nature neuroscience

Attention alters spatial integration in macaque V1 in an eccentricity-dependent manner

Mark Roberts[1,2], Louise S Delicato[1], Jose Herrero[1], Mark A Gieselmann[1] & Alexander Thiele[1]

Attention can selectively enhance neuronal responses and exclude external noise, but the neuronal computations that underlie these effects remain unknown. At the neuronal level, noise exclusion might result in altered spatial integration properties. We tested this proposal by recording neuronal activity and length tuning in neurons of the primary visual cortex of the macaque when attention was directed toward or away from stimuli presented in each neuron's classical receptive field. For cells with central-parafoveal receptive fields, attention reduced spatial integration, as demonstrated by a reduction in preferred stimulus length and in the size of the spatial summation area. Conversely, in cells that represented more peripheral locations, attention increased spatial integration by increasing the cell's summation area. This previously unknown dichotomy between central and peripheral vision could support accurate analysis of attended foveal objects and target selection for impending eye movements to peripheral objects.

Attention exerts a critical influence over information processing in the striate and extrastriate visual cortex[1–5]. This is evident psychophysically, as visual perception becomes more accurate and less strongly influenced by external noise[6] and has a higher resolution[7] at attended locations. Neurophysiological data show that directed attention causes multiplicative enhancements in neuronal response rates when isolated stimuli are attended to[8,9]. However, attentional effects are greater and more complex when attention is directed to one of two stimuli presented in the classical receptive field (CRF)[2,8,10]. Under such conditions, attention alters the interaction between these multiple stimuli, causing the influence of the non-attended stimulus to be suppressed[10,11]. This effect could be mediated by changes in the profile of extrastriate CRFs, which have recently been shown to shift toward, and somewhat shrink around, attended objects[12]. In the primary visual cortex (V1), CRFs are too small to present multiple stimuli within their boundaries, but attention can still influence the interaction between multiple stimuli by acting on the non-classical receptive field (nCRF). A reduction in the strength of the influence of the nCRF during attentive states could potentially mediate the exclusion of noise[6] and enhancement of spatial resolution[7] at attended locations. This would also be expected to reduce contextual influences in visual perception, in line with a number of psychophysical reports[13,14]. The precise mechanisms by which attention mediates changes in the influences of the nCRF are not understood. This study investigates these mechanisms in the V1 of the macaque monkey. We found that attention at parafoveal sites reduced spatial pooling by reducing the size of a neuron's summation area. Notably, at more peripheral sites, attention increased spatial pooling by increasing the size of the summation area and altering the excitatory and inhibitory gain.

RESULTS

Effects of attention on neuronal length tuning

Length tuning is a classic demonstration of nCRF modulation[15]. The analysis of length tuning allows researchers to determine the spatial extent and strength of a neuron's summation area, which consists of the CRF and an excitatory inner fringe of the nCRF[15–17]. It also allows the spatial extent and strength of the neuron's inhibition area to be determined[15–17]. As length is a continuous variable, a model can be fit to the data, thereby allowing changes in summation and inhibition areas to be quantified. Thus, by measuring length tuning, the impact of the nCRF and its modulation by directed spatial attention can be assessed. We measured length tuning under conditions in which the monkey was cued to attend to the stimulus presented in the receptive field (RF; in this case, the CRF) of the neuron under study (attend-RF condition) and when the monkey was cued to attend to a stimulus presented in the opposite hemifield (attend-away condition, see **Fig. 1**). In the majority of cells with parafoveal RFs, the preferred stimulus length was shorter in the attend-RF condition (**Fig. 2**).

We quantified neuronal length tuning by repeatedly fitting a difference of Gaussians (DOG) model[17] to bootstrapped data. For this, we calculated 100 model fits in which the mean firing rate at each bar length in both attention conditions was calculated over a new random-with-replacement selection of trials. We determined goodness of fit in two ways. In the first technique, goodness of fit for each cell was taken to be the variance accounted for[18] that was obtained from fitting the DOG model to the raw, non-bootstrapped data. The model gave good fits (the population median percentage variance accounted for was 95%; 25th percentile 90%; 75th percentile 98%). In the second technique, goodness of fit for each cell was taken to be the median

[1]Institute of Neuroscience, Henry Wellcome Building, Framlington Place, University of Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, UK. [2]Current address: F.C. Donders Centre for Cognitive Neuroimaging, P.O. Box 9101, 6500 HB Nijmegen, The Netherlands. Correspondence should be addressed to A.T. (alex.thiele@ncl.ac.uk).

Received 1 May; accepted 26 July; published online 30 September 2007; doi:10.1038/nn1967

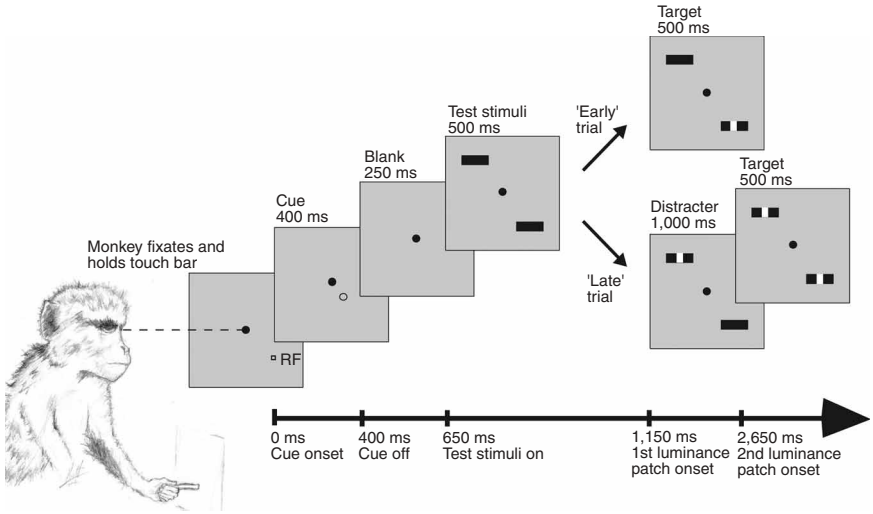

Figure 1 Representation of the main experimental task. The timing of events relative to the start of the trial is marked along the bottom axis. Presentation time is given above each frame. The monkey initiated the trial by fixating centrally (filled circle) and holding a touch-bar. At the start of the trial a cue (open circle) indicated the location to which the monkey should attend; the cue was spatially and temporally separated from the stimulus and thus the attended location. In this example the cue directs attention toward the CRF of the neuron under study. Test stimuli were two identical bars, one presented centered on the CRF of the neuron under study, the other in the opposite hemifield. The monkey's task was to detect the presentation of a $0.1^\circ \times 0.1^\circ$ luminance patch that appeared at the center of the cued bar either 500 ms or 1,500 ms after the onset of the test stimuli. In an 'early' trial the first luminance patch was presented on the cued stimulus ('target'). In a 'late' trial the first luminance patch was presented on the uncued test stimulus ('distracter') and the second patch occurred on the cued stimulus. The monkey had 500 ms to release the touch bar after the presentation of a target, in order to receive a juice reward.

variance accounted for[18] that was obtained from the bootstrap method. This approach resulted in equally good fits (the population median percentage variance accounted for was 96%; 25th percentile 93%; 75th percentile 98%). Each iteration of the bootstrap procedure returned an estimate of the preferred length and of the four fitting parameters for each attention condition. We compared the distributions of these estimates to determine whether changes in length tuning that resulted from directed attention were statistically significant on an individual cell basis (two-sample *t*-test). For statistical comparison across the population, we calculated, for each cell, medians for the preferred length and fitting parameters under both attention conditions. We then calculated the ratio of these medians between the two conditions by dividing the parameter value for the attend-RF condition by the parameter value for the attend-away condition for each cell. This was done separately for high and medium (non-saturating) contrasts (see Methods). At both contrasts, the preferred length was significantly reduced in the attend-RF condition compared with the attend-away condition (signed-rank test (SRT), H_0: average ratio = 1, $P < 0.01$; **Fig. 3**, **Table 1**). The reduction in preferred length was mediated by a reduction in the summation area in all three monkeys (**Fig. 3**, **Table 1**). In addition, the summation gain was significantly enhanced by attention in the high-contrast condition (**Fig. 3**, **Table 1**). The inhibitory area and gain were not significantly affected by attention at either contrast level (**Table 1**). This shows that attention directed to foveal and parafoveal visual field locations reduced the influence of the nCRF mostly by reducing the size of the summation area.

Data recorded at greater retinal eccentricity

In two of the three monkeys (monkey B and monkey H) we collected data from neurons that represented two different retinal eccentricities using medium non-saturating stimulus contrast (10–25% Michelson contrast). In the first 'parafoveal' recording location, the RFs were at an eccentricity of $\sim 2^\circ$ in monkey B ($n = 17$, 25th percentile 2.3°, 50th percentile 2.4°, 75th percentile 2.5°) and $\sim 3^\circ$ in monkey H ($n = 56$, 25th percentile 3.1°, 50th percentile 3.2°, 75th percentile 3.3°). In the second 'peripheral' location, the RFs were at an eccentricity of $\sim 6^\circ$ in monkey B ($n = 22$, 25th percentile 5.6°, 50th percentile 5.8°, 75th percentile 6.5°) and $\sim 7^\circ$ in monkey H ($n = 47$, 25th percentile 6.7°, 50th percentile 6.9°, 75th percentile 7.2°). All cells recorded in monkey D were at a parafoveal eccentricity of around 2° ($n = 37$, 25th percentile 2.2°, 50th percentile 2.3°, 75th percentile 2.4°).

In the ~ 6–7° eccentricity sample ($n = 69$), the effect of attention on length tuning was opposite to the effect at ~ 2–3° eccentricity: that is, the preferred bar length was increased in the attend-RF condition (**Figs. 2c**, **3**). The increase in preferred length was mediated by a significant increase in the summation area in the attend-RF condition, as well as by an increase in summation gain and an increase in inhibition gain ($P = 0.02$, SRT; **Fig. 3**, **Table 1**). The inhibition area was not significantly affected by attention (**Table 1**).

Given that attention affects length tuning differently at parafoveal and peripheral recording sites, it could be predicted that attentional modulation is stronger for shorter bars at parafoveal recording sites, but stronger for medium to larger bars at more peripheral recording sites. We found that this was true (**Fig. 4**). For parafoveal recording sites, attentional modulation was stronger when shorter bars were presented (0.1–0.2° bar length), whereas for peripheral sites attentional modulation was stronger for medium bar lengths (0.6–0.8° bar length). We quantified this finding by calculating the receiver operating characteristic (ROC[19]) as a function of bar length (**Fig. 5**). The time period that was used to calculate the ROC value was 200–500 ms after stimulus onset. For both eccentricities, we found a significant effect of bar length on the attentional modulation (expressed in terms of the ROC value, $P < 0.001$, one way repeated measures ANOVA). Notably, the maximum ROC values for parafoveal sites occurred at a bar length of 0.2°, whereas they were largest for a bar length of 0.8° at more peripheral recording sites (**Fig. 5**).

The difference in the effect of attention on peak length and summation area between the ~ 2–3° and ~ 6–7° eccentricity samples was highly significant ($P < 0.001$, two-sample *t*-test, compare ratios in **Table 1**). Such a marked difference could be mediated by a number of factors beside the simple eccentricity difference, as many neuronal selectivities vary with eccentricity. These include contrast sensitivity (higher near the fovea), spatial frequency preference (also higher in central vision) and RF size (greater in the periphery). Under this hypothesis, any cell with a large RF (or low contrast sensitivity or spatial frequency preference) would have enhanced preferred length under conditions of attention, regardless of the eccentricity of the RF. Attentional modulation would thus be determined by some low-level property of the individual cell, rather than, for example, functional or network differences between central and peripheral vision. We tested

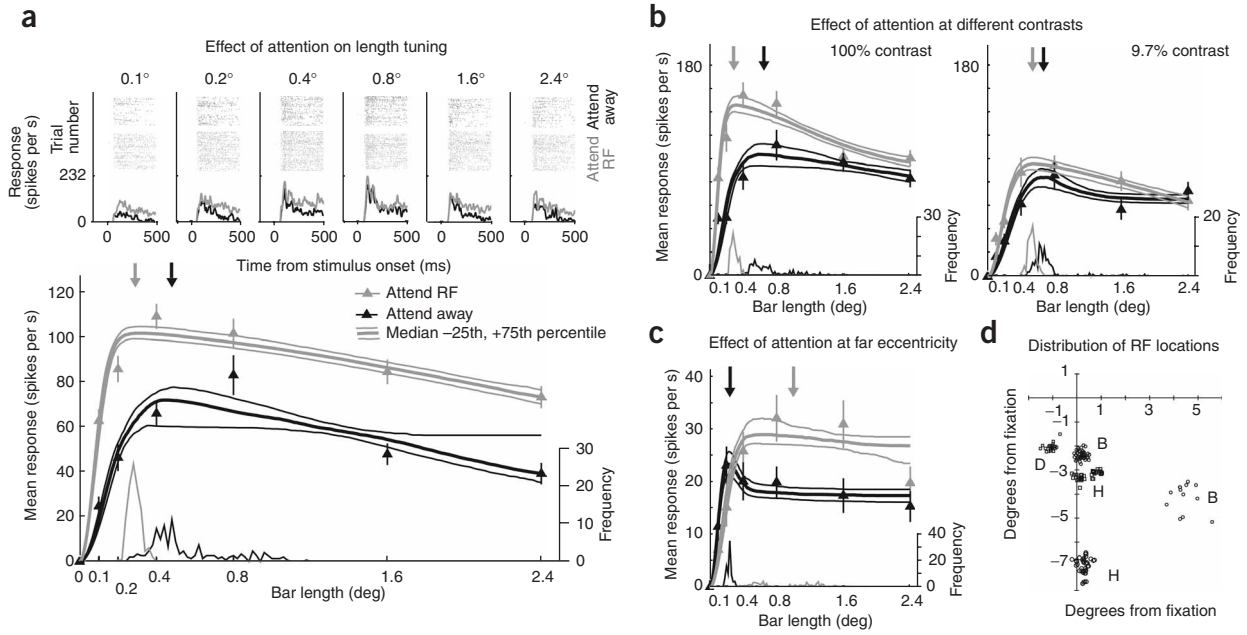

Figure 2 Effect of attention on length tuning for individual cells. (**a**) Top row, raster plots and histograms of single-cell responses for each bar length. Gray, attend-RF condition; black, attend-away condition. Bottom row, effect of attention on length tuning. Triangles, mean response (± s.e.m.) at each bar length. Bold line fitted to the data shows the median DOG model fit from the bootstrap procedure, flanking narrow lines show the 75th and 25th percentile fits. Curves at the base of each plot show the distribution of preferred lengths taken from 100 iterations of the bootstrap procedure. The frequency values of the histogram are shown on the right-hand *y* axis. The median preferred length is marked with the downward-pointing arrow. Grey, attend-RF condition; black, attend-away condition. Error bars, s.e.m. This cell was recorded using high-contrast stimuli. (**b**) Data from example cell showing the effect of attention on length tuning at high and medium contrast. Data are shown in the same format as in **a** and the cell was recorded from monkey D. (**c**) Data from example cell with a receptive field eccentricity of ~6° (monkey B). (**d**) Distribution of RF locations. Each point marks the location of a RF. Letters next to RF clusters indicate the monkey from which the respective cells were recorded.

for this possibility by subdividing the two eccentricity cell groups according the selectivity of the individual cells (where it had been measured). We then compared whether these preferences could account for the effect of attention on length tuning. None of the tested parameters predicted the effect of attention on length tuning in a manner similar to eccentricity (for additional details, see **Supplementary Note 1** online). It could still be the case that ceiling effects, or some other non-uniformity in the data, contribute to our finding of changed summation area (or other parameters of the DOG model). In other words, one might wonder whether cells that belong to the subgroup of 'small receptive fields' for a given eccentricity are just as likely to show attention-induced changes in the summation area as cells that belong to the 'large receptive fields' subgroup. We find no obvious evidence for such differences (see Figure S1 in **Supplementary Note 1**). Although we cannot exclude the possibility that another co-variant of eccentricity, which was not measured in this study, was responsible for our finding, we currently suggest that attentional mechanisms might be implemented differently between parafoveal and peripheral sites, resulting in reduced spatial pooling at parafoveal sites and increased pooling at peripheral sites.

Model comparisons

Our bootstrap procedure indicated that the change in preferred length was mediated by a change in the summation area, as this was the only parameter that was significantly affected by attention in all conditions; the summation gain was not affected by attention at medium contrast at parafoveal sites, and inhibition gain was influenced only among peripheral recording sites (**Table 1**). An alternative account would propose that changes in gain are sufficient to explain the effect of attention on length tuning, rather than changes in the summation or inhibition area. Moreover, a divisive model, such as has been proposed by others[20], might explain a larger amount of variance of the data. To assess these possibilities we repeatedly fitted a DOG and a ratio-of-Gaussian (ROG) model to our bootstrapped data (see Methods). For both models we used three subtypes: a 'full' model in which all parameters were free to vary between the two attentional conditions, a 'gain' model in which the summation and inhibition areas were forced to have the same value in both attention conditions while the gains were allowed to vary, and an 'area' model in which the gains were fixed but the summation and inhibition areas were allowed to vary between attention conditions. We compared the normalized χ^2 values (χ^2_N, normalized by the degree of freedom[20]) between these six models for each monkey and recording condition (eccentricity, contrast level) separately as well as combined across monkeys and conditions. We found that for all conditions and all monkeys, all DOG model subtypes were significantly better than the corresponding ROG models ($P < 0.0001$, repeated measurement ANOVA on ranks). This shows that our data are better described by a DOG model than by a ROG model (for additional detail and discussion see **Supplementary Note 2** online).

When we compared the DOG models, we found that normalized χ^2_N was significantly smaller for the DOG area model and the DOG gain model than the full DOG model ($P < 0.05$, RM-ANOVA on ranks). Moreover, the DOG area model resulted in significantly better fits than the DOG gain model ($P < 0.05$, RM-ANOVA on ranks). Although this was only significant when all conditions (high and medium contrast; parafoveal and peripheral sites) were combined, a trend was present in each individual dataset from each monkey for all conditions. This

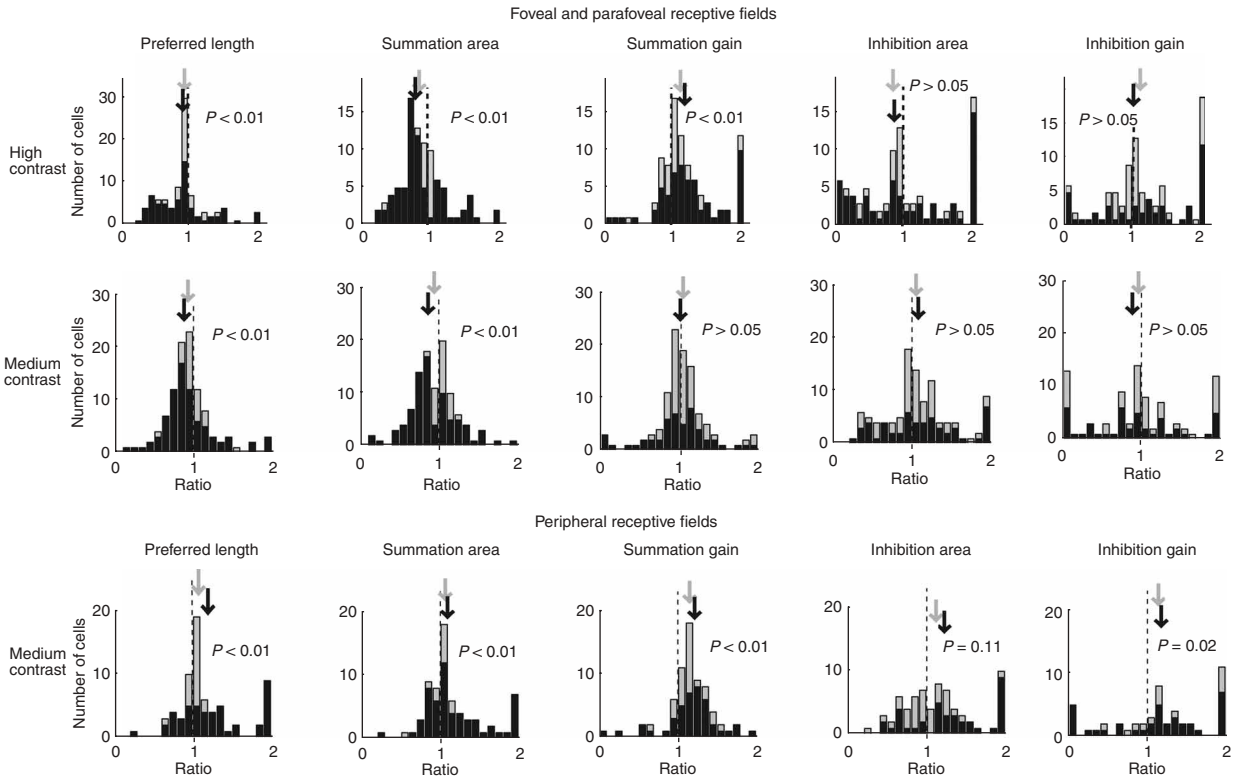

Figure 3 Effect of attention on preferred length and on DOG summation area and summation gain. Top row, high contrast; middle row, medium contrast, both recorded at ~2–3° eccentricity; bottom row, medium contrast recorded at ~6–7° eccentricity. Values below 1 (vertical dashed line) indicate that the parameter of interest was reduced in the attend-RF condition. Light shaded histograms show the distribution of ratios across the population of cells. Dark shaded histograms show the distribution of ratios across cells for which the parameter of interest was significantly different between the two conditions, as assessed by bootstrapping. The median ratio for the whole population and the population of significant cells is marked with downward-pointing arrows, shaded gray and black, respectively. *P* values give the significance of changes in the parameter of interest with attention (whole population signed rank test, H_0 median ratio = 1).

indicates that changes in gain alone are not sufficient to explain our data; a substantial (even larger) amount of variance is explained by changes of the size kernels in the DOG model (summation and inhibition areas). To analyze this further, and to determine the contribution of the individual components of the DOG model (summation area, inhibition area, summation gain and inhibition gain), rather than gains combined or areas combined, we refitted our data with a series of DOG model subtypes in which just one of the four parameters was constrained to have the same value in both attention conditions, while the remaining three parameters could vary between

Table 1 Ratio of DOG model parameters in the attend RF and attend away condition

		Median ratio (25th and 75th percentiles)				
		Preferred length	Summation area	Inhibition area	Summation gain	Inhibition gain
Fovea/parafovea, high contrast	All cells	0.94 (0.69, 1.03) $n = 92$, $P < 0.01$	0.87 (0.72, 1.06) $n = 92$, $P < 0.01$	0.93 (0.52, 1.64) $n = 92$, $P = 0.81$	1.14 (0.99, 1.41) $n = 92$, $P < 0.01$	1.09 (0.78, 1.79) $n = 92$, $P = 0.06$
	Significant cells	0.91 (0.59, 1.07) $n = 66$, $P < 0.01$	0.81 (0.70, 1.14) $n = 75$, $P < 0.01$	0.97 (0.47, 1.80) $n = 66$, $P = 0.88$	1.21 (1.03, 1.58) $n = 62$, $P < 0.01$	123 (0.66, 1.09) $n = 49$, $P = 0.38$
Fovea/parafovea, medium contrast	All cells	0.92 (0.78, 1.06) $n = 106$, $P < 0.01$	0.94 (0.77, 1.09) $n = 106$, $P < 0.01$	1.04 (0.85, 1.29) $n = 106$, $P = 0.47$	1.02 (0.83, 1.19) $n = 106$, $P = 0.41$	0.96 (0.59, 1.28) $n = 106$, $P = 0.22$
	Significant cells	0.88 (0.73, 1.06) $n = 80$, $P < 0.01$	0.86 (0.72, 1.09) $n = 82$, $P < 0.01$	1.08 (0.69, 1.46) $n = 53$, $P = 0.17$	0.99 (0.83, 1.19) $n = 50$, $P = 0.52$	0.88 (0.33, 1.28) $n = 44$, $P = 0.04$
Periphery, medium contrast	All cells	1.08 (0.97, 1.32) $n = 69$, $P < 0.01$	1.07 (0.92, 1.35) $n = 69$, $P < 0.001$	1.12 (0.83, 1.40) $n = 69$, $P = 0.11$	1.16 (1.04, 1.30) $n = 69$, $P < 0.001$	1.15 (0.78, 1.56) $n = 69$, $P = 0.02$
	Significant cells	1.19 (0.96, 1.51) $n = 47$, $P = 0.02$	1.09 (0.92, 1.42) $n = 57$, $P < 0.001$	1.22 (0.83, 1.83) $n = 37$, $P = 0.02$	1.21 (1.04, 1.37) $n = 42$, $P < 0.001$	1.17 (0.64, 1.51) $n = 36$, $P = 0.067$

Each box lists the median ratio (25th and 75th percentiles in brackets) of the parameter of interest (attend-RF/attend-away). The table also lists the number of cells that were recorded, the number of cells for which the parameter of interest was significantly affected (bootstrap method) and the *P* value under the null hypothesis that the average ratio was equal to 1 (SRT). Ratios <1 indicate that the parameter of interest was reduced by attention.

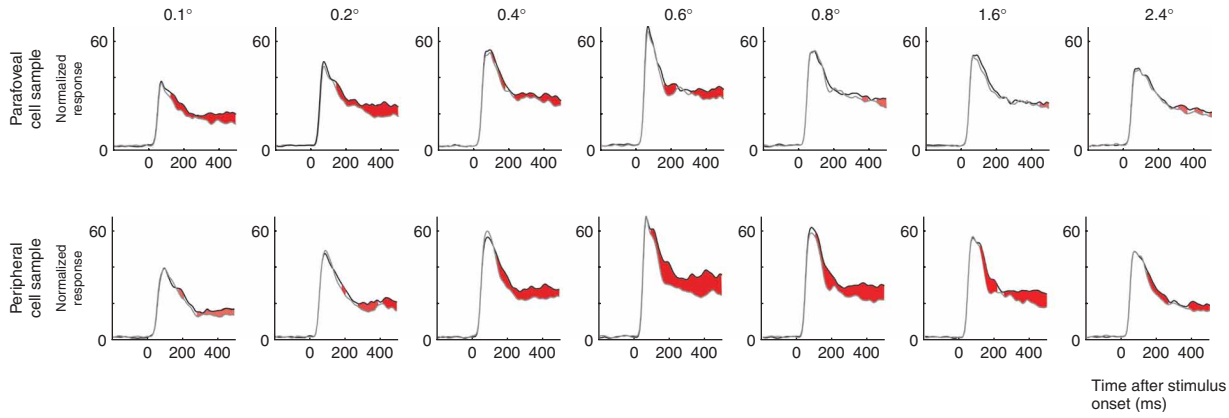

Figure 4 Population response as a function of bar length. Upper row, response from cells recorded in monkeys B ($n = 17$) and H ($n = 56$) at medium contrast from parafoveal sites. Lower row, response from cells recorded in monkeys B ($n = 22$) and H ($n = 47$) at medium contrast from peripheral sites. Black, response for the attend-RF condition; gray, response for the attend-away condition. Red shaded areas, time periods during which response differences were significant for the population ($P < 0.01$, rank sum test). Response normalization was performed for each cell across all conditions initially. Population responses were calculated from these individually normalized responses. Population histogram for bar-length 0.6° is from monkey H only, as recordings in monkey B were restricted to six bar-lengths. Data from monkeys B and H are included as both contributed to our parafoveal and peripheral cell sample.

the attend-away and attend-RF conditions. Fit quality was assessed by calculating χ^2_N. We found that fit quality (χ^2_N) was significantly different for the four models ($P < 0.001$, RM-ANOVA on ranks) for both eccentricities. *Post hoc* testing (Tukey's test) revealed that for the parafoveal sample, constraining the summation area resulted in the highest χ^2_N (that is, the worse fits) of all models. The difference was significant when compared with the model in which the excitation gain was constrained but not for the remaining two models (inhibition area and gain). Unexpectedly, the model in which the excitation gain was constrained gave the best fits. For the cell sample from peripheral sites we found similar results. Constraining the summation area resulted in significantly worse fits than constraining any of the other three parameters ($P < 0.05$, RM-ANOVA on ranks, Tukey's test). This corroborates the previous finding that the change in length tuning in our data cannot be described by changes in the gain parameters alone, and supports the notion that changes in the summation area significantly contribute to changes in preferred length.

Despite these findings, it is worthwhile to bear in mind that the extent of the summation area generally fell within the region that was directly measured in our experiment, whereas the inhibition area often extended beyond that region. Thus, we may have greater confidence in our estimates of the excitatory components of the DOG model than the estimates of the inhibitory components. If, for example, the size of the inhibition area changed from 5° to 10°, our measurements might not reveal these changes, as such a change would occur beyond the maximum extent of our experimental stimuli. Changes in the parameters of the summation area could therefore have a more direct impact on our length-tuning measurements. Thus, even if the inhibitory area changed in conjunction with a change in the summation area, the former might be more difficult to detect given our stimulus protocol.

Influence of eye position

Small differences in eye position or eye movement between the attend-RF and attend-away conditions could potentially contribute to, or contaminate, the effects of attention. To control for this, we used *post hoc* filtering to restrict the eye position window (which was very small to start with: ± 0.30–0.35°). For this analysis we first calculated the mean eye position during the analysis period (30–500 ms after stimulus onset) from all recorded trials. A threshold was set to exclude trials in which the eye position deviated from the mean position by more than the threshold (0.25°, 0.2° or 0.15°) allowed. We then used receiver operating characteristic (ROC) analysis[19,21,22] to quantify the magnitude of attentional modulation of the neuronal response. We compared the ROC values for individual data points (one cell's responses to one bar length) before and after filtered with increasingly restrictive thresholds. Data points where fewer than eight trials remained after filtering were excluded. Filtering the data in this way did not reduce the attentional effect, as would be expected if the difference in response rate between attention conditions was due to differences in eye position (where the largest differences in response would occur in trials with the most deviant eye position).

As we found no significant difference in mean ROC values between *post hoc* filtered and unfiltered data at any eye window threshold, we

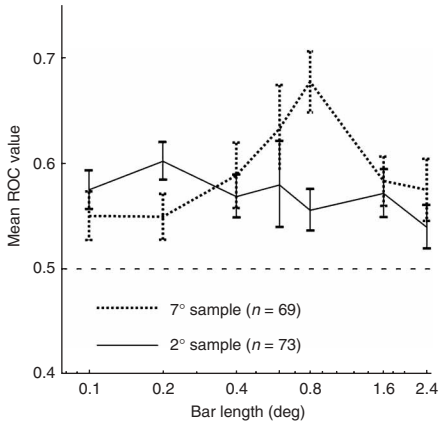

Figure 5 Quantitative comparison of attentional modulation as a function of bar-length and recording location. Attentional modulation was assessed by calculating a receiver operating characteristic (ROC) as a function of bar-length for each cell from monkeys B and H (recordings from medium-contrast experiments) for parafoveal sites (solid curve) and for peripheral sites (dotted curve). ROC values differed significantly as a function of bar-length for both recording sites ($P < 0.001$, ANOVA on ranks). Error bars, s.e.m. Data for bar-length 0.6° are from monkey H only, as recordings in monkey B were restricted to six bar-lengths. Data from monkey D are not included, as he did not contribute to data from peripheral sites.

conclude that the attentional enhancement was not due to small differences in eye movements or position between the two attentional conditions (median difference in ROC after filtering with 0.25° filter 0.00, 25th percentile –0.03, 75th percentile 0.03, $n = 1{,}078$ data points, $P = 0.94$, paired t-test; after filtering at 0.2° median difference 0.01, 25th percentile –0.05, 75th percentile 0.05, $n = 688$, $P = 0.95$; after filtering at 0.15° median difference 0.01, 25th percentile –0.05, 75th percentile 0.08, $n = 118$, $P = 0.2$).

DISCUSSION

We have shown that attention affects spatial integration in primate visual cortex in a manner that depends on eccentricity, by either decreasing (central vision) or increasing (peripheral vision) the summation area. This finding shows that the influence of the nCRF is dynamic and depends on attention. We investigated this by measuring the length tuning of V1 cells under two attentional conditions and at two eccentricities. Attention caused a reduction in preferred length for most cells with RF eccentricities of ~2–3°. This change was mediated by a reduction in the summation area. The inhibitory nCRF subfield was not significantly affected by attention. For cells with eccentricities of ~6–7°, attention caused an increase in preferred length, mediated largely by an increase in the summation area, but also by changes in summation gain and inhibition gain.

Before trying to interpret these findings, we should consider which types of connection should be identified with the different parameters of the DOG model. We would tentatively identify the efficacy of feedforward input (including the efficacy of recurrent excitation within a cortical column) with the summation gain. The efficacy of excitatory lateral connections and feedback connections (which represent visual field locations outside the neuron's CRF) would be identified with the size of the summation area. The latter two types of connection would also be responsible for the size of the inhibitory area when they target local inhibitory interneurons. The inhibition gain is likely to be influenced by a combination of feedforward connections, local recurrent connections, and lateral and feedback connections. Although we think that this could provide a reasonable framework for the current discussion, it is almost certainly an oversimplification and precise identification of the different cortical and subcortical connections with the different parameters of the model will require additional research (see **Supplementary Note 3** online).

It has been argued that attention does not alter neuronal tuning functions[8,9]. However, we found a strong and significant change of length tuning with attention. Length tuning might be a special case of cortical neuronal tuning that is particularly sensitive to changes in the balance between feedforward and lateral or feedback inputs. With increasing stimulus length, an increasing pool of cortical neurons contributes to a cell's response through lateral interactions[23–25] or feedback connections[16,20]. Thus, as stimulus length increases, the balance of inputs shifts from being mostly feedforward contributions at short lengths toward a substantial influence from lateral or feedback contributions at longer lengths. Attention-mediated changes in the synaptic efficacy of the lateral or feedback input will thus alter the responses to long stimuli (which depend heavily on lateral or feedback inputs) but not the responses to short stimuli (which are largely independent of lateral or feedback input), thereby shifting the length-tuning profile. This would not necessarily be the case for other feature domains (for example, orientation or direction of motion), where the relative contribution of feedforward and lateral or feedback connections is less influenced by changing the feature variable.

Length tuning has been shown to be altered by stimulus contrast, with increased contrast leading to reduced spatial summation[17,20,26], although contrast-induced changes in preferred lengths might be due to changes in excitation gain alone[20]. This contrast effect is markedly similar to the effect of attention we found at parafoveal locations, an observation that is in line with suggestions that attention is equivalent to increasing the contrast of a stimulus[11,27]. However, our results from more peripheral locations are incompatible with this idea. Our data contribute to a growing body of recent work[28,29] that shows that the link between attention and contrast cannot always be explained by changes in contrast gain[11,27].

We have shown that the precise nature of the effect of attention on spatial integration depends on retinal eccentricity, and this has important implications for the results of a previous study[30]. Ito and Gilbert[30] reported reduced nCRF facilitation under conditions of focused attention for one of their monkeys (SA), matching their previous psychophysical results[14] and our finding of reduced spatial summation with attention in the parafovea. For their second monkey (UM) they reported increased nCRF facilitation under conditions of focused attention, supporting our data from peripheral vision. The authors suggested that these opposite effects could be explained by differences in training and the strategy of the monkey, but there were also differences in the RF eccentricity between the two monkeys. Monkey SA, whose data were comparable with our data from ~2–3° eccentricity, had RFs with eccentricities in the range 1.85–3.22°. Conversely, monkey UM, whose data were more comparable with our data from ~6–7° eccentricity, had RFs with eccentricities in the range 3.68–5.25° (M. Ito, personal communication). Although the difference in eccentricity between the two monkeys in Ito and Gilbert's study was not as large as the difference between our samples, the pattern of results is consistent with our finding: attention caused reduced summation near the fovea but increased summation further toward the periphery. Therefore, the inconsistency in Ito and Gilbert's data[30] might be explained by differences in eccentricity rather than, or in addition to, differences in training and strategy.

The differential effect of attention on spatial summation as a function of eccentricity could reflect differences in the cortical network between peripheral and parafoveal vision. Evidence for such a difference has come from human psychophysical studies showing that suppressive contextual interactions are stronger for the periphery than for foveal-central vision[31]. This was paralleled by our finding that inhibitory gain makes a significant contribution to changes in length tuning in the peripheral sample but not in the parafoveal sample. For central vision it might be beneficial to exclude contextual information when objects are attended to, allowing unbiased analysis (noise and distracters excluded) of the attended location. In such circumstances, attention should reduce spatial summation. Detailed analysis of visual scenes is not possible in peripheral vision because of reduced visual resolution. Here, enhancement of facilitatory interactions by attention could promote a more integrative scene analysis and highlight attended peripheral objects as targets for impending eye movements, thereby bringing the attended object into foveal vision for detailed analysis. Alternatively, differences in sensitivity between parafoveal vision and peripheral vision (in terms of contrast or spatial sensitivity) might require different amounts of neuronal pooling to solve the task. The change in luminance contrast the animals had to detect was subtle. If contrast sensitivity is higher near the fovea, the animals might need to recruit fewer neurons. In conjunction with better spatial resolution of parafoveal neurons, this might account for the differences we found with respect to spatial integration at parafoveal and peripheral recording sites.

Recently, Womelsdorf *et al.*[12] reported that spatial attention shifts the location of RFs of medial temporal (MT) neurons, while having only a

Table 2 Medians of the parameters of interest obtained from the DOG fits

	n (cells)	Receptive field diameter	Attention condition	Preferred length	Summation area	Inhibition area	Summation gain	Inhibition gain
High contrast	92	0.25 (0.2, 0.3)	Away	0.38 (0.22, 0.52)	0.34 (0.17, 0.44)	1.40 (0.74, 2.42)	69.2 (37.3, 125.4)	41.2 (26.5, 90.9)
			RF	0.31 (0.21, 0.48)	0.28 (0.17, 0.43)	1.23 (0.60, 2.55)	83.3 (47.6, 150.6)	54.5 (31.2, 99.3)
Medium contrast	106	Not mapped with medium contrast	Away	0.47 (0.30, 0.86)	0.42 (0.24, 0.54)	1.50 (0.87, 2.07)	32.93 (20.06, 68.67)	14.5 (0.07, 29.92)
			RF	0.42 (0.28, 0.71)	0.36 (0.21, 0.51)	1.57 (0.88, 2.21)	32.29 (19.97, 65.37)	14.7 (0.03, 35.67)
~6° eccentricity	69	0.33 (0.25, 0.37)	Away	0.29 (0.21, 1.12)	0.23 (0.17, 0.47)	1.46 (0.70, 2.46)	30.96 (16.02, 47.87)	7.19 (0, 25.38)
			RF	0.40 (0.24, 1.24)	0.31 (0.20, 0.51)	1.61 (0.75, 3.46)	37.78 (20.08, 53.23)	11.7 (0, 29.35)

Each table lists the median and 25th and 75th percentiles (in brackets) of the parameter of interest under the condition of attend-RF and attend-away from the RF. The unit for preferred length, summation area, and inhibition area is degrees of visual angle (diameter). Summation and inhibition gains are in arbitrary units. For comparison the receptive field diameter (median, 25th and 75th percentiles) is also listed (in degrees of visual angle), as determined from the initial mapping with 0.1 × 0.1° stimuli under 'neutral' attention conditions.

small effect on the size of the receptive field. At first glance this seems contrary to our findings of a significantly reduced summation area for parafoveal RFs. However, our length-tuning paradigm specifically probed the effect of attention on spatial pooling over an extended area (irrespective of whether it includes the CRF or the nCRF), whereas Womelsdorf *et al.* exclusively measured responses to small stimuli, which were not intended to give rise to different amounts of spatial pooling and thus revealed exclusively the minimum response field. In our data the average summation area under both attention conditions was larger than the CRF and the minimum response field (**Table 2**). Thus, as our experiment probed the effects of attention on the efficacy of spatial pooling, rather than the minimum response field size, it does not contradict but rather complements the finding of Womelsdorf *et al.*[12].

In our task, monkeys had to detect a brightening at a very small location in the visual field. This requires a specific form of attention, in which spatial integration is likely to be detrimental. Under these circumstances we find a reduction in spatial integration at parafoveal sites and an increase at more peripheral sites. Attention might not be a unitary mechanism. It is a mechanism to ensure that task-relevant information (accurately or inaccurately) affects ongoing processing. Therefore, the influence of attention on the underlying computational architecture (for example, interactions between the CRF and the nCRF) might depend sensitively on the specific task. For example, tasks in which attention to large parts of the visual field is required[3,32] might also increase spatial integration at parafoveal locations. Perceptual learning could further alter the network effects of attention[33]. Additional studies are necessary to determine exactly how different attentional task demands alter specific computations within the neuronal architecture.

States of attention are related to the release of acetylcholine (ACh) in the cortex[34]. In a previous study[35] we tested the effect of iontophoretic application of ACh on length tuning in primate V1. Application of ACh caused a significant reduction in preferred length across the population of cells (which we estimated had RF eccentricities in the range of 1–10°). Fitting of the data with a DOG model showed that the reduction in preferred length was mostly mediated by a reduction in a cell's summation area. Thus, the effects of ACh application on length tuning were similar to the effects of directed spatial attention in our sample from parafoveal sites. This similarity in the effects of ACh application and of directing voluntary attention could support the hypothesis that ACh is involved in the neuronal processes that mediate attention. Moreover, our finding that attention mostly affects the later part of the response matches the results of local ACh application[35], and is in line with previous findings in V1 and V4 (refs. 3,11) (but see **Supplementary Note 4** online for a more detailed discussion). Our findings from more peripheral sites are difficult to reconcile with the idea that ACh is the sole agent that mediates mechanisms of attention. We propose, rather, that the effects of spatial attention are mediated by an interaction of cholinergic input and feedback connections (possibly synaptosynaptic) from higher cortical areas. Under this hypothesis, high levels of ACh allow feedback projections to exert their specific influence. This is akin to a recent model in which neuromodulator and feedback interactions allow unsupervised learning[36]. As attention is normally required for learning, attention and learning might share a common neuronal substrate. Future investigations will have to determine the precise underlying neuronal substrate and mechanisms that cause attention to have different effects on spatial integration at foveal-parafoveal as opposed to more peripheral RF locations.

In summary, we have shown that directing spatial attention toward the RF of a V1 neuron significantly alters its length tuning. In cells with parafoveal RFs this change in length tuning was induced by reducing the efficacy of facilitatory nCRF influences in the attend-RF condition. Thus, attention caused the neuronal response to be more strongly driven by visual stimuli within the CRF and less strongly influenced by the surrounding context (nCRF). Reduced spatial integration at foveal-parafoveal locations is likely to aid high-resolution analysis of attended objects and to reduce the effect of distracters or external noise on processing. We also found that attention caused increased spatial integration at more peripheral sites in V1. This shows that cortical processes, and their modulation by attention, are not uniform across visual space. Rather, processing in the periphery might rely on cortical mechanisms fundamentally different from those that operate near to the fovea, reflecting the different requirements of central and peripheral vision.

METHODS

All experiments were carried out in accordance with the European Communities Council Directive 1986 (86/609/EEC), the US National Institutes of Health Guidelines for the Care and Use of Animals for Experimental Procedures and the UK Animals Scientific Procedures Act.

Surgical preparation. After initial training, monkeys were implanted with a head holder, eye coil, and recording chambers above V1 under general anesthesia and sterile conditions. All details of surgical procedures, post-operative care and the cleaning of the implant and recording chambers have been published elsewhere[37].

Electrophysiological recordings. Once monkeys could perform the task reliably, a craniotomy was made above V1. Extracellular responses were recorded using tungsten-in-glass microelectrodes (0.5–2 MΩ, made in-house). Stimulus presentation and behavioral control was managed by Remote Cortex 5.95 (Laboratory of Neuropsychology, National Institute for Mental Health, Bethesda, MD). Neuronal data was collected either by Remote Cortex 5.95

(1-kHz sampling rate) or by Cheetah data acquisition (30-kHz sampling rate) interlinked with Remote Cortex 5.95.

Receptive field mapping. RFs were mapped by presenting a 0.1° black (100% contrast) square at pseudo-random locations on a 10 × 10 grid (a 1 × 1° area; 5 repetitions at each location; 100-ms presentation time with 100-ms gaps), while monkeys fixated centrally on the CRT monitor. To prevent the monkey from attributing a 'special status' to the RF location, an identical stimulus was simultaneously presented in the opposite hemifield. The mean response at each stimulus location (calculated from 30 to 100 ms after stimulus onset) was determined and a two-dimensional Gaussian was fitted to the response distribution. The RF center was taken as the location of the peak of the fitted Gaussian.

Main experimental stimuli and protocol. The monkey's task was to detect a small change in luminance at a cued (attended) location, while ignoring a change that occurred at a non-cued location (**Fig. 1**). Monkeys initiated trials by holding a touch bar and fixating a red fixation point (FP, 0.1° diameter) on a gray background (21 cd m^{-2}) presented centrally on a 20-inch (50.8-cm) analog CRT monitor (75 Hz, 1,600 × 1,200 pixels, 57 cm from the animal). The fixation window was ± 0.3°–0.35° wide, and the animal's eye position had to remain within these boundaries throughout the trial. Eye position was recorded with a scleral search coil. A cue (blue annulus, 0.24° outer diameter, 0.18° inner diameter) was presented for 400 ms on one side of the fixation spot. The location of the cue indicated the location to which the monkey had to attend. The cue was presented displaced along the axis connecting the FP and the RF location by one quarter of the eccentricity of the neuron's RF. The cue was displaced either toward or away from the RF to indicate whether attention should be directed toward or away from the stimulus presented in the RF. After cue offset a 250-ms (900-ms in monkey H) blank period occurred with just the FP present. Spatial and temporal separation of the cue from the test stimuli ensured that it had no direct effect on the neuronal response to the test stimulus. Thereafter, two identical stimuli were presented (test stimuli), one centered on the RF, the other at the same eccentricity in the opposite hemifield. Test stimuli were dark bars of preferred orientation and varying length (see below). After 500 ms a brighter patch (0.1° square) appeared at the center of one of the bars. If presented in the cued location it is referred to as 'target', if presented in the uncued location it is referred to as 'distracter'. The target or distracter was brighter than the test stimuli by 7.3 cd m^{-2} (± 2), depending on the contrast of the test stimulus and on the training of the monkey. After the presentation of a target, the monkey had to release the touch bar within 500 ms to receive a juice reward. If a distracter was presented first, the monkey had to continue to hold the touch bar and maintain fixation until target appearance. This occurred 1,000 ms after the distracter appeared. If the monkey made no response, the trial was terminated 500 ms after presentation of the target or distracter, whichever appeared last. Touch bar releases (correctly or incorrectly) or failure to maintain fixation resulted in immediate trial termination.

Attentional cueing was done in a blocked design, with blocks counter-balanced in random order. Conditions of cueing toward the location of the RF are labeled 'attend-RF', conditions of cueing toward the opposite hemifield are labeled 'attend-away'. Within each block, bar length was varied in either six steps (monkey B and D; 0.1°, 0.2°, 0.4°, 0.8°, 1.6°, 2.4°; bar width: 0.1°) or 7 steps (monkey H, additional 0.6° stimulus). For each bar length the target occurred once 500 ms after bar onset (early target condition) and once 1,500 ms after test bar onset (late target condition). Conditions (bar length, early or late target) were presented in pseudorandom order within each block. If the monkey made an error, the condition would be repeated later in the block. A four-block design was used in sessions where two test stimulus contrasts were presented. Only cells for which there were at least eight trials per length and attention condition were included in the analysis. The median number of trials per condition for neurons reported here was 20 (25th percentile, 16; 75th percentile, 28).

Orientation tuning and contrast response function. For monkeys B and D the preferred orientation was measured by varying test stimuli orientations in 8 steps of 22.5° between 0° and 157.5° (stimulus size: 0.4° × 0.1°, 100% contrast) while the monkey performed the task described above. Each stimulus was presented eight times for both attention conditions. The preferred orientation was taken as the orientation with the highest mean response in either attention condition.

The contrast response function was measured either under passive viewing or by using the attentional task described above. In both conditions we presented bars of the preferred orientation (size: 0.4° × 0.1°), at eight different contrasts (range: 2–100% contrast, individually adjusted to sample the steep part of the contrast response function). Each stimulus was presented at least eight times. A Naka-Rushton function was fit to the data[38] and used to select two contrasts that would give significantly different responses in the length-tuning experiment.

Spatial frequency mapping. Optimal spatial frequency (and orientation) in monkey H was determined by employing a reverse correlation technique[15,39]. Stimuli were 336 circular patches of static sinusoidal gratings (1.0° diameter) varying in orientation (12 orientations, 0–165°), spatial frequency (1, 3, 5, 7, 8, 9, 10 cycles per degree) and phase (0, 0.5π, π, 1.5π). Gratings were presented for ~60 ms in a pseudo-randomized order centered over the minimum response field. Responses were averaged over a 60-ms time window following stimulus onset at + 30 ms, and at + 60 ms. We averaged 5–10 repetitions of each stimulus. The stimulus that yielded the peak response was taken to represent the preferred orientation and preferred spatial frequency in monkey H.

Recording protocol. For each cell we initially mapped the RF, then measured the orientation tuning followed by the contrast response function and then the length tuning (in monkey H we also measured the spatial frequency preference, while contrast tuning was measured at the end of the session, provided recording stability still allowed for it). To test that our results concerning the effect of attention on length tuning were not simply due to a saturation effect, we measured length tuning at two contrast categories in monkeys B and D: high and medium contrast. In recordings defined as high contrast, the contrast of the test bar was always 100% relative to the background, and therefore it is possible that the cell's response might have been saturated. However, in recordings defined as medium contrast, a lower contrast was used and the cell's response was demonstrably not saturated (the highest response to a medium-contrast stimulus was significantly lower than the highest response to a high-contrast stimulus ($P < 0.05$, one-tailed two-sample t-test)). The range of contrasts used in medium-contrast recordings differed slightly between the two monkeys. For monkey B contrasts were between 9% and 48% (median contrast of 18%), whereas for monkey D the range was between 7% and 22% (median contrast of 10%). Data obtained using stimuli from either contrast category are referred to as 'high-contrast data' and 'medium-contrast data', respectively, throughout the text. Depending on the training and motivational status of the monkey, we measured the effect of attention on length tuning at either high or medium contrast or at both contrast levels. For monkey H we used a fixed contrast of 25% for our medium-contrast recordings.

Calculating stimulus-driven responses. We measured the neuronal response to each bar length in the attend-RF and attend-away conditions. We calculated this response from 30 ms to 500 ms after stimulus onset (that is, up to the time of the appearance of an early target). Spontaneous firing rates were calculated separately for each attention condition from responses during the 250 ms preceding the presentation of the test stimuli. All stimulus-driven activity presented herein was corrected for spontaneous activity (that is, spontaneous activity was subtracted). This was done to fulfill the assumption of the fitting model that the response is 0 with 0° bar length (no stimulus).

Length tuning analysis and fitting. Length tuning data, given by the mean response at each bar length, was initially fit with a DOG model[17]. In this model the narrower Gaussian represents the RF's excitatory center and an excitatory fringe of the nCRF, and the broader Gaussian represents the inhibitory surround (see **Supplementary Notes 3** and **5** online for more detail). Each Gaussian is described by a gain and an area constant, determining its height and width, respectively. The response to any bar length is modeled by the difference between the integrals of the area of each mechanism up to the length of the stimulus. This function captures the shape of measured length-tuning curves and allows the relative strength and size of excitation (summation) and

inhibition areas to be determined (for details of the DOG function, see ref. 40). Fits of the summation area and inhibitory area were constrained so that the inhibitory area was larger than the summation area. We optimized fits to minimize the summed squared error between the model's prediction and the mean firing rate. To take the variance in the data into account and to assess the significance of changes in peak length and fitting parameters, we used a bootstrap method as described previously[35]. The quality of the model fit was assessed by calculating the percentage of variance accounted for by the fitted model[18]. Additional fitting was performed by using an ROG model[20]. This model assumes divisive inhibitory mechanisms rather than subtractive ones. Fitting was performed in an identical manner as described for the DOG otherwise.

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

ACKNOWLEDGMENTS

We thank P. Dayan for discussions and comments on the paper. The staff of the Comparative Biology Centre (University of Newcastle upon Tyne) provided excellent technical support. The work was supported by the BBSRC (BBS/B/09325), the Wellcome Trust (070380/Z/03/Z), and the MRC (G0100407; G78/7853).

AUTHOR CONTRIBUTIONS

M.R. and A.T. conceived the experiments and performed data analysis. M.R., L.S.D., J.H., M.A.G. and A.T. performed the experiments. M.R., L.S.D. and A.T. wrote the paper.

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

1. Haenny, P.E. & Schiller, P.H. State dependent activity in monkey visual cortex. I Single cell activity in V1 and V4 on visual tasks. *Exp. Brain Res.* **69**, 225–244 (1988).
2. 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).
3. 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).
4. Spitzer, H., Desimone, R. & Moran, J. Increased attention enhances both behavioral and neuronal performance. *Science* **240**, 338–340 (1988).
5. Treue, S. & Maunsell, J.H.R. Attentional modulation of visual motion processing in cortical areas MT and MST. *Nature* **382**, 539–541 (1996).
6. Lu, Z.L., Lesmes, L.A. & Dosher, B.A. Spatial attention excludes external noise at the target location. *J. Vis.* **2**, 312–323 (2002).
7. Yeshurun, Y. & Carrasco, M. Attention improves or impairs visual performance by enhancing spatial resolution. *Nature* **396**, 72–75 (1998).
8. Treue, S. & Martinez-Trujillo, J.C. Feature-based attention influences motion processing gain in macaque visual cortex. *Nature* **399**, 575–579 (1999).
9. McAdams, C.J. & Maunsell, J.H.R. Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *J. Neurosci.* **19**, 431–441 (1999).
10. Reynolds, J.H., Chelazzi, L. & Desimone, R. Competitive mechanisms subserve attention in macaque areas V2 and V4. *J. Neurosci.* **19**, 1736–1753 (1999).
11. Reynolds, J.H., Pasternak, T. & Desimone, R. Attention increases sensitivity of V4 neurons. *Neuron* **26**, 703–714 (2000).
12. 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).
13. Zenger, B., Braun, J. & Koch, C. Attentional effects on contrast detection in the presence of surround masks. *Vision Res.* **40**, 3717–3724 (2000).
14. Ito, M., Westheimer, G. & Gilbert, C.D. Attention and perceptual learning modulate contextual influences on visual perception. *Neuron* **20**, 1191–1197 (1998).
15. DeAngelis, G.C., Freeman, R.D. & Ohzawa, I. Length and width tuning of neurons in the cat's primary visual cortex. *J. Neurophysiol.* **71**, 347–374 (1994).
16. Angelucci, A., Levitt, J.B. & Lund, J.S. Anatomical origins of the classical receptive field and modulatory surround field of single neurons in macaque visual cortical area V1. *Prog. Brain Res.* **136**, 373–388 (2002).
17. Sceniak, M.P., Ringach, D.L., Hawken, M.J. & Shapley, R. Contrast's effect on spatial summation by macaque V1 neurons. *Nat. Neurosci.* **2**, 733–739 (1999).
18. Carandini, M., Heeger, D.J. & Movshon, J.A. Linearity and normalization in simple cells of the macaque primary visual cortex. *J. Neurosci.* **17**, 8621–8644 (1997).
19. Thiele, A., Distler, C. & Hoffmann, K.P. Decision-related activity in the macaque dorsal visual pathway. *Eur. J. Neurosci.* **11**, 2044–2058 (1999).
20. Cavanaugh, J.R., Bair, W. & Movshon, J.A. Nature and interaction of signals from the receptive field center and surround in macaque V1 neurons. *J. Neurophysiol.* **88**, 2530–2546 (2002).
21. Celebrini, S. & Newsome, W.T. Neuronal and psychophysical sensitivity to motion signals in extrastriate area MST of the macaque monkey. *J. Neurosci.* **14**, 4109–4124 (1994).
22. Britten, K.H., Newsome, W.T., Shadlen, M.N., Celebrini, S. & Movshon, J.A. A relationship between behavioral choice and the visual responses of neurons in macaque MT. *Vis. Neurosci.* **13**, 87–100 (1996).
23. Shapley, R., Hawken, M. & Ringach, D.L. Dynamics of orientation selectivity in the primary visual cortex and the importance of cortical inhibition. *Neuron* **38**, 689–699 (2003).
24. Angelucci, A. *et al.* Circuits for local and global signal integration in primary visual cortex. *J. Neurosci.* **22**, 8633–8646 (2002).
25. Ferster, D., Chung, S. & Wheat, H. Orientation selectivity of thalamic input to simple cells of cat visual cortex. *Nature* **380**, 249–252 (1996).
26. Kapadia, M.K., Westheimer, G. & Gilbert, C.D. Dynamics of spatial summation in primary visual cortex of alert monkeys. *Proc. Natl. Acad. Sci. USA* **96**, 12073–12078 (1999).
27. Carrasco, M., Ling, S. & Read, S. Attention alters appearance. *Nat. Neurosci.* **7**, 308–313 (2004).
28. Williford, T. & Maunsell, J.H. Effects of spatial attention on contrast response functions in macaque area V4. *J. Neurophysiol.* **96**, 40–54 (2006).
29. Buracas, G.T. & Boynton, G.M. The effect of spatial attention on contrast response functions in human visual cortex. *J. Neurosci.* **27**, 93–97 (2007).
30. Ito, M. & Gilbert, C.D. Attention modulates contextual influences in the primary visual cortex of alert monkeys. *Neuron* **22**, 593–604 (1999).
31. Xing, J. & Heeger, D.J. Center-surround interactions in foveal and peripheral vision. *Vision Res.* **40**, 3065–3072 (2000).
32. Freeman, E., Sagi, D. & Driver, J. Lateral interactions between targets and flankers in low-level vision depend on attention to the flankers. *Nat. Neurosci.* **4**, 1032–1036 (2001).
33. Li, W., Piech, V. & Gilbert, C.D. Perceptual learning and top-down influences in primary visual cortex. *Nat. Neurosci.* **7**, 651–657 (2004).
34. Everitt, B.J. & Robbins, T.W. Central cholinergic systems and cognition. *Annu. Rev. Psychol.* **48**, 649–684 (1997).
35. Roberts, M.J. *et al.* Acetylcholine dynamically controls spatial integration in marmoset primary visual cortex. *J. Neurophysiol.* **93**, 2062–2072 (2005).
36. Roelfsema, P.R. & van Ooyen, A. Attention-gated reinforcement learning of internal representations for classification. *Neural Comput.* **17**, 2176–2214 (2005).
37. Thiele, A., Delicato, L.S., Roberts, M.J. & Gieselmann, M.A. A novel electrode-pipette design for simultaneous recording of extracellular spikes and iontophoretic drug application in awake behaving monkeys. *J. Neurosci. Methods* **158**, 207–211 (2006).
38. Thiele, A., Distler, C., Korbmacher, H. & Hoffmann, K-P. Contribution of inhibitory mechanisms to direction selectivity and response normalization in macaque middle temporal area. *Proc. Natl. Acad. Sci. USA* **101**, 9810–9815 (2004).
39. Ringach, D. & Shapley, R. Reverse correlation in neurophysiology. *Cognit. Sci.* **28**, 147–166 (2004).
40. Sceniak, M.P., Hawken, M.J. & Shapley, R. Visual spatial characterization of macaque V1 neurons. *J. Neurophysiol.* **85**, 1873–1887 (2001).