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CHAPTER 13

The role of feedback connections in shaping the responses of visual cortical neurons

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Abstract: The results of a previous study [Hupé et al. (1998) *Nature*, 394: 784–787] led us to conclude that feedback connections are important for differentiating a figure from the background, particularly in the case of low salience stimuli. This conclusion was principally based on the observation in area V3 neurons that inactivating MT by cooling led to a severe weakening of the center response and of the center–surround interactions, and that these effects were particularly strong for low salience stimuli. In the present paper, we first show that the results extend to areas V1 and V2. In particular, the inhibitory center–surround interactions in areas V1, V2 and V3 disappear almost completely in the absence of feedback input from MT for low salience stimuli, whereas the effects are much more limited for stimuli of middle and high salience. We then compare the results obtained in studies of feedback connections from MT to those obtained in a study of the feedback action of area V2 onto V1 neurons [Hupé et al. (2001) *J. Neurophysiol.*, 85: 146–163], in which the same effects were observed on the center mechanism (decrease in response), but no effects were seen on the center–surround interactions. We conclude that feedback connections act in a non-linear fashion to boost the gain of the center mechanism and that they combine with horizontal connections to generate the center–surround interactions.

Introduction

Despite the large number of feedback connections between visual cortical areas of the mammalian brain, very few studies have been devoted to elucidating the role of these connections in cortical processing. These studies generally demonstrated that lesion or inactivation of a higher order area leads to a decrease of the neuron response in the lower order area to a stimulus activating the RF center (Mignard and Malpeli, 1991; Sandell and Schiller, 1982; Vanduffel et al., 1997; Wang et al., 2000). Thus, feedback connections appear to potentiate the RF center response of neurons in lower order areas.

In a series of publications in the 1990s, we studied the visuotopic organizations of feedforward and feedback connections and concluded that feedback connections are not visuotopically organized in the same manner as feedforward connections (Salin et al., 1992; Salin and Bullier, 1995). Recipient neurons of feedforward connections have RF centers that include those of their inputs. This corresponds to the strategy employed at numerous levels of the visual system that consists in increasing the specificity of the receptive field properties of neurons in higher-order areas by convergence of appropriate feedforward inputs. Feedback connections, on the other hand, link neurons in such a way that the RF centers of neurons providing the feedback connections cover a much wider part of the visual field than

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that represented in the RF center of the recipient neuron. For this reason, we concluded that the feedback connections are organized in a non-retinotopic or a loose retinotopic fashion.

The loose retinotopic character of the feedback connections suggested that these connections may be involved in controlling the modulatory influences of the RF surround on the response elicited by stimulating the RF center. This was tested in a first series of studies in the monkey in which we inactivated the superior temporal sulcus at the location of visual cortical area MT, and observed the responses of neurons in areas V1, V2 and V3. The stimuli were similar to those illustrated in the bottom part of Fig. 1. A central bar of variable luminance moved back and forth across the cell RF center. This bar was superimposed on a background composed of gray rectangles of same width and orientation. The contrast of the background checks was too low to activate the RF center of the neuron when it was moving (see responses corresponding to bkg alone in Fig. 1). The contrast was nonetheless sufficient to activate the surround mechanism, as seen in Fig. 1 by comparing the responses to the bar moving on a stationary background (BS histograms) with the responses to the bar moving together with the background (BM histograms). The response decrease for stimulus BM compared to BS is due to the suppressive effect of the moving background on the response of the neuron to the bar alone. This suppressive effect is principally due to activation of the inhibitory surround of the receptive field.

Area MT neurons show vigorous responses at low contrast (Sclar et al., 1990) and we were therefore particularly interested in studying the responses of neurons in lower order areas to activation by a moving bar of low contrast. Because the structured background stimulus acted as a mask, such a low contrast bar was hardly seen when stationary and became visible when it started to move. To quantify the visibility of the bar, we defined the salience of the stimulus by the ratio of the contrast of the central bar divided by that of the background. We subdivided the scale of salience in three categories: low salience (from 1 to 7), middle salience (from 7 to 15) and high salience (above 15; see Hupé et al., 1998) for further details).

From the results of these studies, we concluded that the role of feedback connections is to help differentiate the figure from the background, particularly in the case of stimuli of low salience. This conclusion was principally based on the observation in area V3 that inactivating MT by cooling led to a severe weakening of the center response and of the center–surround interactions, and that these effects were particularly strong for low salience stimuli (Hupé et al., 1998). In the present paper, we report the results concerning areas V1, V2 and V3, as we wished to determine to what extent the findings observed in V3 were also observed in the other two areas. The first two sections of this paper are devoted to this question of the generality of our original findings in area V3. We then draw some general conclusions concerning the role of the feedback connections from MT in differentiating figures from the background in lower order areas.

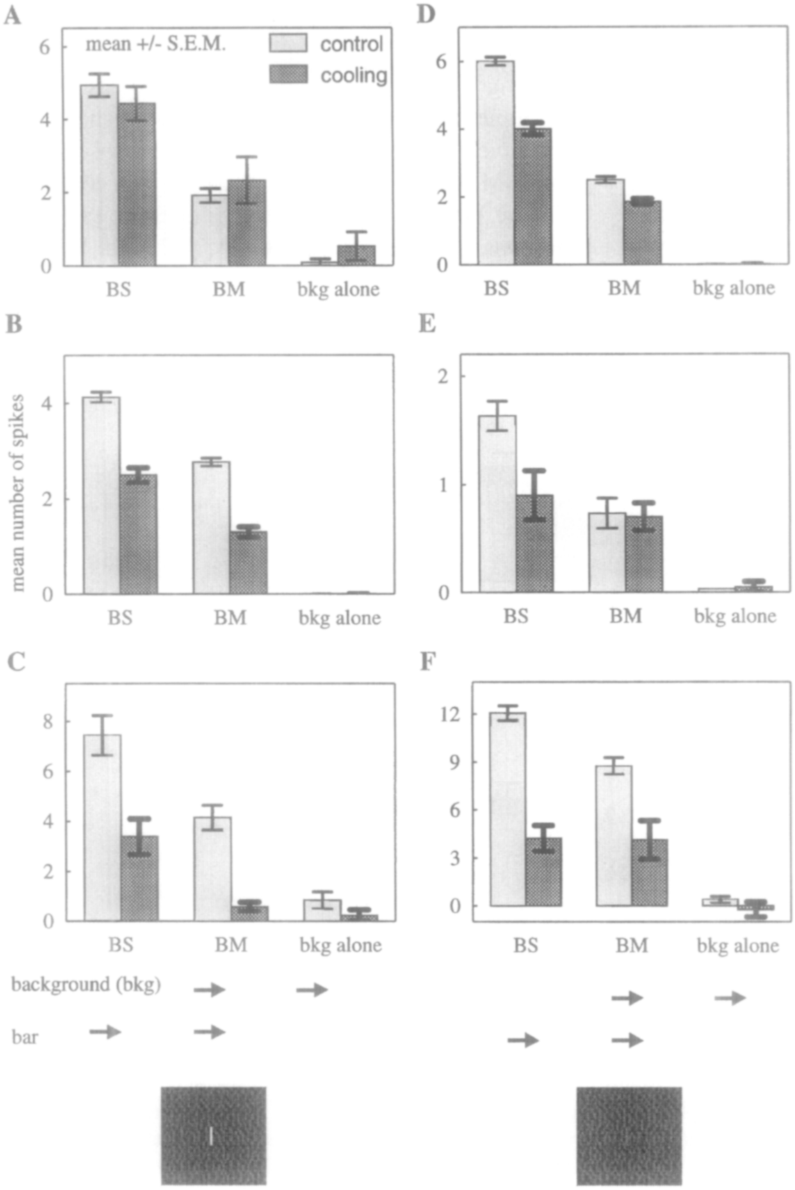
In the final two sections, we compare the results obtained in studies of feedback connections from MT to those obtained in a study of the feedback action of area V2 onto V1 neurons, and we discuss the possible role of feedback connections in controlling the gain of center–surround interactions in lower order areas.

All experiments were conducted on anesthetized and paralyzed macaque monkeys. Details of experimental methods can be found in the figure legends of the present paper or in the methods sections of our earlier publications (Hupé et al., 1998, 2001a,b).

Effect of stimulus salience on feedback action

Fig. 1 illustrates the effects of inactivating MT on the responses of selected neurons in areas V1, V2 and V3 to the central bar moving across the RF center with the background stationary (BS), and to the bar moving together with the background (BM). Mean responses per stimulus presentation of these different stimuli are shown for both the control runs and the runs when MT was inactivated by cooling. Two groups of examples are presented: on the left, responses to high salience stimuli (Fig. 1A–C); and on the right, responses to low salience stimuli (Fig. 1D–F).

Fig. 1A illustrates a case with no statistically significant change during MT inactivation. Fig. 1B and C present cases for which decreases in response are observed during MT cooling for the central moving



high salience stimulus **low salience stimulus**

Fig. 1. Examples of neurons for which the response to the moving bar is decreased by a moving background. (A–C) Neurons tested with a high salience stimulus. There is no significant change of the background suppression index (BM − BS)/BS) when MT is inactivated. (D–F) Neurons tested with a low salience stimulus. There is a decrease of the background suppression index or even a disappearance of background suppression during the cooling of MT. (A) Layer 2 V1 neuron, single unit, case lba14. (B) Layer 2/3 V1 neuron, single unit, case lca24. (C) Layer 2/3 V2 neuron, single unit, case kal21. (D) Layer 2/3 V1 neuron, single unit, case lcb14. (E) Layer 2/3 V1 neuron, single unit (but not isolated), case lcb15. (F) Layer 2/3 V2 neuron, single unit, case kbt24.

bar (BS) and for the bar moving together with the background (BM). During inactivation, the amount of suppression of the response to the central bar induced by the moving background is maintained or only slightly changed relative to the control situation.

In contrast, for low salience stimuli (Fig. 1D–F), the response suppression induced by the moving background is strongly diminished by MT inactivation. This can be seen by comparing BS and BM responses during the control condition and during cooling. Background suppression is decreased in the example in Fig. 1D and completely abolished in the examples shown in Fig. 1E and F (responses to BS and BM stimuli become equal during MT cooling).

The population data are illustrated in Fig. 2 for neurons recorded in areas V1, V2 and V3 with

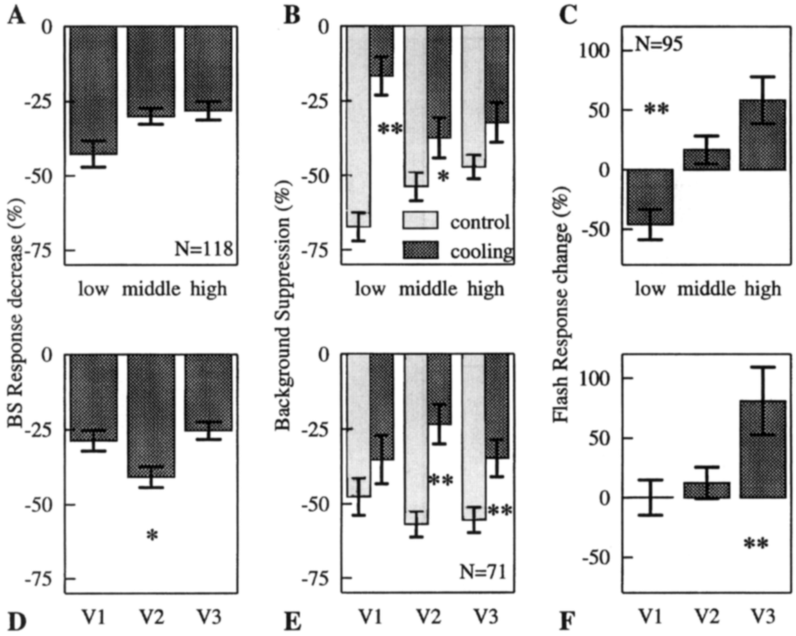


Fig. 2. (A,D) Mean (± SEM) decrease (neurons showing increases are excluded) of the response to the stimulus BS during the inactivation of MT for neurons tested at low, middle and high salience stimulus (A) in areas V1, V2, V3 (D). We carried out a two-way ANOVA with the independent variables 'area' and 'salience' (the variances are homogenous, and the distribution of the residuals is not different from a Normal distribution). There is a significant effect of the salience of the stimulus ($P = 0.046$, A) and of the area of recording ($P = 0.002$, D). The interaction between these two factors is not significant ($P = 0.21$). The asterisks on this graph and all the others (unless specified) correspond to the results of 2 × 2 post-hoc comparisons (Tukey test): $^{*}P < 0.05$; $^{**}P < 0.01$; and $^{***}P < 0.001$. (B,E) Mean (± SEM) change of the background suppression index during the inactivation of MT for neurons tested at low, middle and high salience stimulus (B) in areas V1, V2, V3 (E). The background suppression index (also called bsup in Table 1) is defined as $100 \times (BM - BS)/BS_c$ where BS and BM are the responses to the BS and BM stimuli during control or during MT inactivation and BS_c is the response to BS during control. Normalization was done with respect to BS_c to limit the influence of large changes in the BS responses during inactivation which produced many outliers. All these 71 neurons were significantly suppressed by the moving background before the cooling of MT. A three-way ANOVA was done (Table 1). There is a significant dependence on the salience of the stimulus for the effect of cooling on the background suppression (salience × treatment: $P < 10^{-3}$, B): the effect is stronger at low salience. The effect on the background suppression does not significantly depend on the area of recording (area × treatment: $P = 0.064$, E): the background suppression decreased during cooling in areas V1, V2 and V3. (C,F) Mean (± SEM) change of the ON response to the flash stimulus during the inactivation of MT for all the neurons ($n = 95$) tested at low, middle and high salience stimulus (C) in areas V1, V2, V3 (F). A two-way ANOVA could not be performed as the distributions were far away from the Normal distribution. Two one-way non-parametric ANOVA were done instead. There is a significant effect of the salience of the stimulus (Kruskal–Wallis test, $P = 0.003$, C): the mean response decreased for neurons tested at low salience, whereas it increased for the neurons tested at high salience. The area where the neurons were recorded has also a significant effect (Kruskal–Wallis test, $P = 0.006$, F): there is a strong increase of the responses in V3. Here (C and F), the two asterisks mean that the group was significantly different ($P < 0.01$, Mann–Whitney) from the two other groups.

stimuli at different levels of salience. Fig. 2A illustrates how the mean decrease in BS response during MT inactivation varies as a function of stimulus salience ($P = 0.046$, see legend of Fig. 2) for the neurons in V1/V2/V3 showing BS response decreases (118/154 neurons). The response decrease is more pronounced for low salience stimuli (Tukey, $P = 0.08$). This suggests that the potentiating effect of the feedback connections on the center response is stronger for poorly visible stimuli than for highly salient stimuli.

A similar but stronger effect of stimulus salience on the suppression of the center response by the moving background ($P < 10^{-3}$; see Table 1) is illustrated in Fig. 2B for all the neurons showing statistically significant background-induced suppression (71 neurons/135 neurons tested for background suppression). For low salience stimuli, the background suppression changes from about 70% to 15%. In other words, under MT inactivation, the background suppression is almost totally abolished for low salience stimuli. For middle and high salience stimuli, the background suppression also decreases but to a much smaller extent (significant at the 0.05 level for middle salience; $P = 0.058$ for high salience)

Fig. 2C illustrates the observation that stimulus salience is also an important factor governing the cooling-induced changes in response to a small bar flashed in the RF center (Hupé et al., 2001b). During MT inactivation at low stimulus salience, the response decreases by almost 50%, whereas it increases by the same amount for high salience stimuli.

The scattergram presented in Fig. 3 shows how the background suppression (bsup) varies between the control and the cooling condition for different levels of salience of the stimulus (same data as shown in Fig. 2B). For middle and high salience, there are a few neurons for which the background suppression increases (below the 45° line) and some for which there is little change or some decrease during MT inactivation. For low salience on the other hand, all the neurons show a decrease of the background suppression (above the 45° line). For a few cases, background suppression is converted to facilitation during MT inactivation (points above the horizontal line at zero bsup).

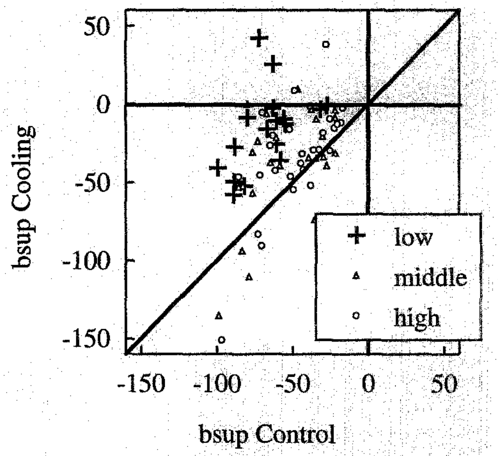


Fig. 3. Scattergram of the values of background suppression (bsup) during control and cooling runs for different categories of stimulus salience: +, low salience; triangle, middle salience; circles, high salience. Note that bsup increases for all neurons tested at low salience, whereas variable effects are observed for the middle and high salience cases.

Effect of MT inactivation in different cortical areas at different saliences

Recordings were done in areas V1, V2 and V3 and we were interested in determining whether similar results are found in these different areas. The bottom histograms in Fig. 2 show the influence of the area in which the neurons were recorded. Response decreases to the central bar (BS) are stronger in V2 than in V1 or V3 (Fig. 2D). Although the background suppression varied in the same direction (decrease) for neurons in all three areas (no significant interaction, $P = 0.064$, see Table 1), there was also a tendency for the decrease to be more marked in area V2 (Fig. 2E). Finally, for flashed stimuli, increases are principally observed in V3 whereas variable effects (increases and decreases) are recorded in areas V1 and V2 (Fig. 2F).

Next, we wished to determine whether similar effects of salience were observed in all three visual areas. Interactions between salience and area are presented in Fig. 4. The interaction for the response decreases to the central bar (BS) is not significant (two-way ANOVA, $P = 0.21$); however, we can see that in areas V2 and V3, the decrease is more pronounced for low salience than for medium or high salience stimuli (Fig. 4B,C),

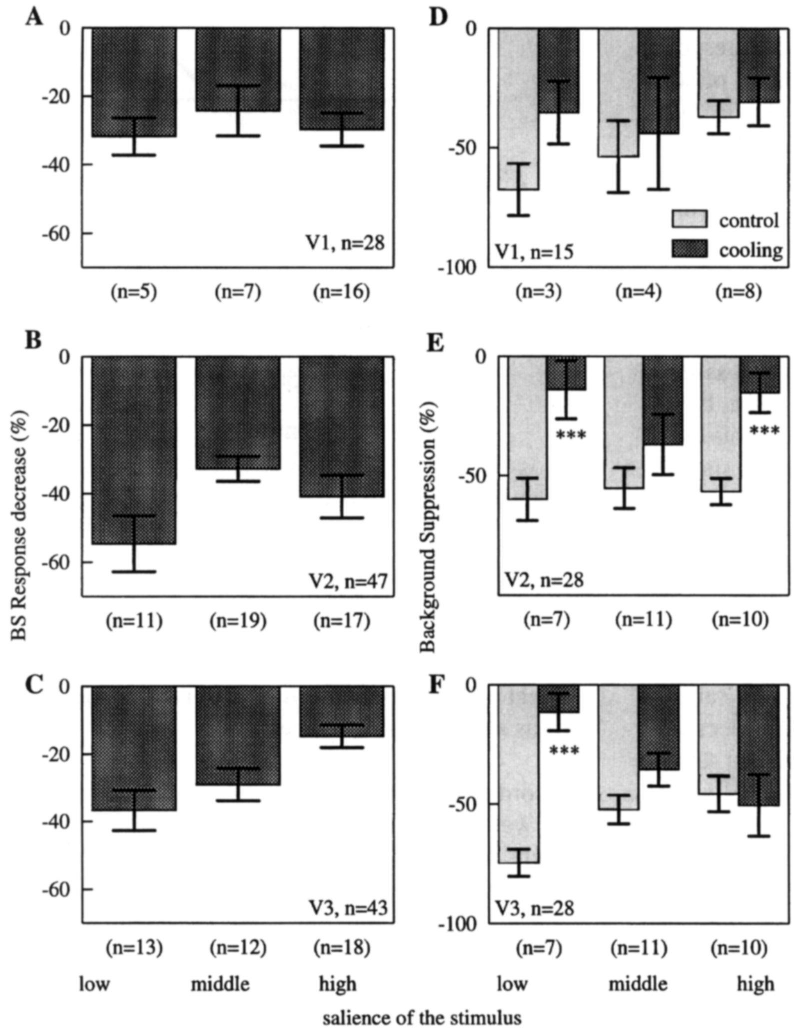


Fig. 4. (A–C) Interactions between area and stimulus salience for the BS response in the 118 neurons with decreased responses during MT inactivation. The post-hoc 2 × 2 comparisons (Tukey test) are not significant. (D–F) Interactions between area and stimulus salience for the background suppression in the 71 neurons for which the moving background decreased significantly the response to the center stimulus. In all three areas, the background suppression is decreased strongly at low salience, and this decrease is significant in V2 and V3 (Tukey post-hoc 2 × 2 comparison, $P < 10^{-3}$). In addition, in V2 some decreases of background suppression at high salience were also observed (E, right columns). These effects are responsible for the significant three-way interaction (see Table 1).

whereas the salience effect is not apparent in V1 (Fig. 4A).

Table 1 summarizes the results obtained by a three-way ANOVA on the bsup values (background suppression values in per cent; see legend of Fig. 2 for definition) with the independent variables ‘area’ and ‘salience’ and the repeated measured variable ‘treatment’ (cooling or control). The ANOVA was made on the bsup values of the 71 neurons showing statistically significant background suppression. The results indicate that treatment (cooling/control) had a highly significant effect. Interaction between area and treatment is not significant (Fig. 2E). Interaction between salience and treatment is highly significant (Fig. 2B), which supports our claim that the effect on background suppression is much stronger at low salience. The three-way interaction between salience, area and treatment is also highly significant.

The dependence of the background suppression on stimulus salience is particularly strong in area

TABLE 1

Summary of the results of the three-way ANOVA done on background suppression values for the 71 neurons showing significant background suppression with the three factors: area, salience and treatment

Area (1)	$F(2, 62) = 0.35$	0.707
Salience (2)	$F(2, 62) = 0.47$	0.626
Treatment (3)	$F(1, 62) = 64.18$	0.000
1 × 2	$F(4, 62) = 0.51$	0.726
1 × 3	$F(2, 62) = 2.88$	0.064
2 × 3	$F(2, 62) = 9.99$	0.000
1 × 2 × 3	$F(2, 62) = 4.12$	0.005

V3 (Fig. 4F), as reported earlier. The background suppression at low salience changes from 75% to less than 10% when MT is inactivated, whereas no significant change is observed for medium and high salience stimuli. In V3, the decrease in background suppression at low salience is due to a decrease in BS response and to an increase in BM response (Hupé et al., 1998). This was not the case in V2 and V1 in which the BS response decreases, but the BM remains unchanged (Hupé, 1999). In V2 also, the decrease in background suppression is marked at low salience, not significant at medium salience, but is strong and highly significant for high salience stimuli (Fig. 4E). This effect is mainly responsible for the three-way significant interaction. It should be noted that among the 10 neurons tested at high salience in V2, three had an almost complete response suppression to the BS stimulus and two had color-selective responses. In V1, the trend is also observed of stronger effects on background suppression for low salience stimuli (Fig. 4D), despite the lack of statistical significance due to the small sample at low salience.

Thus, the effects of salience on the response changes to BS and BM stimuli during MT cooling tend to be observed in all three areas but are particularly strong in areas V2 and V3: during MT inactivation, the BS response and the background suppression both show a stronger decrease at low salience.

What does this effect on center and surround mechanisms mean for the role of feedback connections in information processing in the visual system? Fig. 5 summarizes in a schematic fashion the effects of inactivating area MT on the cortical responses of neurons in a lower order area such as V1, V2 or V3. The cortex is seen from above and the white or gray rectangles represent the neuronal activity evoked by a low salience bar moving across the stationary background (BS stimulus, left) or together with the background (BM stimulus, right). The white area in the cortex for the BS stimulus (Fig. 5A) represents the robust responses of neurons with RF centers crossed by the moving bar. In normal conditions, because of the strong inhibitory influences of surround stimulation for most neurons (Hupé et al., 2001a; Knierim and Van Essen, 1992; Li and Li, 1994; Nothdurft et al., 1999), the cortical activation by the BM stimulus is much weaker, as illustrated by the dark gray color of the activated cortical region (Fig. 5B).

When area MT is inactivated, the response to the central bar is decreased by 40% on average, which corresponds to the light gray color of the activated cortical region (Fig. 5C). Because of the almost complete disappearance of the background-induced suppression when MT is blocked, the response to the BM stimulus differs only slightly from that of the BS stimulus, as illustrated by the gray color of the activated cortical region (Fig. 5D).

The consequence of inactivating the feedback is therefore that the cortical response to the BS stimulus is strongly reduced and that it is no longer substantially different from that to the BM stimulus. In other words, in the absence of feedback connections, the cortical area loses the ability to differentiate the BS and BM stimuli, particularly at low salience. This led us to conclude that feedback connections act to differentiate figure from background in low visibility conditions (Hupé et al., 1998).

Effects of V2 inactivation on responses in area V1

In another series of experiments published elsewhere (Hupé et al., 2001a), we studied the effects of inactivating with GABA a small region (around 2–3 mm in diameter) of V2 on the responses of neurons in the retinotopically corresponding region in V1. The stimuli used were similar to those used by Knierim and Van Essen (1992): the RF center was activated by a small flashed bar of optimal orientation and the surround was stimulated by an array of flashed bars with different positions and orientations (optimal or orthogonal to the optimal orientation).

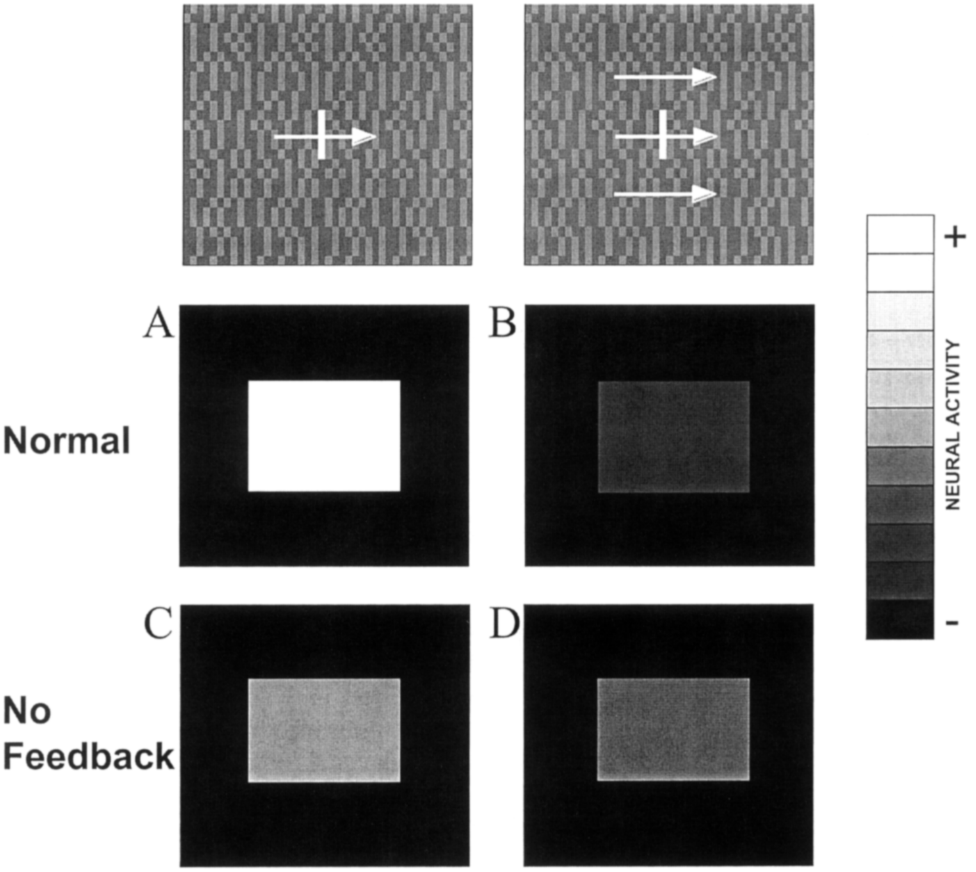


Fig. 5. Schematic representation of the effects of feedback removal on the ability of cortical neurons to differentiate between the BS and BM stimuli at low salience. The rectangular white or gray squares in A–D represent the average neural activity of neurons activated by the stimulus. A single bar moving on a stationary background (BS stimulus) strongly activates the neurons whose RF centers are on the trajectory of the stimulus. (B) Because of the strong background suppression, the response to the BM stimulus is much weaker (dark gray). When the feedback is removed, the response to the BS stimulus is decreased by 40% on average (C) and the background suppression is strongly decreased (D). As a result, the cortical area responds more weakly to the BS stimulus and does not properly differentiate between the BS and BM stimuli.

In keeping with an earlier preliminary report (Bullier et al., 1996), we observed statistically significant changes in the responses to the bar flashed in the RF center for 10% of the sampled neurons. In all cases, the response was a decrease of the V1 response when V2 was inactivated. The average response decrease was around 30%. Thus, the feedback connections from V2 to V1 appear to play a similar role in boosting the response to a central stimulus as observed in the feedback from MT to V1, V2 and V3.

Using sets of oriented bars flashed in the RF surround we also studied the center–surround interactions in V1 neurons during V2 inactivation. Contrary to what we had observed in the study of MT feedback, we could not find any change in surround suppression in V1 neurons during V2 inactivation (Hupé et al., 2001a). We also failed to replicate an earlier observation of general response increases to surround stimulation during V2 inactivation (Bullier et al., 1996). We interpreted the differences between these two studies as due to the strict monitoring of the EEG traces during control and V2 inactivation in the second set of experiments. Indeed, it has recently been shown (Worgotter et al., 1998) that during phases of power increases of low frequency components of the EEG, RF centers of cortical neurons tend to increase in such a way that could have produced the effects we observed in our earlier study.

Conclusion: feedback influences on center responses and center–surround interactions

Center responses

In both systems of feedback connections that we studied, the effect of inactivation of a higher order area led to a decrease of the center response: this was observed for 85% of the neurons that were affected by MT inactivation and for 100% of the V1 neurons that were affected by V2 inactivation. This is in keeping with earlier results concluding that feedback connections tend to boost the responses in lower order areas (Mignard and Malpeli, 1991; Sandell and Schiller, 1982; Vanduffel et al., 1997). The higher proportions of response decreases versus increases during inactivation in our results compared to those of Sandell and Schiller (1982) may be due to different inactivation techniques and to a more rigorous statistical treatment of the data that allowed us to eliminate many false-positive results.

The fact that we observed effects on a smaller proportion of neurons in V1 after inactivation of V2 than in areas V1, V2, V3 after MT inactivation may be due to the fact that the inactivation of V2 by GABA was less extensive than that of MT by cooling. Another possibility is related to the fact that the central stimulus in the V1/V2 experiment was highly salient. If feedback connections from V2 to V1 are particularly important for differentiating figure from background in the case of low salience stimuli as it is for the MT feedback (Figs. 3–5), we may have missed the major effects that could be seen with other types of low salience or ambiguous stimuli such as Kanisza-type stimuli. Responses to such stimuli have been reported for neurons in areas V1 and V2 (Peterhans and von der Heydt, 1989; Von der Heydt and Peterhans, 1989; Grosof et al., 1993; Leventhal et al., 1998) and in imaging studies (Hirsch et al., 1995; Sheth et al., 1996; Seghier et al., 2000).

The effects of feedback connections can be surprisingly strong: during MT inactivation, the responses of some neurons appear to be almost completely abolished (Hupé et al., 1998). Despite this strong influence, it appears that the feedback connections do not drive their target neurons as feedforward connections do. This conclusion is based on two observations.

(1) When V1 is reversibly blocked, practically all neurons in V2 loose their visual responses (Girard and Bullier, 1989), despite the presence of a strong residual activity in area MT (Girard et al., 1992) that should be able to drive V2 neurons if feedforward and feedback connections were combined in a linear fashion.

(2) If feedback connections acted in a linear fashion, we should have observed activity changes outside the RF center of V1/V2/V3 neurons during MT inactivation. This results from the fact that the moving stimulus activates the RFs of several feedback neurons before entering the RF center of the recorded neuron, because of the loose visuotopic nature of feedback connections. However, the changes in responses of neurons in areas V1, V2 and V3 during MT inactivation are observed only during the period of response to the central bar (BS) in the RF center. No significant changes of activity are observed when the bar crosses the surround region. This restriction of changes to the RF center was observed both for response increases and for response decreases during MT inactivation (Hupé et al., 2001b).

Thus, feedback connections appear to interact in a non-linear fashion with feedforward and horizontal connections to boost the center response by controlling the gain of the center mechanism. Although we lack experimental evidence, it is likely that the effect of feedback connections on center–surround mechanisms also corresponds to a non-linear mechanism such as gain control.

These differences in mechanisms between feedforward and feedback connections are in keeping with differences in anatomy (for example laminar distributions of terminals) and synaptic mechanisms (Felleman and Van Essen, 1991; Salin and Bullier, 1995; Shao and Burkhalter, 1996).

Center–surround interactions

As suggested by many authors, horizontal connections are the most likely basis for center–surround interactions. This possibility is supported by measurements of timing of responses. With the exception of fibers in layer 4B, horizontal connections in primate area V1 are non-myelinated and very fine in diameter, and are therefore likely to be slow conducting. From electrical stimulation experiments in monkey V1 we concluded that their median conduction velocity is 0.3 m/s (Girard et al., 2001). This value is consistent with those found for center–surround interactions using optical imaging (Grinvald et al., 1994) and for long distance interactions in the receptive field demonstrated by intracellular recordings in the cat (Bringuier et al., 1999). Thus, at least in terms of conduction speed, horizontal connections could be the main basis of center–surround interactions.

On the other hand, there are reasons to think that horizontal connections cannot be the sole substrate of center–surround interactions in cortical neurons and that feedback connections are involved in these effects. Horizontal connections have a limited spread and therefore cannot be the substrate of long-range lateral interactions in the visual field, at least monosynaptically. For example, in area V1 at 2.5° eccentricity (corresponding to our recording position), an axonal length of 3 mm corresponds to approximately 0.5° in the visual field (Dow et al., 1981). This is much smaller than the maximal extent of the modulatory surround region of neurons in this area (Levitt and Lund, 1997). Indeed the extent of cortex spanned by horizontal connections in macaque V1 appears to correspond to the RF center and the most proximal part of the surround (Angelucci et al., 2000). Reaching out to several degrees in visual field would require multisynaptic connections. On the other hand, because of their loose visuotopic organization, feedback connections could transfer information from distant regions of the visual field and could therefore be the substrate of distant influences in the RF surround.

In that case, one could expect that these distant influences should be delayed, because of the supposedly slow nature of feedback connections and the delayed activation of higher order areas. The orientation-selective component of the surround effect in V1 is indeed delayed by 15–20 ms with respect to the onset of the population response (Knierim and Van Essen, 1992; Nothdurft et al., 1999), and by about 40 ms at the single cell level (Hupé et al., 2001a). But, in fact, we showed that feedback connections have a very rapid action (Hupé et al., 2001b), and there appears to be no participation of feedback connections from V2 in center–surround interactions tested with such stimuli in V1 (Hupé et al., 2001a). The delay for the observed surround modulations agrees therefore better with the horizontal connection hypothesis.

The results obtained at high salience in the study of MT feedback point to the same conclusion: at middle and high salience, there is on average a minimal change in the suppression of the center response by activating the surround with a moving background. This suggests that our failure to observe strong effects of feedback inactivation on center–surround interactions in V1 was not simply due to an incomplete inactivation of V2.

The most likely explanation of our failure to demonstrate strong feedback influences on center–surround interactions at middle and high salience is that the different sets of feedback connections from different cortical areas and the horizontal connections combine with an OR-gate mechanism to control the gain of the inhibitory surround. Thus, for high salience stimuli, all feedback and local inputs are active, and removal of one has a minimal effect on center surround interactions. If feedback and horizontal connections combine their effects in this way, one should be able to demonstrate effects on center–surround mechanisms by activating neurons in a single area by chemical means or by inactivating most cortical areas providing feedback connections. Another way to address specifically the role of feedback connections from one area on center–surround interactions would be to work near the threshold limits for responses in that area, by adjusting parameters such as speed differences, spatial or temporal frequencies, or chromatic differences. This is probably what we did by using low contrast moving stimuli that activated mostly area MT.

For reasons explained above, it appears difficult for horizontal connections to mediate the longest range interactions measured physiologically in V1 (Levitt and Lund, 1997; Angelucci et al., 2000). It is therefore likely that feedback connections are involved in these long-range center–surround interactions. In our study of feedback from MT we used a large background stimulus that did not enable us to study specifically some parts of the surround. The stimuli used in the V1–V2 study were mostly confined to the proximal part of the surround as we wished to activate the most sensitive part of the surround. Thus we have not specifically tested the role of feedback connections in providing surround effects for large distances in the visual field and this remains to be done.

Another way to interpret our failure to identify strong feedback effects on center surround interactions for high salience stimuli is to consider the possibility that this is simply not the main role of feedback connections. Center–surround interactions are present from the earliest stages of processing in the retina and orientation-specific surround effects could be provided by horizontal connections at least for proximal interactions. Feedback connections may be important for providing an 'intelligent' input to different sets of neurons in lower order areas depending on interpretations reached at higher levels of the hierarchy (Gilbert et al., 2000). In a recent publication, we showed that feedback connections act on the early part of the visual responses of neurons in lower order areas (Hupé et al., 2001b). Information can be rapidly transferred to higher order areas through the population of magnocellular neurons that are activated early (Nowak and Bullier, 1997) and a first-pass analysis can be performed in higher order areas. According to this first-pass analysis, the gains of the center mechanism and the center–surround interactions could be adjusted in lower order areas to perform an optimal processing of the second wave of information carried by the parvocellular neurons. Recent results of feedback inactivation on neural activity evoked by plaid patterns in cat area 18 are in keeping with such an interpretation of the role of feedback connections in providing a global-to-local interface to neurons in low order areas (Schmidt et al., 2000).

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