the longest trials (3 s), probably because they became impatient while waiting for the target (3 s was the maximum time duration at which they would perform this task).

We calculated the frequency of microsaccades using a method described in a previous study[41]. First, we plotted the vertical and horizontal eye movement recordings from 800 to 0 ms before the grating changed color and created a table of change (dx and dy) for each trial, computed as the difference between successive 1-ms intervals. Then, we smoothed the differential values with a 31-ms-wide boxcar filter and converted the dx and dy values to polar coordinates, which represented the instantaneous direction (θ) and amplitude of the microsaccade (r). The number of microsaccades was estimated as the r values that exceeded a threshold of 3 arcmin. The frequency of microsaccades was obtained by averaging the number of microsaccades across 800-ms trials.

We measured possible differences in eye position and fixation stability across testing conditions and cell types. We used four different time windows (800, 400, 200 and 100 ms) and found no significant differences in the average eye position in >76% of cases tested, including all multiple conditions and multiple time windows (Wilcoxon test). In a minority of the cases, we did find statistically significant differences ($P < 0.05$, Wilcoxon test), but these differences were too small ($\leq 0.25^\circ$) to be a concern. In fact, if we had removed these cases from our sample, the main conclusions would stay the same. Moreover, these small offsets in eye position were not correlated with the location of attention and/or task difficulty, indicating that they were probably produced by a small drift in the eye coil measurements rather than a real drift in eye position. The distributions of differences in fixation position and fixation stability did not differ across conditions and cell types (**Supplementary Fig. 3**). The size of the attentional effect was not correlated with the eccentricity of the cell recorded ($r = -0.06$, $P = 0.7$, mean attentional ratio was 0.09 both at $<10^\circ$ and 10–20°). Finally, our main results could be replicated when the measurements were performed in selected trials without microsaccades. Consistent with our results (**Fig. 3**), in the selected trials without microsaccades, the mean attentional ratio was 0.09 for the hard task and 0.04 for the easy task, the mean difficulty ratio was 0.03 for attention inside of the receptive field and –0.03 for attention outside of the receptive field, and the response changes inside and outside of the receptive field were correlated ($r = 0.49$, $P < 0.002$).

Significant differences throughout the paper were assessed with a Wilcoxon test when comparing visual responses from the same cell or behavioral parameter (for example, **Fig. 3**) and a Mann-Whitney test when comparing the response properties of different cells (for example, **Table 1**).

Note: Supplementary information is available on the Nature Neuroscience website.

ACKNOWLEDGMENTS

The research was supported by NIH EY14345 (J.-M.A.), MH-64024 (H.A.S.), The Research Foundation at the SUNY College of Optometry (J.-M.A.), The Barrow Neurological Foundation (S.M.-C. and S.L.M.), NSF 0643306 (S.M.-C.), the Science Foundation Arizona (S.L.M.) and Arizona Biomedical Research Commission 07-102 (S.M.-C.) and 06-083 (S.L.M.).

Published online at http://www.nature.com/natureneuroscience/
Reprints and permissions information is available online at http://npg.nature.com/reprintsandpermissions/

1. Posner, M.I. Orienting of attention. *Q. J. Exp. Psychol.* **32**, 3–25 (1980).
2. Carrasco, M. & McElree, B. Covert attention accelerates the rate of visual information processing. *Proc. Natl. Acad. Sci. USA* **98**, 5363–5367 (2001).
3. Pestilli, F. & Carrasco, M. Attention enhances contrast sensitivity at cued and impairs it at uncued locations. *Vision Res.* **45**, 1867–1875 (2005).
4. Lu, Z.L. & Dosher, B.A. External noise distinguishes attention mechanisms. *Vision Res.* **38**, 1183–1198 (1998).
5. Lavie, N. & Cox, S. On the efficiency of visual selective attention: efficient visual search leads to inefficient distractor rejection. *Psychol. Sci.* **8**, 395–398 (1997).
6. LaBerge, D., Brown, V., Carter, M., Bash, D. & Hartley, A. Reducing the effects of adjacent distractors by narrowing attention. *J. Exp. Psychol. Hum. Percept. Perform.* **17**, 65–76 (1991).
7. Yantis, S. Attentional capture in vision. in *Converging Operations in the Study of Selective Attention* (ed. Kramer, A.F. & Coles, G.H.) 45–76 (American Psychological Association, Washington, DC, 1996).
8. Desimone, R. & Duncan, J. Neural mechanisms of selective visual attention. *Annu. Rev. Neurosci.* **18**, 193–222 (1995).
9. Maunsell, J.H. & Cook, E.P. The role of attention in visual processing. *Phil. Trans. R. Soc. Lond. B* **357**, 1063–1072 (2002).
10. Reynolds, J.H. & Chelazzi, L. Attentional modulation of visual processing. *Annu. Rev. Neurosci.* **27**, 611–647 (2004).
11. Roelfsema, P.R., Lamme, V.A. & Spekreijse, H. Object-based attention in the primary visual cortex of the macaque monkey. *Nature* **395**, 376–381 (1998).
12. Carrasco, M. Covert attention increases contrast sensitivity: psychophysical, neurophysiological and neuroimaging studies. *Prog. Brain Res.* **154**, 33–70 (2006).
13. Ress, D., Backus, B.T. & Heeger, D.J. Activity in primary visual cortex predicts performance in a visual detection task. *Nat. Neurosci.* **3**, 940–945 (2000).
14. Rees, G., Frith, C.D. & Lavie, N. Modulating irrelevant motion perception by varying attentional load in an unrelated task. *Science* **278**, 1616–1619 (1997).
15. Schwartz, S. *et al.* Attentional load and sensory competition in human vision: modulation of fMRI responses by load at fixation during task-irrelevant stimulation in the peripheral visual field. *Cereb. Cortex* **15**, 770–786 (2005).
16. Spitzer, H., Desimone, R. & Moran, J. Increased attention enhances both behavioral and neuronal performance. *Science* **240**, 338–340 (1988).
17. Boudreau, C.E., Williford, T.H. & Maunsell, J.H. Effects of task difficulty and target likelihood in area V4 of macaque monkeys. *J. Neurophysiol.* **96**, 2377–2387 (2006).
18. Spitzer, H. & Richmond, B.J. Task difficulty: ignoring, attending to and discriminating a visual stimulus yield progressively more activity in inferior temporal neurons. *Exp. Brain Res.* **83**, 340–348 (1991).
19. Bichot, N.P., Thompson, K.G., Chenchal Rao, S. & Schall, J.D. Reliability of macaque frontal eye field neurons signaling saccade targets during visual search. *J. Neurosci.* **21**, 713–725 (2001).
20. Hasegawa, R.P., Blitz, A.M. & Goldberg, M.E. Neurons in monkey prefrontal cortex whose activity tracks the progress of a three-step self-ordered task. *J. Neurophysiol.* **92**, 1524–1535 (2004).
21. Maunsell, J.H.R. The role of attention in visual cerebral cortex. in *The Visual Neurosciences* (ed. Chalupa, L.M. & Werner, J.S.) 1538–1545 (MIT Press, Cambridge, Massachusetts, 2004).
22. Ito, M. & Gilbert, C.D. Attention modulates contextual influences in the primary visual cortex of alert monkeys. *Neuron* **22**, 593–604 (1999).
23. McAdams, C.J. & Reid, R.C. Attention modulates the responses of simple cells in monkey primary visual cortex. *J. Neurosci.* **25**, 11023–11033 (2005).
24. Motter, B.C. Focal attention produces spatially selective processing in visual cortical areas V1, V2 and V4 in the presence of competing stimuli. *J. Neurophysiol.* **70**, 909–919 (1993).
25. Luck, S.J., Chelazzi, L., Hillyard, S.A. & Desimone, R. Neural mechanisms of spatial selective attention in areas V1, V2 and V4 of macaque visual cortex. *J. Neurophysiol.* **77**, 24–42 (1997).
26. McAdams, C.J. & Maunsell, J.H. Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *J. Neurosci.* **19**, 431–441 (1999).
27. Gilbert, C.D. & Sigman, M. Brain states: top-down influences in sensory processing. *Neuron* **54**, 677–696 (2007).
28. Roelfsema, P.R., Lamme, V.A. & Spekreijse, H. Synchrony and covariation of firing rates in the primary visual cortex during contour grouping. *Nat. Neurosci.* **7**, 982–991 (2004).
29. Mitchell, J.F., Sundberg, K.A. & Reynolds, J.H. Differential attention-dependent response modulation across cell classes in macaque visual area V4. *Neuron* **55**, 131–141 (2007).
30. Swadlow, H.A., Bereshpolova, Y., Bezdudnaya, T., Cano, M. & Stoelzel, C.R. A multichannel, implantable microdrive system for use with sharp, ultra-fine 'Reitboeck' microelectrodes. *J. Neurophysiol.* **93**, 2959–2965 (2005).
31. Hartigan, J.A. & Hartigan, P.M. The dip test of unimodality. *Ann. Stat.* **13**, 70–84 (1985).
32. Ringach, D.L., Shapley, R.M. & Hawken, M.J. Orientation selectivity in macaque VI: diversity and laminar dependence. *J. Neurosci.* **22**, 5639–5651 (2002).
33. Movshon, J.A. & Newsome, W.T. Visual response properties of striate cortical neurons projecting to area MT in macaque monkeys. *J. Neurosci.* **16**, 7733–7741 (1996).
34. Womelsdorf, T., Anton-Erxleben, K., Pieper, F. & Treue, S. Dynamic shifts of visual receptive fields in cortical area MT by spatial attention. *Nat. Neurosci.* **9**, 1156–1160 (2006).
35. Kelley, T.A., Serences, J.T., Giesbrecht, B. & Yantis, S. Cortical mechanisms for shifting and holding visuospatial attention. *Cereb. Cortex* **18**, 114–125 (2008).
36. Super, H. & Roelfsema, P.R. Chronic multiunit recordings in behaving animals: advantages and limitations. *Prog. Brain Res.* **147**, 263–282 (2005).
37. Yoshor, D., Ghose, G.M., Bosking, W.H., Sun, P. & Maunsell, J.H. Spatial attention does not strongly modulate neuronal responses in early human visual cortex. *J. Neurosci.* **27**, 13205–13209 (2007).
38. Bahrami, B., Lavie, N. & Rees, G. Attentional load modulates responses of human primary visual cortex to invisible stimuli. *Curr. Biol.* **17**, 509–513 (2007).
39. O'Connor, D.H., Fukui, M.M., Pinsk, M.A. & Kastner, S. Attention modulates responses in the human lateral geniculate nucleus. *Nat. Neurosci.* **5**, 1203–1209 (2002).
40. Martinez-Conde, S. Fixational eye movements in normal and pathological vision. *Prog. Brain Res.* **154**, 151–176 (2006).
41. Martinez-Conde, S., Macknik, S.L. & Hubel, D.H. Microsaccadic eye movements and firing of single cells in the striate cortex of macaque monkeys. *Nat. Neurosci.* **3**, 251–258 (2000).
42. Lavie, N. Perceptual load as a necessary condition for selective attention. *J. Exp. Psychol. Hum. Percept. Perform.* **21**, 451–468 (1995).
43. Silver, M.A., Ress, D. & Heeger, D.J. Neural correlates of sustained spatial attention in human early visual cortex. *J. Neurophysiol.* **97**, 229–237 (2007).
44. Ardid, S., Wang, X.J. & Compte, A. An integrated microcircuit model of attentional processing in the neocortex. *J. Neurosci.* **27**, 8486–8495 (2007).
45. Treue, S. & Martinez Trujillo, J.C. Feature-based attention influences motion processing gain in macaque visual cortex. *Nature* **399**, 575–579 (1999).
46. Connor, C.E., Gallant, J.L., Preddie, D.C. & Van Essen, D.C. Responses in area V4 depend on the spatial relationship between stimulus and attention. *J. Neurophysiol.* **75**, 1306–1308 (1996).
47. Moore, T. & Armstrong, K.M. Selective gating of visual signals by microstimulation of frontal cortex. *Nature* **421**, 370–373 (2003).
48. Swadlow, H.A. Fast-spike interneurons and feedforward inhibition in awake sensory neocortex. *Cereb. Cortex* **13**, 25–32 (2003).
49. Liu, T., Pestilli, F. & Carrasco, M. Transient attention enhances perceptual performance and fMRI response in human visual cortex. *Neuron* **45**, 469–477 (2005).
50. Somers, D.C., Dale, A.M., Seiffert, A.E. & Tootell, R.B. Functional MRI reveals spatially specific attentional modulation in human primary visual cortex. *Proc. Natl. Acad. Sci. USA* **96**, 1663–1668 (1999).