

Spatial integration and its moderation by attention and acetylcholine

Mark J. Roberts, Alexander Thiele

Institute of Neuroscience, University of Newcastle upon Tyne, Newcastle upon Tyne, NE2 4HH, United Kingdom

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1. ABSTRACT

Attention is often regarded as a mechanism by which attended objects become perceptually more salient, akin to increasing their contrast. We demonstrate by means of human psychophysics that attention is better described as a mechanism that reduces contextual integration, thereby ensuring that task irrelevant information is prevented from influencing the processing of task relevant information. To investigate possible neuronal bases of this phenomenon we studied the effects of attention on spatial integration in V1 of the macaque monkey. In line with our psychophysical results, attention directed to parafoveal locations reduced spatial integration by reducing the summation area of V1 neurons. Additionally we measured length tuning in V1 in the presence and absence of externally applied acetylcholine in V1 of the marmoset monkey. The effects of acetylcholine application and attention were largely similar. Acetylcholine reduced spatial integration by reducing the neuron's summation area. These data demonstrate that attention can alter perceptual and neuronal spatial integration, and that acetylcholine might contribute to task dependent receptive field dynamics.

2. INTRODUCTION

Local context influences the ability to detect and discriminate visual targets (1-6). Certain contextual configurations result in pop-out which enhance stimulus detection (7-9), while others result in crowding and impair stimulus detection (10). Neural correlates of these perceptual phenomena have been found in sensory visual areas, where responses to a stimulus in the classical receptive field (CRF) are facilitated or suppressed by stimuli presented in the non-classical receptive field (nCRF) (11-13). Whether context results in facilitation or suppression depends on a variety of factors, including the luminance contrast of the target (or central stimulus). At high target contrast, contextual stimuli mostly have a suppressive effect (12-15), but facilitation can occur if low contrast targets are surrounded by high (2, 3, 13, 16-19) or low contrast contextual stimuli (13, 15, 20). While the stimulus configuration in the external world determines to a large extent how low level stimulus features are processed, visual processing is also influenced by selective attention. Selective attention is generated and maintained in 'higher' cortical areas (21-28). These areas exert top-down control

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over processing in sensory cortex (22-24, 29-33), thereby ensuring that task relevant information is processed at the expense of task irrelevant information. Attention has been shown to affect virtually all aspects of visual processing (23-26, 29, 31-47). Attending to low luminance contrast stimuli increases their apparent contrast (48). At the neuronal level this is mirrored by the finding that attention boosts neuronal responses to match responses elicited by higher contrast stimuli, thereby shifting contrast response functions (41, 49) (but see (50)). Thus attending to a stimulus is sometimes compared to increasing its luminance contrast (48, 51). Intuitively, the idea that attention is equivalent to a signal increase is appealing (making the attended objects appear brighter, louder, or more intense). But it is unlikely to be the sole mechanism by which attention acts. In line with this suggestion, psychophysical studies have shown that attention in noisy environments is better described as a mechanisms of noise exclusion (52, 53), than as a mechanisms of signal enhancement. In principle, the effect of context on visual processing should be task dependent. If context can help to solve the task, attention should increase its influence, if context is akin to noise, attention should decrease its influence. In line with this prediction psychophysical studies have shown that contextual integration was increased when attention was directed simultaneously to the stimulus *and* the context (2, 54, 55). However, attention served to reduce the influence of contextual stimuli which were behaviorally irrelevant 'distracters' and should therefore have been excluded from processing to optimize performance (4, 6).

At the neuronal level attention directed to isolated stimuli can result in multiplicative enhancements of response rates (42, 56), while more complex effects occur when attention is directed to one of two stimuli presented inside the CRF (43, 45, 57). In the latter condition, attention reduces the influence of the non-attended stimulus (45, 57). This effect could be mediated by changes in the profile of CRFs, which can shift towards attended objects (44, 58). Another form of attention-dependent contextual modulation was recently described in area V2 where neurons respond optimally for object borders and signal border ownership. Here the effects of attention depended on whether an objects' border crossing the CRF was part of an attended or unattended object, responses to the borders of attended objects were enhanced, while responses to the borders of objects that touched attended objects but were not themselves part of the attended object were suppressed, resulting in a relative suppression in the representation of objects surrounding the attended object (59). Thus, a variety of attentional influences on spatial (contextual) integration have been demonstrated for extrastriate cortical areas. It is currently unknown whether similar effects occur in primary visual cortex (V1). Due to the small size of V1 CRFs, attention induced changes of spatial integration should be best detectable by investigating nCRF influences. A reduction in nCRF inputs during attentive states would promote noise exclusion (53), improve spatial resolution (60), and thus aid perception.

While the precise attentional conditions which mediate alteration of CRF and nCRF influences are still poorly understood, even less is known about the cellular and molecular mechanisms mediating such effects. Changes in spatial integration occur if the efficacy of selected synapses is up- or down- regulated, and/or by the activation of inhibitory connections which can selectively gate the flow of information in the cortex. It is widely accepted that feedback plays a substantial role in mediating attentional effects (21, 61-66). In addition to these, the neuromodulator acetylcholine (ACh) seems to be important in mediating (or enabling) states of attention (22, 28) and may have a role in altering CRF-nCRF influences as suggested by *in vitro* studies (67-73). These *in vitro* studies have demonstrated that ACh selectively alters the flow of feed-forward and lateral/feed-back information in the cortex. ACh suppresses the efficacy of intra-cortical synapses by activating muscarinic receptors (67-73), and increases the efficacy of feed-forward/thalamocortical input (74), by acting on presynaptic nicotinic receptors located on thalamocortical synapses (75). In primary visual cortex the thalamocortical input is largely responsible for the CRF response properties (76), while lateral and feed-back connections are often identified with mediating the nCRF influences (77-79). Thus, ACh applied *in vivo* should result in reduced impact of stimuli presented in the nCRF while increasing the effect of stimuli placed within the CRF. If true, the effects of ACh would be similar to the predicted effects of attention.

To test the above proposals we performed three sets of experiments. Firstly, we investigated whether attention reduces contextual influences in an orientation discrimination task employing human psychophysics. In line with previous physiological (13, 19) studies we found that stimulus contrast determined whether contextual influences were facilitatory or inhibitory, which in the case of our study made targets appear more context like (facilitation) or less context like (inhibition). The even more important finding of our psychophysical study was that attention reduced contextual influences irrespective of the sign of these influences. Secondly, we investigated neurophysiologically, whether attention affected spatial integration of V1 neurons in macaque monkeys, and, thirdly, whether local application of acetylcholine to V1 neurons results in similar effects on spatial integration. We found that attention directed to parafoveal receptive fields of V1 neurons, and the application of acetylcholine to V1 neurons in anesthetized monkeys resulted in a reduction of spatial integration in a manner comparable to our psychophysical results. Overall, this suggests that attention is not just a mechanism by which neuronal activity is increased at the attended location. Attention can alter spatial integration at the perceptual and neuronal level, whereby task relevant information is highlighted for further processing, while task irrelevant information is filtered out.

3. EFFECTS OF ATTENTION ON SPATIAL INTEGRATION IN HUMAN PSYCHOPHYSICS

Human subjects reported the orientation of a target bar in relation to a reference bar. Both bars were

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Table 1. Stimuli used in human psychophysics

Exp #	Target to Reference orientation difference	Target to Context orientation difference	Number of Subjects
1	-3 -2 -1 0 1 2 3	-4 -3 -2 -1 0 1 2 3 4	3 high contrast
2	-6 -4 -2 0 2 4 6	-8 -6 -4 -2 0 2 4 6 8	3 high contrast
3	-3 -2 -1 0 1 2 3	-12 -9 -6 -3 0 3 6 9 12	2 high contrast 1 low contrast
4	-6 -4 -2 0 2 4 6	-12 -9 -6 -3 0 3 6 9 12	5 high contrast 4 mid contrast 6 low contrast 2 no context bars

Our experimental design was based around nine different target orientations relative to the context bar orientation. For each target orientation we presented seven reference orientations. The exact values of the target-to-context bar orientation differences and the target-to-reference orientation differences varied between experiments. The table gives these values for each of the four settings and gives the numbers of subjects measured in each contrast condition using each setting.

displayed simultaneously opposite from a fixation spot (Figure 1) for a brief period of 80 ms. Contextual information was provided by a spatio-temporal bar sequence that preceded target and reference bar presentation. Specifically, the target appeared as the 5th bar in the sequence of 4 preceding context bars. The sequence of bars resulted in a diagonal apparent motion stimulus (see figure 1). The target bar could have 9 different orientations relative to the context bar (Table 1), while the reference bar could have 7 different orientations relative to each target bar orientation (figure 1 and table 1). A highly similar stimulus has been used before to show that human perception (80) and neuronal representation (in macaque area V1 (81)) of the target orientation is altered by the presentation of the context bars in a Bayesian like manner. Subjects reported whether the orientation of the target was ‘counter-clockwise’, ‘same’, or ‘clockwise’ relative to the reference bar by pressing keyboard letters ‘j’, ‘k’, and ‘l’ respectively. We manipulated the subjects’ attention between two conditions. In one condition subjects could fully attend to the orientation discrimination task (single task condition). In a second condition (dual task) subjects were required to additionally perform an attentionally demanding color-counting task. In the dual task subjects first reported the number of times a central patch was presented as either red or green, and thereafter indicated their perception of the target orientation relative to the reference orientation. The color of the circular patch changed randomly four times during each trial between seven possible colors (red, green, blue, magenta, grey, dark yellow and bright yellow), at a rate of 5.4 Hz (for additional details see figure legend 2). For both tasks we collected data from three target contrast conditions; high target contrast (82%), medium target contrast (10%) and low target contrast (<4%). The context bars were of high contrast (82%) in all conditions. Subjects were instructed to maintain fixation at the fixation point throughout all trials.

We found that the influence of the context on the perceived orientation was dependent on the level of

attention subjects could devote to the orientation discrimination, the contrast of the target bar, and the orientation difference between the target and context bars. We will first describe the effects from the single task condition where subjects could fully attend to the orientation discrimination task. This will be followed by a description of the dual task data, where attention was focused on the color counting task.

3.1. Single task data

When the target had high luminance contrast, subjects perceived it to be tilted further from the context bar orientation than was the case. Specifically we found a high proportion of ‘clockwise’ responses when the target was counter-clockwise to the reference *but clockwise to the context bars*, and a high proportion of ‘counter-clockwise’ responses when the target was clockwise to the reference *but counter-clockwise to the context bars*. Thus, orientation differences between the context bars and the target were perceptually exaggerated indicating that the presence of the context bars had a repulsive effect on the perceived target orientation. We transformed the data such that the subject’s ‘clockwise’ and ‘counter-clockwise’ responses were represented in a more meaningful framework that describes whether the subject perceived either the target or the reference as being most similar to the context bar orientation. Specifically, we determined whether the absolute target-to-context bar orientation difference (T-C) was perceived to be larger or smaller than the reference-to-context orientation difference (R-C). These alternative responses are abbreviated as T-C>R-C and T-C<R-C respectively for the remainder of the text. We will refer to conditions where the target orientation is perceived to be more dissimilar to the context bar orientation than it really was as *contextual repulsion*. Thus, if subjects indicated a larger proportion of ‘T-C>R-C’ responses, when in fact the physical display for these trials corresponded to T-C<R-C, then the condition of contextual repulsion was fulfilled. Conversely, in conditions where subjects indicated a larger proportion of ‘T-C<R-C’ responses, when in fact the physical display for these trials corresponded to T-C>R-C, the target orientation was perceived to be more similar to the context bar orientation than it really was. These conditions are referred to as *contextual attraction*.

At high luminance contrast we found high proportions of ‘T-C>R-C’ responses when in reality the orientation difference was T-C<R-C. The proportion of these misjudgments indicated the strength of the repulsion effect induced by the context bars. The strength of repulsion was dependent on two factors: the orientation difference between the target and context bars, and the allocation of voluntary attention. The repulsion effect was largest in conditions where there was a large orientation difference between the target and context bars, and in conditions of reduced attention, i.e. in the dual task (see below).

To quantify the strength of the repulsion we took the difference between proportions of ‘T-C>R-C’ and ‘T-

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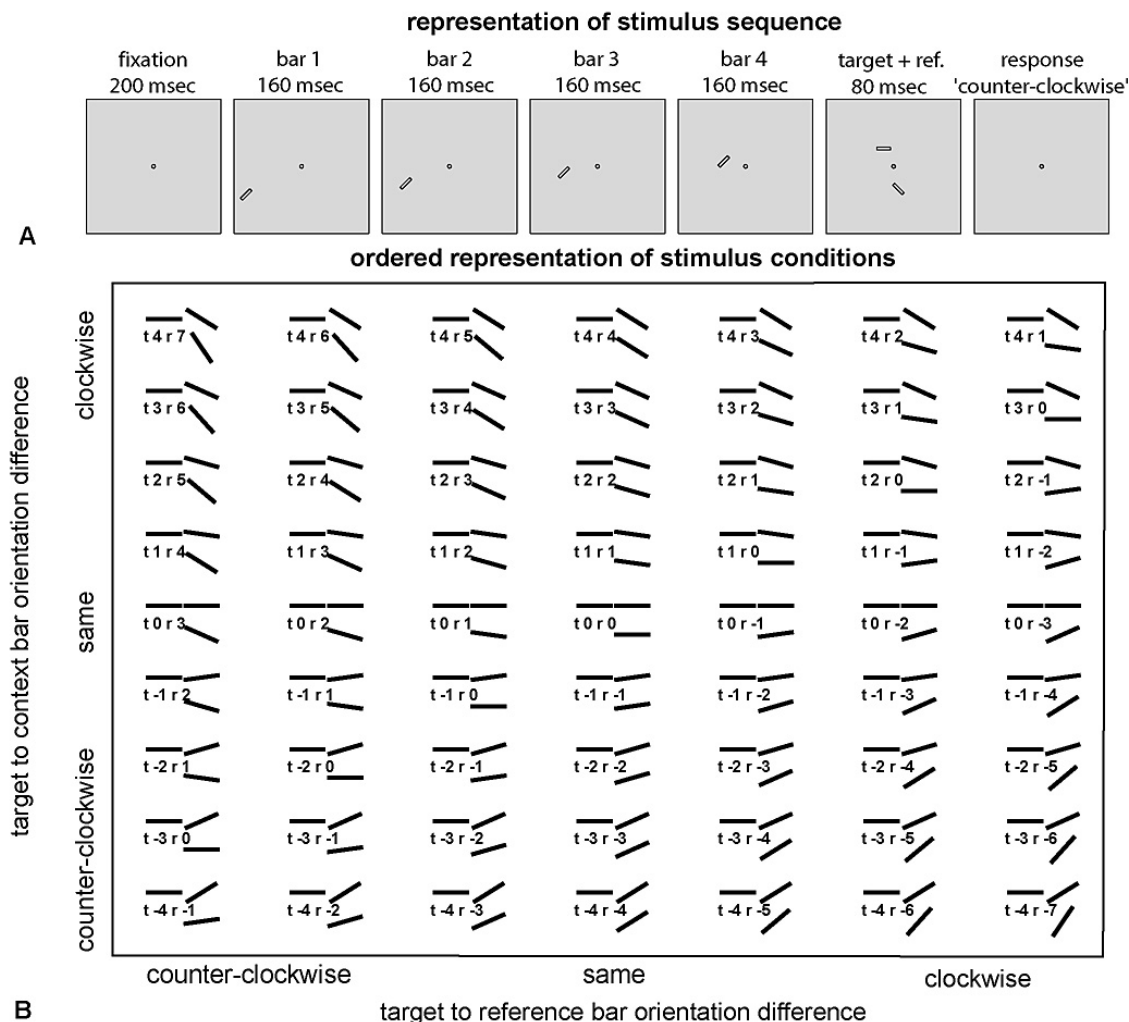


Figure 1. A. Representation of stimulus sequence. The presentation time of each frame is given above each panel. Bars 1-4 provided the spatio-temporal context. They appeared from either the lower left, or the upper right (assigned randomly). Bar size was $0.8 \times 0.07^\circ$. Bar 5 was always the target stimulus which appeared at an eccentricity of 1.1° to the upper left of the fixation spot. The reference bar appeared simultaneously with the target bar. It was presented to the lower right of the fixation spot, displaced by half its length along the screen diagonal relative to the target bar. Target bar orientation was varied pseudo-randomly in 9 steps relative to the context bar. Reference bar orientation was varied pseudo-randomly in 7 steps relative to the target bar orientation. Bars were brighter than the uniform gray background (13.6 cd/m^2). Four circular color colored patches were presented simultaneously in sequence at the fixation spot location starting 109 ms after the first context bar appeared (78ms presentation time, 109 ms gaps; 7 possible colors: red, green, blue, magenta, grey, dark yellow and bright yellow). Subjects were asked to ignore these patches in the single task, but count and report the number of red and green patches in the dual task before reporting the orientation of the target relative to the reference (a number of 1-4). The colored patches are not shown here. B. Ordered representation of stimulus conditions. Each combination of target and reference orientation is represented as a triplet of lines. The horizontal line on the left represents the final context bar, the line adjacent to it represents the target. The reference is represented below the target. The orientation difference between target and reference changes across columns. Columns to the left show conditions where the target was counter-clockwise to the reference. Columns to the right show conditions where the target was clockwise to the reference. The central column shows conditions where the target and reference had the same orientation. The orientation difference between the target and the context bars changes across rows. Upper rows show conditions where the target was clockwise to the context bar, lower rows show conditions where the target was counter-clockwise to the context bars. The central row shows conditions where the target had the same orientation as the context bars. The full raw data set shown in Figure 2 is shown according to these stimulus conditions. Next to each triplet of lines the relative orientation difference between the target and context bars is given by the value 't'. The relative orientation difference between the reference and context bars is given by the value 'r'. The values given here are generic for all experiments, the exact values are given in table 1. For data transformation (see also figure legend 2), data were combined from conditions of equal value of t and r but opposite sign, for example the condition at the top left ($t = 4, r = 7$) is a mirror image match for the condition at the bottom right ($t = -4, r = -7$). Responses along the central row were not combined.

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C<R-C' responses for each possible target-reference orientation. This resulted in a matrix of 5*7 data points which we then fitted with a 3-dimensional curved surface (see figure 2 and its legend for additional detail). This surface gave good fits to the data, evident by a relatively high percentage of variance accounted for (median =90.1%, 25th percentile 86.6%, 75th 92.8%). Of the five fitting parameters, two are relevant to the performance of the subject, the remaining three being essentially scaling factors. The slope of the sigmoidal component of the surface, which describes responses as a function of the target-to-reference orientation difference (legend of figure 2), is related to the reliability of the subjects' responses. The gradient of the straight line fitting parameter, which describes response differences as a function of the target-to-context bar orientation difference, corresponds to the amount by which the subject's perception was shifted as a function of the angular difference between the target and context bars. Positive values indicate that the context bars resulted in attraction, while negative values indicate contextual repulsion. Thus, the gradient is the main parameter of interest here. The median gradient in the high contrast experiments was -0.24 (25th percentile = -0.13, 75th percentile -0.33, n=13), meaning that for each degree of angular difference between the target and context bar orientation, the subject's perception of the target was shifted away (repelled) from the context bars by 0.24°.

In the medium contrast condition (target bar at 10% contrast) the data were essentially identical to those in the high contrast condition. The median gradient of the straight line component was -0.3 (25th percentile = -0.25 75th = -0.36; n=4), i.e. for each degree of difference between target and context bars the perceived target orientation would be shifted away from the context bar orientation by 0.3°. There was no significant difference between the gradient values in the medium contrast experiments and those from the high contrast experiments (two sample t-test p=0.43 CI -0.26, 0.12).

In the low contrast experiments the target bar was presented at <4% luminance contrast, while the context and reference bars were kept at 82%. Here, the pattern of responses was opposite to that found in the high and medium contrast experiments. Thus, lowering the luminance contrast of the target to <4% reversed the repulsion effect seen in the high (82%) and medium (10%) contrast conditions, and caused an attractor effect on the perceived orientation of the target. The median gradient of the straight line component in the fitted surface was 0.21 (25th percentile 0.03, 75th 0.28, n=7), meaning that for each degree of angular difference between the target and context bars, the perceived target orientation was shifted towards the context bar orientation by 0.21°.

Did the subjects still reliably perceive the target at this low contrast? To test this we included an additional 10% of trials in which the target was not presented. On these trials the subjects should report that the target was not presented. Subjects correctly identified that the target was not presented on 72% (median) of trials in which the target was not presented (25th percentile = 39%, 75th percentile =

94%, chance performance = 10%). Subjects correctly identified the presence of the target (by making a 'clockwise', 'counter-clockwise' or 'same' response) on 96.5% of trials in which the target was presented (25th percentile 85.5%, 75th percentile 99.0%). Thus subjects reliably perceived the absence and presence of the target.

3.2. Dual task data

Context bars influenced perception more strongly in the dual task (reduced attention condition) than in the single task (full attention condition). This occurred irrespective of whether context bars caused repulsion or attraction of the perceived target orientation. We quantified the effect of attention on contextual modulation by comparing the gradient of the shifting parameter 'g' in the 3D surface fits (figure 2) between the single and dual task data. In the high contrast experiments the median gradient was -0.24 in the single task (25th percentile = -0.13, 75th percentile -0.33) and -0.37 in the dual task (25th percentile = -0.27, 75th -0.51). In the medium contrast data the median gradient was -0.3 in the single task (25th percentile = -0.25, 75th -0.36) and -0.8 in the dual task (25th percentile = -0.52, 75th -1.24). In the low contrast experiments the median gradient in the single task was 0.21 (25th percentile 0.03, 75th 0.28), and it was 0.41 (25th percentile 0.28, 75th 0.49) in the dual task. Thus directing full attention towards the orientation discrimination task reduced the context induced shift of perceived orientation (be it repulsion or attraction) by more than 0.1° per degree of angular difference between the target and context bars. This corresponds to a reduction of contextual influence of almost 50% in the full attention condition (median percentage change = 48%, 25th percentile = 28%, 75th percentile = 87%) when compared to the reduced attention condition.

Figure 2 D shows the individual comparisons between the single and dual task of the gradient component 'g'. Significance was tested for each contrast condition separately, and for all contrasts combined using a signed rank test (SRT). For the combined data we used the absolute values of the fitting parameters to account for the fact that an increase in repulsion effect (high/medium contrast experiments) was associated with the gradient of the straight line becoming more negative in the dual task, while an increase in the attractor effect (low contrast experiments) was associated with a more positive gradient in the dual task. In line with the previous description of the data, the dual task was associated with an increase in the gradient component 'g' which was significant for the high contrast data separately (values in Table 2, p=0.005, SRT) and low (values in Table 2, p=0.031, SRT), but was not significant for the medium contrast data (values Table 2, p=0.25 SRT) possibly due to the small sample size (n=4). The change in the gradient 'g' was highly significant for the absolute values when the data from all contrast levels were combined (values in Table 2, p=0.00014, SRT). There was a trend for a reduction in the slope of the sigmoidal function between the single and dual task (data not shown), which quantifies the accuracy of the subjects responses (steep slopes indicate high accuracy). This trend was significant for the high contrast data (values in Table 2, p=0.033), but did not reach significance either for the

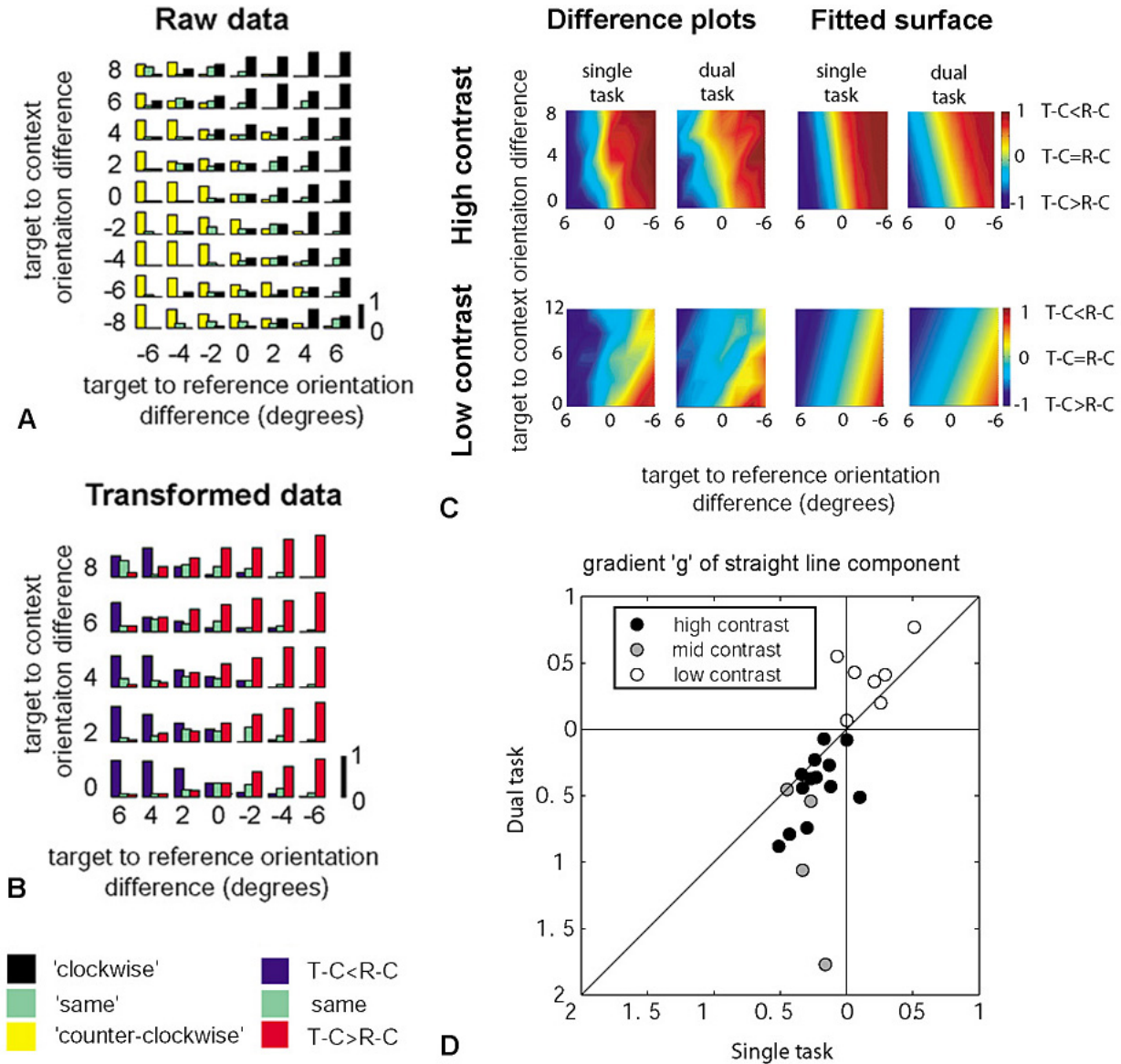


Figure 2. A. Example of raw data: proportions of ‘clockwise’ (black bars), ‘same’ (green) and ‘counter-clockwise’ (yellow) responses in each condition. Rows show data from conditions of equal target-to-context orientation differences, columns show conditions of equal target-to-reference orientation differences. B. Transformed data. In Figure 2A each individual condition is the mirror image of another condition in the set. Thus it is possible to combine opposite responses from conditions of equal but opposite target-to-reference and target-to-context orientation differences. To find the corresponding mirror image it is necessary to first reflect all conditions along the central column and then along the central row. Each of these mirror image conditions correspond to the absolute angular distance of the ‘target-to-context’ and of the ‘reference-to-context’, thus replacing the nomenclature ‘clockwise’, ‘same’, and ‘counter-clockwise’. Such a data reduction allows for a description of the data in the more meaningful reference frame of the angular distance of the target and reference to the context bar orientation. After transformation the respective response proportions show the number of trials in which the perceived target-to-reference orientation difference was larger or smaller than the target-to-context orientation difference (T-C<R-C or T-C>R-C, blue and red bars respectively). Green bars show proportion ‘same’ responses, i.e. where the subject perceived both bars to have the same angular distance relative to the context bar. Rows of bars show data from conditions of equal target-to-context orientation differences, columns show conditions of equal target-to-reference orientation differences. The angular difference between reference and context bars is given by the sum of the X and Y axis values, thus for the condition in the upper right the target was 8° from the context bars, and the reference was 2° from the context bars, meaning that T-C>R-C (red) was the correct response. Therefore the x-axes run from 6 to -6. C. Difference plots and fitted surfaces: colored surface shows the difference between T-C<R-C and T-C>R-C responses for each triplet data point after transformation. Blue indicates a high proportion of T-C<R-C responses, red a high proportion of T-C>R-C responses. Green/yellow shows either an equal proportion of T-C<R-C and T-C>R-C responses or a high proportion of ‘same’ responses. The upper row shows example data of the context bar influence on the perceived orientation with a high contrast target bar for

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the single and dual task condition. The tilt of the yellow/green border between blue and red indicates the strength of the contextual influence. No tilt angle (border between blue and red runs along the vertical) indicates absence of any influence, a leftward tilt is indicative of perceptual repulsion, i.e. the target was perceived to be tilted more from the context than it really was. The lower row shows example data from the low contrast experiment. The rightward tilt indicates that the context had an attractor effect on the perceived target orientation. For high and low contrast data sets the tilt angle of the yellow/green line was larger in the dual task condition (relative to the vertical). To quantify the strength of attractor and repulsion effects we fitted the difference plots with a 3D surface from a sigmoidal function along the target-to-reference axis and a sloping straight line along the target-to-context bar axis. The form of this surface was:

$$P(X, Y) = R_{\max} * \left(\frac{(X - (g * Y))}{i^n + (X - (g * Y))^n} \right) + R_{\min}$$

where the ‘X’ dimension is the orientation difference between target and reference and the ‘Y’ dimension is the orientation difference between the target and context bar. Rmax and Rmin are scaling factors determining the upper and lower range of the surface. The inflection point of the surface is determined by the parameters ‘i’ this relates to a bias the subject may have for reporting either ‘T-C<R-C’ or ‘T-C>R-C’, and so is essentially a third scaling factor. The parameter ‘n’ determines the slope of the sigmoid (i.e. the slope along the target-to-reference dimension) and so relates to the reliability of the subject’s responses. The parameter ‘g’ determines the gradient of the straight line component (i.e. along the target-to-context bar dimension) and so measures the strength of the contextual influence. We adjusted these five parameters (Rmax, Rmin, i, n and g) to fit the surface to the matrix of difference values by minimizing the summed squared error. The gradient parameter ‘g’ was most relevant in the context of our study, as it shows the strength of the influence of the context on perception. D) Fitted gradient parameter ‘g’ for all experiments as a function of attention condition (single vs. dual task). Data from high contrast experiments are marked by filled black circles, data from the mid contrast condition are marked by a filled gray circle and data from low contrast experiments are marked by open circles. Data points above the horizontal indicate that context had an attractor effect (low contrast target), data points that fall below the horizontal indicate that context had a repulsive effect (mid and high contrast target). Attention reduced the strength of these effects irrespective of their sign. This is evident by the leftward displacement of open circles (low contrast) relative to the diagonal, i.e. larger ‘g’ values in the dual task condition, and by the rightward displacement of gray and black circles relative to the diagonal, i.e. more negative ‘g’ values (more repulsion) in the dual task at medium and high contrast.

Table 2. Fitting parameters from human psychophysics

High Contrast					Medium Contrast					Low Contrast				
Subject	n		g		Subject	N		g		Subject	n		g	
	single task	dual task	single task	dual task		single task	dual task	single task	dual task		single task	dual task	single task	dual task
KW	0.3	14.62	-0.43	-0.79	CP	0.11	0.98	-0.16	-1.77	MR	8.43	8.42	0.00	0.07
WS	22.26	0.6	-0.10	-0.51	DC	0.91	4.91	-0.33	-1.06	NT	0.54	2.05	-0.07	0.55
CS	12.10	0.7	-0.12	-0.43	SJH	0.18	0.8	-0.27	-0.54	YL	9.14	6.77	0.26	0.20
DB	13.21	0.3	-0.24	-0.23	TE	0.13	0.71	-0.45	-0.45	ZI	3.93	7.16	0.21	0.36
AT	11.86	4.07	-0.23	-0.36						EA	7.61	3.07	0.29	0.41
AG	16.83	5.01	-0.33	-0.44						IS	7.63	9.10	0.06	0.43
DH	3.58	4.07	-0.34	-0.34						ER	3.49	2.45	0.51	0.77
JS	0.18	0.08	-0.30	-0.74										
NT	3.54	2.39	0.00	-0.08										
YL	12.39	7.4	-0.17	-0.07										
BP	10.8	0.15	-0.51	-0.88										
PA	5.50	0.39	-0.27	-0.37										
HS	4.03	0.35	-0.13	-0.27										
Median	10.8	0.70	-0.24	-0.37	Median	0.15	0.89	-0.30	-0.80	Median	7.61	6.77	0.21	0.41
25th	3.58	0.35	-0.33	-0.51	25th	0.12	0.78	-0.36	-1.24	25th	3.71	2.76	0.03	0.28
75th	12.39	4.79	-0.13	-0.27	75th	0.36	1.96	-0.25	-0.52	75th	8.03	7.79	0.28	0.49
SRT	P=0.033		P=0.005		SRT	P=0.13		P=0.25		SRT	P=0.94		P=0.031	
SRT Comp	P=0.077		P=0.00014											

Fitting parameters to quantify the influence of the context bar and the influence of attention on orientation discrimination. Parameters were obtained by fitting a tilted 3D surface to the data (for details see Figure 2 legend). The parameter ‘n’ corresponds to the slope of the surface along the target-to-reference axis and so relates to the reliability of the response. The parameter ‘g’ corresponds to the gradient of the surface along the target-to-context bar axis and so relates to the influence of the context bar on the perceived target orientation. Lower rows give the median, 25th and 75th percentiles over the population. P-values indicate whether a significant difference for the parameter of interest occurred between single and dual task for each contrast condition separately (signed rank test, SRT) and for all contrasts combined (SRT Comb.).

combined data (values Table 2, p=0.077, SRT), or for any other individual contrast level (values in Table 2, medium p=0.13, low p=0.94 SRT). The steepening of the sigmoid slope in the single task condition demonstrates the well known enhancement in perceptual accuracy under conditions of full attention. This effect is distinct from the attention mediated reduction of contextual influences, which also led to fewer incorrect responses in the single task in our experiment. An improvement in accuracy reduces random errors, while suppressing in contextual

influences reduces the consistent bias in subjects’ responses. These distinct sources of error could be separated in our experiment thanks to the two dimensions of ‘target-to-reference’, which measured random errors, and ‘target-to-context bar’ which measured consistent biases in responses caused by contextual influence.

3.3. Human psychophysics summary

Spatio-temporal context systematically influences orientation discrimination in human subjects. The nature of

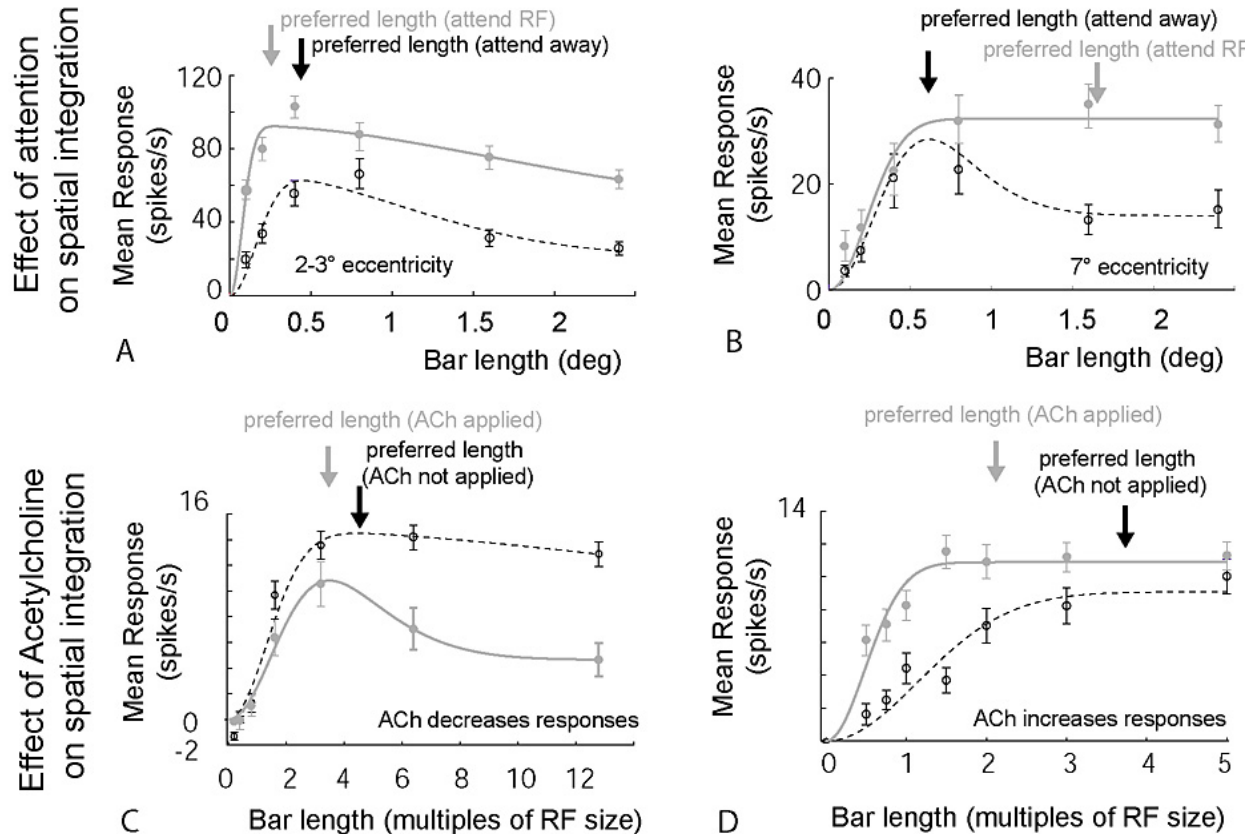


Figure 3. Effect of attention and acetylcholine on length tuning in V1. A. Example of how attention affected length tuning in a cell recorded at a parafoveal location (2.8° eccentricity). Grey data points show the activity as a function of bar length when attention was directed to the CRF, black data points show the activity when attention was directed into the opposite hemifield. Solid curves represent fitted data based on a Difference of Gaussian model. Arrows show the preferred length when attention was directed to the CRF (grey) and when it was directed away from the CRF (black). B. Example of attention induced changes in spatial integration for a cell with a peripheral receptive field (7.1° eccentricity). Attention still increased firing rates at this eccentricity, but the increase was more pronounced at medium length bars, thus resulting in increased spatial integration when attention was directed to the CRF. All symbols as in A. C. Length tuning in a cell which was facilitated by acetylcholine. Grey symbols, errorbars and fitted line (based on a Difference of Gaussin fit) show activity when acetylcholine was applied, black symbols, errorbars and dashed line show activity when it was not applied. Acetylcholine increased firing rates at all bar length, but proportionally more at shorter bars, thus resulting in reduced preferred bar length. D. Length tuning in a cell which was inhibited by acetylcholine. All symbols are as described in C. The cell was inhibited by acetylcholine mostly at longer bar lengths, resulting in a reduction of preferred length. Errorbars show s.e.m.

the influence was dependent on the luminance contrast of the target. At high and medium contrasts the perceived orientation difference between the target and context bar was enhanced, i.e. context bars had a repulsion effect. At low contrast the perceived orientation difference between the target and context bars was reduced, i.e. context bars had an attractor effect. The magnitude of the influence of the context bars was dependent on the orientation difference of the target from the context bars and on the allocation of voluntary attention. In the full attention condition the influence of the context bars was reduced by almost 50% compared with the divided attention condition.

4. EFFECTS OF ATTENTION ON SPATIAL INTEGRATION IN MACAQUE V1

We measured the effects of attention on spatial integration in V1 in a total of 73 cells with parafoveal CRF

locations in 2 monkeys using medium contrast stimuli (for details see (82)). The CRF eccentricity of these cells was similar to the eccentricity explored in human psychophysics (in the human psychophysics studies stimuli occurred ~1.1° away from the fovea, while the CRFs were located at 2-3° away from the fovea). An example of the effect of attention on firing rates and length tuning for a single cell is shown in figure 3A. When attention was directed to the CRF, firing rates were increased, especially for short bar stimuli. As a consequence the preferred length shifted towards shorter bar lengths (compare grey and black arrows). A shift of the preferred length towards shorter bar length when attention was directed to the CRF was a consistent finding for our parafoveal cell sample. The population data are shown in figure 4A. Figure 4 plots the preferred length and the parameters of the difference of Gaussian (DOG) model fits (82) when attention was directed to the CRF and when it was directed into the

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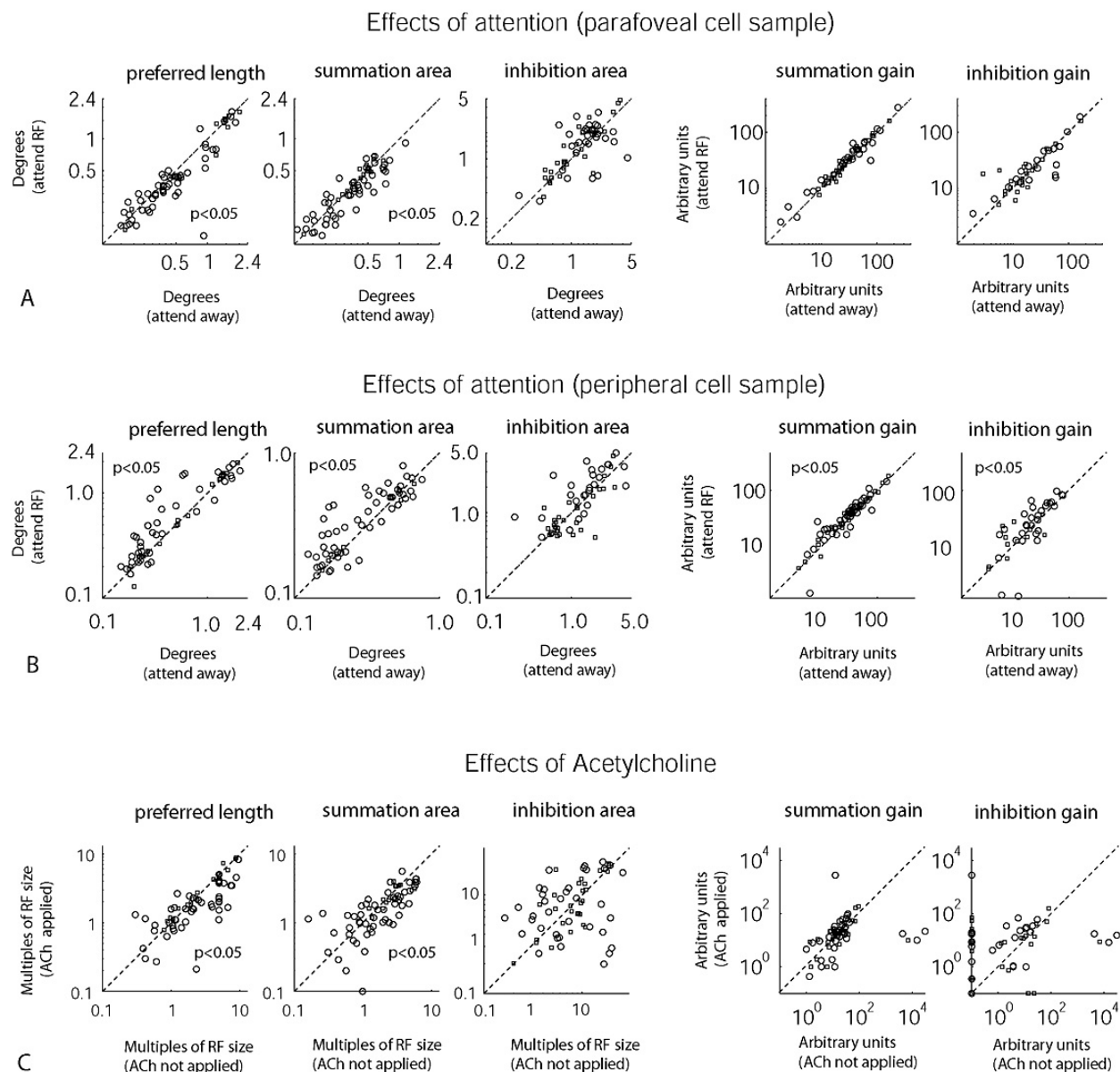


Figure 4. Population data regarding the effect of attention and acetylcholine on spatial integration. A. Population data of the cell sample which had parafoveal receptive fields, recorded at medium contrast. X-axis shows parameter of interest when attention was directed away from the receptive field, y-axis shows the respective parameter when attention was directed to the receptive field. This cell sample showed a significant reduction of preferred length and a significant reduction of the summation area. None of the other parameters were significantly affected by attention. B. Population data of the cell sample which had peripheral receptive fields, recorded at medium contrast. For this sample attention resulted in a significant increase of preferred length, mediated by an increase in the summation area in conjunction with increased excitation and inhibition gain. C. Effects of acetylcholine application on spatial integration. Application of acetylcholine resulted in significantly reduced preferred length, mediated by a significant reduction of the summation area. Circles in all plots denote cells where the parameter of interest was significantly affected by the respective manipulation (significance was determined by bootstrap methods), while squares show cells where the parameter of interest was not significantly affected. Only cells that were significantly affected by acetylcholine were included in the analysis, as the absence of an acetylcholine effect could be due to non susceptibility of the cell to the drug, but equally (or even more probably) due to a failure in the application method (e.g. a blocked pipette).

opposite hemifield. The preferred length was significantly shifted towards shorter bar length when attention was directed to the CRF ($p < 0.01$, Wilcoxon signed rank test). Fitting the DOG model to our data revealed that the

reduction of preferred length was mediated by a reduction in the spatial summation area ($p < 0.01$, Wilcoxon signed rank test). None of the other parameters of the model were systematically affected by attention. This suggests that the

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effects of attention seen psychophysically could be due to a change in the spatial summation properties in primary visual cortex, whereby attention causes neurons to pool more from their CRF inputs, and less from their nCRF inputs.

In both animals we additionally investigated the effect of attention on spatial integration in more peripheral vision. Here we recorded from 69 neurons with CRFs located at an eccentricity of $\sim 7^\circ$ from the fovea (82). In these cells the effects of attention on spatial integration were opposite to those at parafoveal sites. For these cells we found that attention increased the preferred length. An example neuron is shown in figure 3B. Attending to the CRF still resulted in increased firing rates, but the increase occurred mostly for bars of medium length (0.6° - 1.6°). The corresponding result for the population of cells is shown in figure 4B. For the majority of cells we found that attending to the CRF resulted in an increased preferred length ($p < 0.01$, Wilcoxon signed rank test). This was mediated by an increase in the size of the spatial summation area ($p < 0.01$, Wilcoxon signed rank test). Furthermore, the summation gain ($p < 0.01$, Wilcoxon signed rank test) and the inhibition gain ($p < 0.01$, Wilcoxon signed rank test) also increased when attention was directed to the CRF of this cell sample.

5. EFFECTS OF ACETYLCHOLINE ON SPATIAL INTEGRATION IN V1

In vitro studies suggest that ACh should alter spatial integration properties in a manner similar to the effect of attention found in our psychophysical study and in our alert macaque cell sample from parafoveal sites. We investigated this proposal in V1 of anesthetized marmoset monkeys, and found indeed that application of ACh resulted in a reduction of preferred length. RF eccentricity was 1 - 10° , unfortunately we do not know the exact eccentricity locations for our V1 recordings from the anesthetized marmoset on a cell by cell basis. When we conducted the experiments we were unable to map the fundus of the retina with high precision. Based on our mappings, we believe that most of our recordings were within the central 5 deg, but the possible error margin associated with these measurements limits a more detailed account.

Two example neurons which exhibited a change in spatial integration with ACh application are shown in figure 3C and D. The effect for the population is shown in figure 4C. ACh application resulted in a significant reduction of the preferred length ($p < 0.01$, Wilcoxon signed rank test), which was mediated by a reduction of the spatial summation area ($p < 0.05$, Wilcoxon signed rank test). None of the other DOG model parameters were significantly affected by ACh application, although there was a trend towards an increased inhibition area ($p = 0.09$, Wilcoxon signed rank test). Thus, the results in principle suggest a possible mechanism by which attention could affect spatial integration perceptually and neuronally in parafoveal vision. Before we discuss this in more detail, it is worthwhile to highlight additional similarities between

ACh application and focused attention, but equally to emphasize important differences between the two.

Previous studies on the effect of attention in V1 and V4 have noted that attention mostly influences the sustained part of the response with less of an influence on the initial phasic part (49, 82, 83), and this effect is mirrored by ACh application. ACh significantly affected the tonic part of neuronal responses, i.e. the relative strength of the later response part (> 200 ms after response onset), when compared to the first 200 ms of the response ($p < 0.01$, signed rank test). Despite these similarities, we also found important differences between ACh application and the allocation of attention. ACh applied in V1 of the anaesthetized animal often resulted in increased ongoing activity (the activity that was measured before a stimulus was presented in the CRF). The effect of ACh on ongoing activity was significant in 55/66 cells ($p < 0.05$, rank sum test). At the population level spontaneous activity increased by almost 100% (mean spontaneous activity ACh not applied: 5.9 ± 7.3 sp/s; mean spontaneous activity ACh applied: 10.6 ± 11.5 sp/s; $p < 0.001$, paired t-test). Attention, in comparison, had much less of an effect on spontaneous activity. Spontaneous activity was significantly affected by attention in 13/73 cells at parafoveal recording sites. Of these 13 cells, attention increased spontaneous activity in 7 cells and decreased spontaneous activity in 6 cells. At the population level attention marginally decreased spontaneous activity overall for these recording sites, however, the effect was not significant (mean spontaneous activity attend away: 3.7 ± 11.1 sp/s; mean spontaneous activity attend RF: 3.6 ± 10.9 sp/s; $p = 0.605$, paired t-test). At peripheral recording locations attention significantly affected spontaneous activity in 8/69 cells. In 7 of these attention resulted in decreased spontaneous activity. At the population level there was a small but significant decrease in spontaneous activity when attention was directed to the CRF (mean spontaneous activity attend away: 2.3 ± 3.5 sp/s; mean spontaneous activity attend RF: 2.1 ± 3.1 sp/s; $p = 0.006$, paired t-test). Thus, while ACh application resulted in an increase in spontaneous activity, attention in V1 either showed no consistent effect (parafoveal sites), or resulted in a small decrease of spontaneous activity (peripheral sites).

The application of ACh often (37.9% of cells) resulted in decreased stimulus driven firing rates (relative to spontaneous activity) while attention rarely did ($< 15\%$, somewhat dependent on bar lengths, see fig. 5A). Figure 5 shows the effects of stimulus driven firing rates as a function of bar length for the ACh and the attention experiments. Figure 5B plots the ratio of firing rates when ACh was applied vs. when it was not applied. Although on average the stimulus driven firing rate increased when ACh was applied (the majority of cells at all bar length showed ratios > 1), a reasonable fraction of cells showed the opposite effect. This was much less the case when attention was directed to the receptive field of the neuron under study (Figure 5A). When attention was directed to the CRF only a few cells showed a significant decrease of firing rates (black bars show cells which exhibited a significant effect of attention on firing rates). Across the population of

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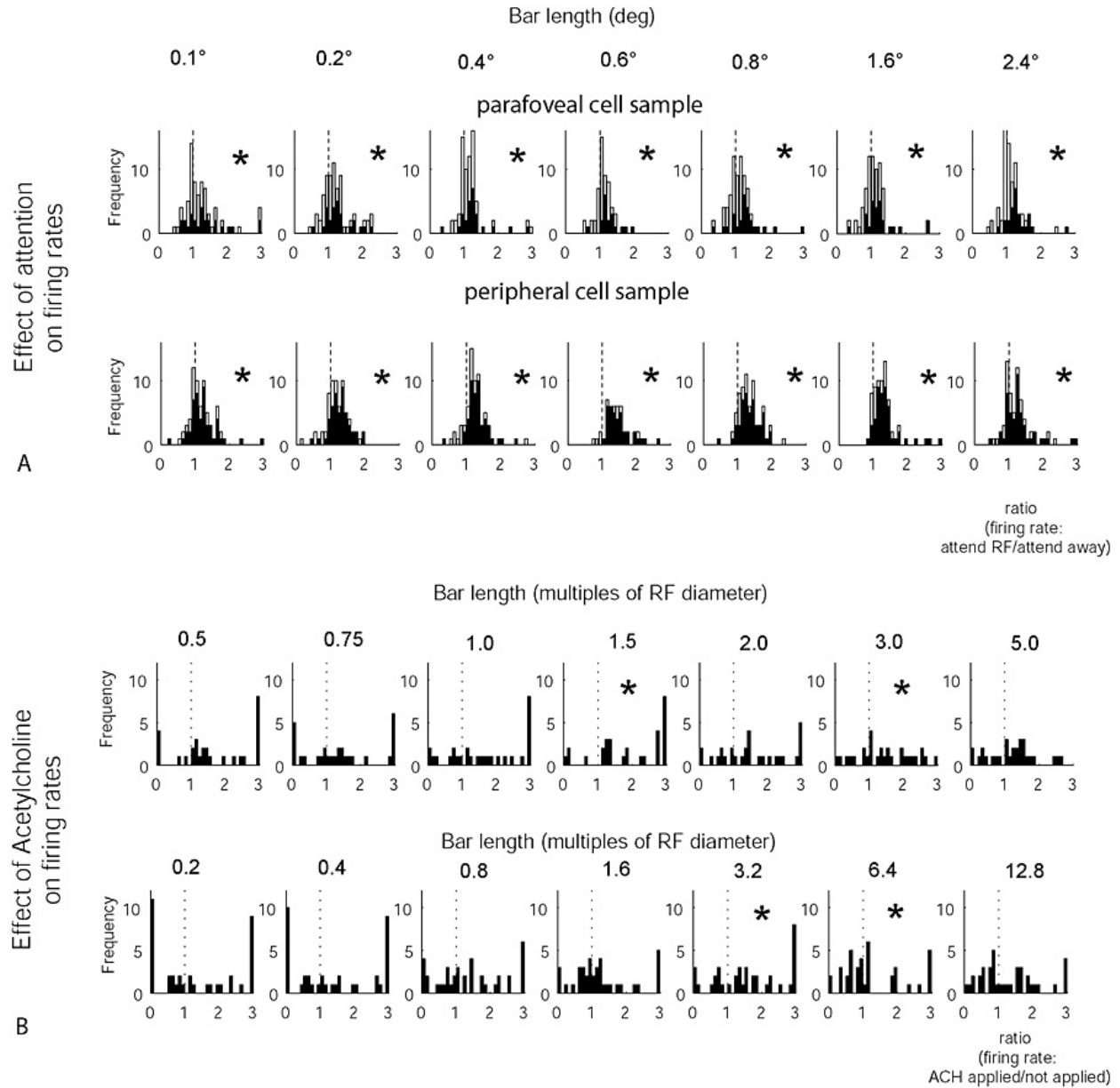


Figure 5. Effect of acetylcholine and attention on firing rates as a function of bar length. A. Attention significantly increased firing rates for all bar lengths (denoted by *). The increase was somewhat larger for the parafoveal cell sample. Moreover the proportion of cells which were significantly affected by attention was somewhat larger in the peripheral sample than the parafoveal sample. Black bars show the distributions for cells significantly affected by attention, empty bars show the distributions for all cell. B. Acetylcholine generally increased firing rates (ratio values >1), but reductions (after subtraction of spontaneous activity) could also occur, particularly for shorter bar lengths. As a consequence, the median of the ratio distributions was only rarely significantly different from 1 (indicated by the *). Upper row shows data where one set of bar lengths was used, lower row shows data where the other set of bar lengths was used. Only cells that were significantly affected by acetylcholine were included in the analysis.

cells, the ratios of firing rates were significantly larger than 1 for all bar length in the attention paradigm. This was not the case for all bar lengths in the ACh experiment, although this difference may be partially accounted for by smaller sample sizes in the ACh experiments.

6. ATTENTION AND SPATIAL INTEGRATION: CURRENT RESULTS IN A WIDER CONTEXT

Here we investigated how attention and contrast influence spatial integration of human orientation

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perception, how attention affects spatial integration in macaque primary visual cortex, and whether cholinergic mechanisms could contribute to dynamic changes of spatial integration in visual cortex. Our psychophysical results showed that when a target was presented at high and medium contrast, its perceived orientation was shifted away from the orientation of the context bars. When targets were presented at low contrast the perceived orientation of the target was shifted towards the orientation of the context bars. Both effects (repulsion and attraction) were smaller when attention was fully devoted to the orientation discrimination task, i.e. attention resulted in a reduction of contextual influences, irrespective of their sign. We found matching effects of attention in parafoveal V1. For these cells attention reduced spatial integration (and thus contextual influences). Furthermore, we found that ACh applied to V1 neurons resulted in a reduction of spatial integration, suggesting that ACh may be one of the neuropharmacological agents by which attention exerts its influence. Despite these striking similarities between our psychophysical study and our neurophysiological studies, we also found some important differences which require further exploration. Before we discuss these, we will first discuss similarities and differences in the experimental approaches in relation to stimulus choice and state of the animals.

The human psychophysical study and the electrophysiological studies used related, but somewhat different stimuli. We chose the spatio-temporal context in the psychophysical studies, as it allowed investigating a variety of different aspects simultaneously. Firstly, the single-dual task setting allowed an investigation of the role of attention in contextual integration, under conditions where context is equivalent to noise. Secondly, the stimuli allowed to investigate the influential idea that vision is a process of Bayesian inference (80, 81, 84-86). If true, the spatiotemporal context should have resulted in attractor effects at high and low contrast. The stimuli used in the two electrophysiological experiments were similar, they were bars of different lengths presented at the preferred orientation centred on the neuron's RF. These bars can be considered 'context' in the attention demanding task, as the animals were required to detect an increase in luminance at a small patch in the centre of the RF after the bars had been presented. Thus, the bars themselves were behaviourally irrelevant. Although it was not a spatio-temporally context as in the human psychophysics, it was comparable. Notably, the effect of attention in reducing the contextual influence at parafoveal sites was also similar between the two experiments.

Ideally, one would like to compare the influence of attention and ACh on spatial integration in the same animals in an awake preparation, as the effects of ACh application can be influenced by anaesthesia (for review see (87)). Despite this caveat, the choice of our anaesthetic minimized the possibility of such confounds (88). Moreover, the current results suggest a possible neuropharmacological basis for our human psychophysical and awake monkey data, and are thus a step towards a detailed understanding of attentional modulation, which we currently follow up in an awake behaving setting.

In the following we will briefly discuss each finding separately, before we discuss how they relate to one another in more detail.

6.1. Human psychophysics

We manipulated the allocation of voluntary attention on human orientation perception using a single/dual task paradigm. We found that for high and medium contrast stimuli, the perceived target orientation was shifted away from the orientation of the context bars. This effect is similar to Westheimer's 'simultaneous orientation contrast' effect (89). At low target contrast the effect was reversed. Contrast-dependent switching of contextual influences have been demonstrated by a number of physiological studies (13, 15, 19), but have not, to our knowledge, been previously reported in a psychophysical setting. Notably, we found that the withdrawal of visual attention in the dual task condition enhanced the effect of the context bars on the perceived orientation of the target. Before discussing this in detail, we address the possibility that the effects were simply due to increased accuracy under conditions of full attention. We can discount this explanation for the following reason: If withdrawal of attention simply reduced accuracy, one would expect to see an increase in error rate that is unbiased, i.e. we would expect to see a more noisy distribution of choices, rather than a selective bias of specific errors. To give a concrete example, imagine the condition where target and reference are physically identical, i.e. they have the same tilt relative to the spatio-temporal context. If attention simply decreased accuracy, we would expect to see an increase in the number of erroneous reports that the target is more similar to the context bars and the same increase in the number of reports that the target is more dissimilar to the context bars. This is not what we saw. We saw a strong bias towards only one of the two possible errors. This bias reflected increased attraction (i.e. increased number of reports that target is more similar to the context bars than the reference is to the context bars) for low contrast stimuli, and the opposite bias of errors for the high contrast target stimuli. This shows that withdrawal of attention did not simply increase error rates; it increased reports of a specific error which reflected the sign of the influence of the spatio-temporal context. Thus, attention reduced the influence of the context, irrespective of whether stimulus conditions resulted in an attractor effect or whether they resulted in repulsion. This conclusion is in line with Ito's finding of reduced surround facilitation under conditions of focused attention versus distributed attention (3, 4) and is supported by Zenger's finding that surround modulation is weaker in a single task than a dual task condition (6). However, our conclusion is at odds with Freeman's proposition that attention enhances contextual influences (2, 54). These apparently contradictory conclusions reflect differences in the experimental approach. While we specifically addressed the issue of how spatial and temporal integration is influenced by varying levels of attention directed to the *target location*, Freeman's experiments addressed the separate issue of whether attending to different parts of the *surround* can alter their influence on processing the central location. The different findings are therefore not necessarily contradictory. Rather they are complementary

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and together show that attention alters the flow of information within the neuronal network such that task relevant information impacts on the processing at attended locations while task irrelevant information is excluded and has little impact on the processing of information at the attended location. Such flexibility could be achieved by selectively enhanced efficacy of feed-forward connections to neurons representing attended stimuli, while simultaneously suppressing lateral inputs to those neurons. The processing of attended stimuli would thus be less affected *by* surrounding stimuli (suppressed afferent lateral inputs) as demonstrated herein, but would have a greater influence *on* surrounding stimuli (enhanced feed-forward input with no suppression of lateral afferents) as demonstrated by Freeman's findings.

The interaction between attention and contrast has been a topic of much debate. It is well known that high levels of attention enhance performance in a number of tasks, particularly in crowded/noisy displays and when task demands are high (6, 52, 53, 90). Given that increasing the luminance contrast of a test stimulus can also improve performance in a number of tasks, some authors have suggested that the effect of attention is akin to increasing the 'effective contrast' of a stimulus (48-50, 56). Such a model of attention supposes that increasing attention and increasing luminance contrast are essentially interchangeable. Our data allowed us to explicitly test this proposal, because, unlike in previous studies where lowering the contrast essentially weakened but did not change the perception of the target, we demonstrate a reversal in the perception of the target between high and low contrast. Due to this dissociation, the effect of attention was much easier to distinguish from the effect of contrast. For the low contrast experiments we demonstrated that the perceived orientation of the target was shifted towards the orientation of the context bars. This effect was reduced in the full attention condition. The attractor influence of the context bars could also be reduced by increasing the contrast of the target to an intermediate level, before the repulsion effect took over. Hence when the target was presented at low contrast, the effect of attention was similar to increasing the contrast of the target. With a further increase of the target contrast, the effect of the context bar changed sign from attraction to repulsion. If attention increased the 'effective contrast' of the target, one would expect to find the strongest repulsion effect in the high contrast, full attention condition, as this condition should result in the highest 'effective' contrast. Contrary to this proposal we found the strongest repulsion effect in the divided attention condition. Devoting full attention to the orientation discrimination task reduced the strength of repulsion, rather than increasing it. One could argue that at high contrast attention cannot increase the perceived contrast any further due to saturation effects. However, we found strong perceptual repulsion already at a luminance contrast of 10% (medium contrast experiment). Here, attention decreased the repulsion, whereas the contrast gain model of attention would predict that attention should increase the repulsion. Hence, while data from the low contrast condition demonstrate how the effect of attention can appear similar to the effect of increased contrast, data

from the high and medium contrast conditions clearly show that increasing the level of attention is not necessarily interchangeable with increasing the contrast of the target, in effect they had opposite effects in our study.

These data show that contrast determines the nature of contextual influences (repulsion or attraction) in human orientation perception, while the level of attention determines the strength of this influence. Attention can thus alter spatial integration perceptually.

6.2. Attention in V1

To investigate possible neuronal substrates of the attention mediated reduction of contextual influences, demonstrated in our psychophysical experiments, we recorded from V1 neurons while animals attended to the CRF of the neuron under study and when they attended away from the CRF. We found that attention affected spatial integration in primate V1 in an eccentricity dependent manner, by either decreasing (central vision) or increasing (peripheral vision) the summation area. This shows that the influence of the nCRF is dependent on attention. The finding of decreased spatial integration with attention at parafoveal locations parallels our human psychophysical results. Our electrophysiology data are also relevant for the relation between attention and contrast. Stimulus contrast affects length tuning in V1, whereby increasing contrast reduces spatial summation (91-93). This effect of contrast mirrors the effect of attention at parafoveal locations. At first glance it thus supports the idea that attention is equivalent to increasing the contrast of a stimulus (48, 49). However, our results from peripheral locations contradict this idea, where attention resulted in increased, not decreased spatial summation. Our data thus contribute to mounting evidence (50, 94), that attending to a stimulus is not necessarily equivalent to increasing the stimulus' luminance contrast (48, 49).

We also found that attention decreased spontaneous activity in V1. This is different from results in extrastriate cortex (50, 56), where an increase in spontaneous activity with attention counteracted a sensitivity gain (50), thereby leaving neuronal contrast thresholds unaffected. The decrease of spontaneous activity in V1 when attention is directed to the RF of a neuron could increase the signal to noise ratio, and thus result in increased sensitivity, an issue to be clarified in future studies.

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. For central vision it may be beneficial to exclude contextual information when objects are attended to, allowing unbiased analysis (noise and distracters excluded) of the attended location. This was the main finding of our human psychophysical study, where attention reduced spatial summation. Detailed analysis of visual scenes is not possible in peripheral vision due to reduced visual resolution for these locations. Here, attention mediated pooling over extended areas could promote a more integrative scene analysis and highlight

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attended peripheral objects as targets for impending eye movements, thereby bringing the attended object into foveal vision for detailed analysis. It will be important to determine whether attending to more eccentric locations also results in increased spatial integration measured psychophysically. In light of the differences between parafoveal and peripheral vision, it is important to highlight that attention can also influence spatial integration in a task dependent manner. Optimal performance in our tasks (human and monkey) benefited from exclusion of 'contextual' information. Matching this behavioral requirement, we found a reduction in spatial integration at parafoveal sites. We believe that attention is not a unitary mechanism. It is a mechanism that enables task-relevant information to affect ongoing processing. Thus, if attention to large parts of the visual field is required (2, 18, 54, 83), the effects might be different than those seen in our study. Additional studies are necessary to delineate how different attentional task demands alter specific computations within the neuronal architecture.

6.3. Effects of acetylcholine in V1

The release of acetylcholine in the cortex has often been linked to states of attention (22, 28). Results from slice studies (67, 68, 71, 73, 74) led us to propose a specific role of ACh in dynamically changing spatial integration. These changes should be similar to the effects of focused spatial attention. To test this proposal we measured the effects 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°). This change was mediated by a reduction in a cell's summation area. Thus, the effects of ACh application on length tuning were in line with the predictions generated from the slice studies, and they were similar to the effects of directed spatial attention at parafoveal sites. These findings could support the idea that ACh is involved in the neuronal processes that mediate attention. However, there were also some important differences which require further investigation. Our results of the effect of attention in monkeys at more peripheral sites are difficult to reconcile with the idea that ACh is the sole agent which mediates mechanisms of attention, unless we speculate that there may be anatomical differences (e.g. a different distribution of muscarinic and nicotinic cholinergic receptors) between visual cortical regions representing central and peripheral vision. Moreover, ACh application generally increased the spontaneous activity in V1 and, in a substantial fraction of cells, suppressed stimulus driven responses. In contrast, attention either had no effect on spontaneous activity, or even slightly reduced it. Finally, attention caused suppression of the stimulus driven response only in a very small number of cells. These differences may, to some extent be due to the methodology of our ACh application. Our application of ACh was probably restricted to the vicinity of the recorded cell (estimated to be within ~200-800 μm of the electrode tip). This is in contrast with endogenous ACh efflux, which is likely to affect virtually all layers and consequently large parts of the network simultaneously and mediate its effects through a large variety of receptor mechanisms and in a

location dependent manner (88). Furthermore, the dosage of ACh we applied may not have been within the normal physiological range. In addition to these concerns, the anesthesia may have interacted with the effect of ACh. Thus, it is unsurprising that external application of ACh does not fully match the effects that would occur when ACh is released endogenously in relation to specific task demands.

If ACh were to play a major role in mediating attentional control of cortical processes a high degree of specificity of the cholinergic input would be required, such that only neurons processing attended stimuli receive cholinergic modulation. This level of specificity is probably not existent, although the output of the basal forebrain is sufficiently restricted to yield modality specificity (95). Beyond modality specificity, reasonable doubts exist whether input from the basal forebrain has the spatial precision to influence only those cells that represent the attended location. This not withstanding, recently described cholinergic cells within the cortex (96) could yield the required specificity. Cortical cholinergic neurons are located in layers 2/3 of nearly all cortical areas. These cells (96) receive input from adjacent pyramidal cells and from various types of interneurons. Their activation increased the excitability of neighbouring cells. Thus, extremely local (column specific) cholinergic effects could be generated through the activation of these intrinsic cells, potentially moderating responses to specific stimuli. Irrespective of these recent findings, we do not propose that ACh is the only agent responsible for attentional effects in the cortex. It is more likely that the effects of spatial attention are mediated by an interaction of cholinergic inputs and feedback connections from higher cortical areas (21, 61, 62). High levels of ACh may enable feedback projections to exert their specific influence. This would match a recent model where neuromodulator and feedback interactions mediate unsupervised learning (97). As attention is normally required for learning, attention and learning may share a common neuronal substrate.

6.4. Summary and common themes

We investigated how attention influences contextual/surround effects in vision. Previous psychophysical studies demonstrated that attention has a role in modulating contextual influences, however these studies failed to adequately account for the three-way interactions of attention, contrast and context. This is important since attention is sometimes described as influencing vision by modulating 'effective contrast', and contextual influences are known to be strongly dependent on contrast. Thus, attention could modulate contextual influences indirectly, through its influence on effective contrast. We discounted this hypothesis and showed that attention has a direct negative influence on contextual processing in a contrast-independent manner. At the neuronal level, response modulation from non-classical parts of the receptive field is analogous to, and is likely to be the substrate of, contextual modulation in vision. A convenient way to assess the strength and form of the nCRF is to measure the cell's length tuning. The shape of the length tuning curve, for example the location and

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height of the peak and the degree of end-stopping, demonstrates the relative strengths of facilitation and inhibition coming from the nCRF. Our psychophysical studies suggested that, at the neuronal level, attention should reduce nCRF influences thereby resulting in changes of the length tuning profile. In line with this hypothesis we found that attending towards the RF of a V1 neuron representing central vision significantly reduced its length tuning preference, by reducing the efficacy of facilitatory nCRF influences. Surprisingly, the reverse was true for cells representing peripheral vision, where attention increased summation from the nCRF. Future studies will address whether there is a psychophysical correlate of this interesting reversal at the physiological level.

There has been considerable interest and research into uncovering the biological mechanisms by which attention exerts its pervasive influence. The understanding of these mechanisms will be important in improving the understanding and treatments of cognitive disorders related to attentional processing, such as attention deficit disorder, spatial neglect etc. A substantial body of research has highlighted the importance of feedback mechanisms which modulate processing in 'lower' cortical areas. In addition to these mechanisms, neuromodulators are also likely to play a role in mediating attentional effects. Of particular interest to the understanding of the attentional modulation of nCRF and contextual influences is the neuromodulator ACh. Levels of cortical ACh are strongly linked with levels of attention, moreover, ACh alters the flow of information in cortical networks, such that lateral inputs, which largely give rise to nCRF influences, are suppressed relative to thalamic inputs. In the final experiment presented here we investigated whether raising the level of cortical ACh *in-vivo* could have a similar effect on nCRF processing to the effect of attention. This is what we indeed found; the application of ACh in anesthetized animals caused a reduction in summation from the nCRF, thus we suggest that modulation of ACh could be, at least in part, the mechanism underlying attentional modulation of surround influences. Future studies, where selective ACh antagonists are applied while animals attend to the CRF of the recorded neuron will be necessary to delineate the precise role of ACh in the mediation of attention and the receptors that are involved in this process.

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Send correspondence to: Alexander Thiele, Institute of Neuroscience, Henry Wellcome Building for Neuroecology, University of Newcastle upon Tyne, Newcastle upon Tyne NE2 4HH, United Kingdom, Tel: 441912227564, Fax: 441912225622, E-mail: alex.thiele@ncl.ac.uk

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