Neuron
Article

Privileged Processing of the Straight-Ahead Direction in Primate Area V1

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DOI 10.1016/j.neuron.2010.03.014

SUMMARY

Gaze direction modulates the gain of neurons in most of the visual cortex, including the primary visual (V1) area. These gain modulations are thought to support a mechanism involved in the spatial localization of objects. In the present study, we show that part of them may reflect an additional function: enhancing the visual processing of the objects located straight ahead. Using single- and multiunit recordings in behaving macaques, we found that in peripheral V1, the gain of most neurons increases as their receptive fields (RF) are brought closer to the straight-ahead direction by changing the direction of gaze. No such tendency was observed in central V1, although the influence of gaze direction is similar in term of strength. This previously unknown organization of the gaze-related gain modulations might insure that objects located straight ahead still receive a privileged processing during eccentric fixation, reflecting the ecological importance of this particular egocentric direction.

INTRODUCTION

In a seminal electrophysiological study, Andersen and Mountcastle (1983) showed that in macaque monkeys involved in a fixation task, changing the direction of gaze modulated the excitability (or gain level) of a majority of visual neurons in the parietal cortex. The authors interpreted these modulations as reflecting the integration of visual and eye position signals for recovering the egocentric (i.e., head-centered) location of visual objects, a proposal that has received support by further theoretical works (Bremmer et al., 1998; Pouget and Snyder, 2000; Zipser and Andersen, 1988). Since then, this initial observation has been extended to most of the visual cortex (Andersen et al., 1985; Bremmer, 2000; Bremmer et al., 1997a, 1997b; Dobbins et al., 1998; Galletti and Battaglini, 1989; Galletti et al., 1995; Li et al., 1989; Nakamura et al., 1999; Nowicka and Ringo, 2000; Rosenbluth and Allman, 2002; Squatrito and Maioli, 1996; Toyama et al., 1984), including the primary visual (V1) area (Dobbins et al., 1998; Guo and Li, 1997; Rosenbluth and Allman, 2002; Trotter and Celebrini, 1999; Trotter et al., 1992; Weyand and Malpeli, 1993), and it has been put forward that spatial localization processes might involve both dorsal and ventral visual streams and start in the early visual cortex (Pouget et al., 1993).

But what impact these gaze-related gain modulations have on the visual processing per se? Most previous studies support the view that, despite their omnipresence in the visual cortex, these gain modulations are uniquely involved in spatial localization and do not leave a significant trace on the visual processing. Note that this is not true at the level of single gain-modulated neurons, since the level of activity evoked by stimuli in their retinal receptive fields (RF) depends on gaze direction or, equivalently, on the egocentric location of the stimuli impinging their RF (Andersen et al., 1985). However, it is generally admitted that this "egocentric tuning" differs across neurons with overlapping RF and cancels out at the population level (Bremmer, 2000). Consequently, population responses to visual stimuli are thought to be largely independent of the stimuli egocentric location.

In the present study, we bring evidences that in area V1, this dominant view holds for neurons coding the central part of the visual field, but not for neurons in charge of the peripheral visual field. A first experiment was initially designed to test whether the influence of gaze direction described in area V1 for the central portion of the visual field could be generalized to the whole visual field. Unexpectedly, we found that the gain level of most peripheral V1 neurons increased as their RF were brought closer to the head/body mid-sagittal plane (i.e., the straight-ahead direction) by changing the direction of gaze. These results were fully confirmed in a second experiment designed to test more specifically, through multiunit recordings, this systematic preference for the straight-ahead direction across peripheral V1 neurons.

Thus, our results reveal the presence of an egocentric tuning centered on the straight-ahead direction at the population level in peripheral V1. An important functional consequence of this tuning is that during eccentric fixation, when the objects located straight-ahead are not processed by central vision, they still receive a privileged processing in area V1. This mechanism could reflect the behavioral importance of objects located straight ahead, notably for obstacle avoidance during navigation. With this study, we bring the first evidence that part of the gaze-related gain modulations occurring in the visual cortex are not directly, or uniquely, linked to spatial localization, but rather reflect a mechanism for enhancing the early visual processing of objects occupying relevant egocentric locations.

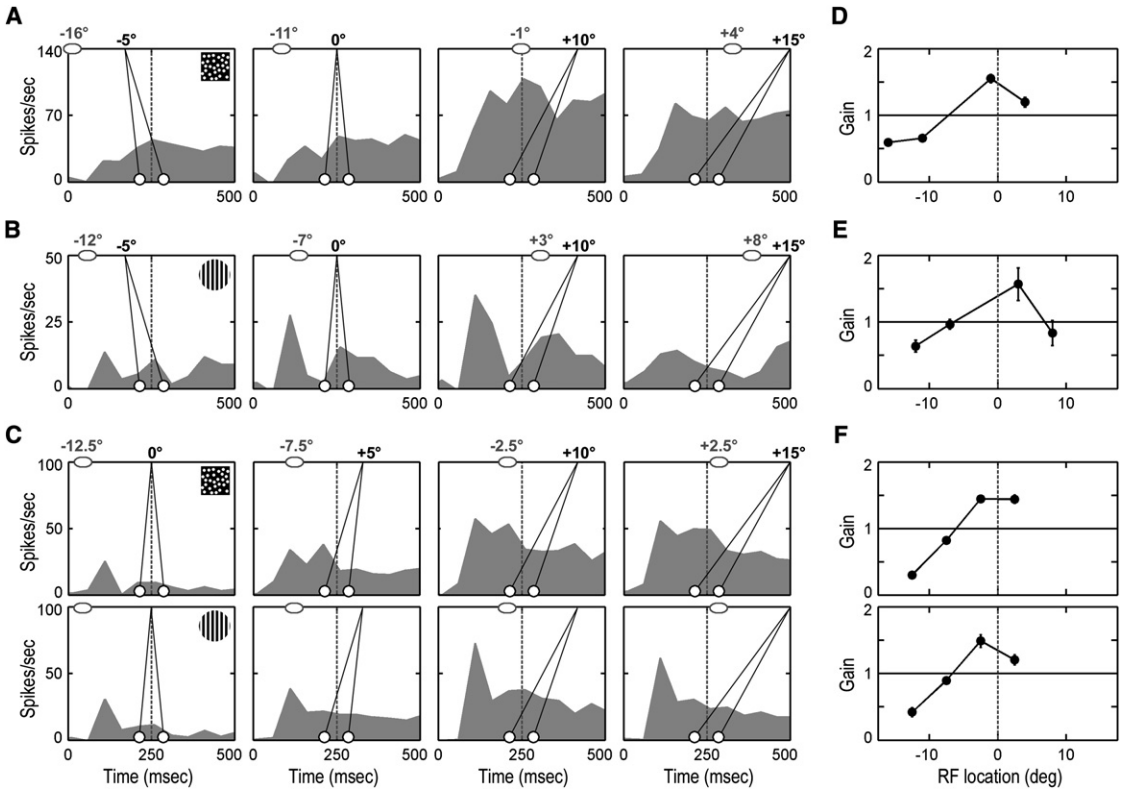

Figure 1. Examples of Gaze-Related Gain Modulations in Peripheral V1 Neurons (Single Units)

(A–C) Three example peripheral V1 neurons tested with dynamic random dots and/or gratings. Mean temporal response profiles (bins of 50 ms) are shown in the background (gray areas). Corresponding gaze directions are illustrated on top, together with the receptive fields (RF) location (ellipses) relative to the straight-ahead direction (dashed lines).

(D–F) Gain profiles for the three example neurons, obtained by plotting gain values as a function of RF location relative to the straight-ahead direction (dashed lines). Error bars indicate standard errors of the mean.

RESULTS

Gaze-Related Gain Modulations and the Influence of RF Location in Central and Peripheral V1: Single-Unit Recordings

The first experiment was initially designed to compare the influence of the direction of gaze on the excitability (or gain) of V1 neurons coding the central and peripheral portions of the visual field. In two macaque monkeys involved in a fixation task, we recorded the activity of neurons in response to similar visual stimuli (dynamic random dots and/or optimally oriented gratings) presented in their RF for 3 to 6 directions of gaze, varied along the horizontal dimension and tested one after each other, in line with a previous experiment (Trotter and Celebrini, 1999). The first tested direction was repeated at the end and only cells that did not show recording instability were kept for further analysis (see Experimental Procedures section). In total, we analyzed the activity of 97 dorsal (or central) V1 neurons (median RF eccentricity = 3.2°, range 1°–5.1°), and 85 calcarine (or peripheral) V1 neurons (median RF eccentricity = 14.8°, range 7.3°–28.5°).

We found similar proportions of neurons showing a significant effect of gaze direction on the level of visual activity (one-way ANOVA, $p < 0.05$) in central and peripheral V1 (62% and 61% respectively; $\chi^2 = 0.01$, $p = 0.92$). Among these cells, the median increase of activity level between the preferred and worst gaze directions was also comparable (201% in central V1 and 206% in peripheral V1; Wilcoxon rank-sum test, $p = 0.96$). In line with a previous study (Trotter and Celebrini, 1999), we found only a marginal influence of gaze direction on the level of spontaneous activity, reaching significance for 8% of the cells in central V1 (median increase of activity level = 125%) and 11% in peripheral V1 (median increase = 138%). Together, these results indicate that the direction of gaze influences mainly the visually evoked activity, with a comparable strength in the central and peripheral representations of the visual field.

Three examples of peripheral V1 neurons showing a significant effect of gaze direction when tested with dynamic random dots and/or gratings are presented in Figures 1A–1C. Mean temporal response profiles are shown in the background, and the corresponding gaze directions are illustrated on top. For these neurons, we derived a gain value for each direction of gaze by dividing the associated level of activity by the overall activity across all directions (see Experimental Procedures section). We also derived the corresponding RF location (ellipses) relative to the straight-ahead direction (dashed lines) by combining the

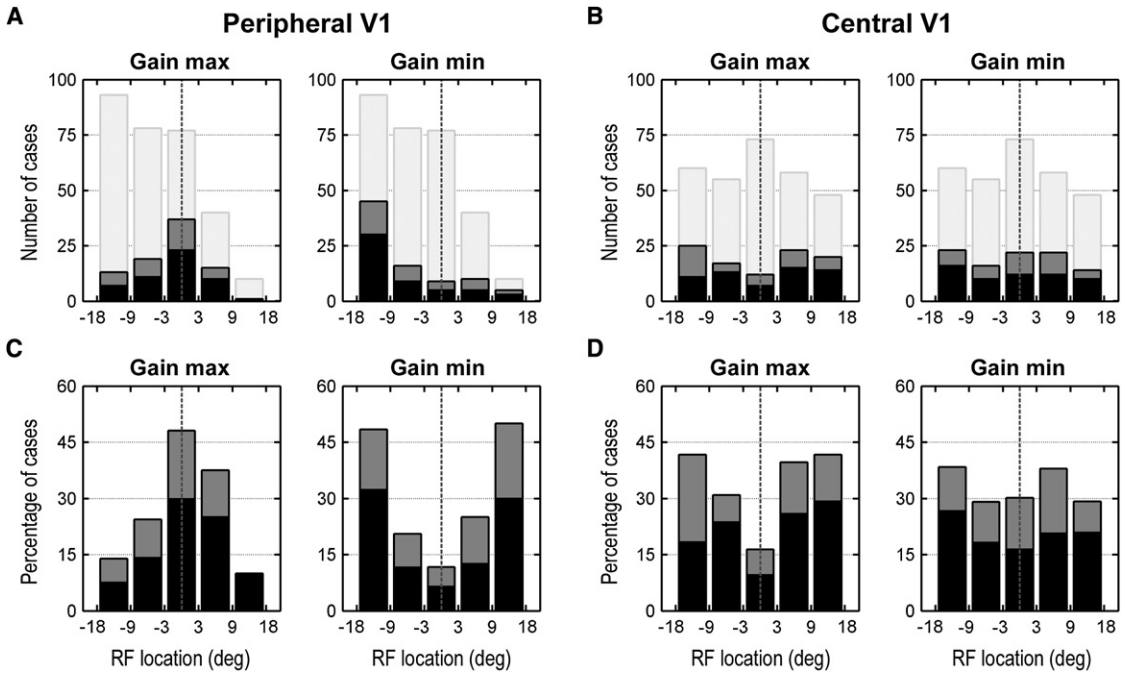

Figure 2. Distributions of RF Egocentric Locations Associated to Maximum and Minimum Gains (Single Units)

(A and B) Distributions of receptive field (RF) egocentric locations (relative to the straight-ahead direction) associated to the maximum and minimum gain values for all neurons in peripheral V1 (A) and central V1 (B). Dark gray histograms represent all the neurons and black histograms only those showing significant gain modulations. Pale gray histograms indicate the total number of gain values sampled in each interval.

(C and D). The distributions shown in (A) and (B) are expressed as a percentage of the total number of samples. Dashed vertical lines indicate the straight-ahead direction.

retinal location of the RF and the tested gaze direction. Gain profiles were then constructed by plotting the gain as a function of the egocentric RF location, as shown in Figures 1D–1F. The first important point regarding these profiles is that they are not monotonic, indicating that gain levels are not linearly related to rightward of leftward shifts of the RF. Rather, in these examples, the gain level appears to increase (or decrease) as the RF is moved closer (or farther) from the straight-ahead direction by changing the direction of gaze.

To assess the generality of this unexpected relationship between gain level and RF location, we first looked at where the RF of each neuron was located with respect to the straight-ahead direction in the conditions eliciting their maximum and minimum gain levels. RF locations were classified as central (within ±3°), intermediate (between ±3° and ±9°), or eccentric (beyond ±9°). Results with dynamic random dots and gratings were grouped based on the very good agreement ($r = 0.75$, $p < 10^{-5}$) between gain values obtained with both types of stimuli on the same cells (e.g., Figures 1C and 1F). In peripheral V1 (Figure 2A) maximum gains were concentrated close to the straight-ahead direction (dashed line), and minimum gains were encountered mainly at eccentric locations on the left side of the head, confirming the trend described in Figure 1. In total, 74% of all the tested cells (dark gray histograms in Figure 2A), and 77% of those showing significant gain modulations (black histograms) were found to have their RF closer to the straight-ahead direction for the condition eliciting maximum gain than for the condition evoking minimum gain. These percentages are significantly higher than the 50% expected by chance (Binomial test; $p < 10^{-5}$ for all the cells, $p < 10^{-4}$ for the gain-modulated cells). Note that because these neurons had RF in the periphery of the left visual hemifield (e.g., Figure 1), there is a sampling bias toward intermediate and eccentric RF locations on the left side of the head. This bias is indicated by the pale gray histograms in Figure 2A, which represent the total number of gain values sampled in each interval (number of tested cells × number of time each cell was sampled within the interval). Thus, for instance, 76 cells were tested 1.22 times on average in the interval [−18°, −9°], while only 10 cells were tested once in the interval [9°, 18°]. In order to compensate this sampling bias, the number of cells showing maximum and minimum gain values in each interval was expressed as a percentage of the total number of samples within that interval (Figure 2C). This procedure clearly indicates (1) that the maximum and minimum gains were actually concentrated on central and eccentric locations respectively and (2) that eccentric locations for the minimum gains were symmetrically distributed on both sides of the straight-ahead direction. These results differ greatly from those obtained for the population of central V1 neurons (Figures 2B and 2D), for which we did not find any obvious relationship between gain level and RF location. Only 52% of all the cells (dark gray histograms) and 47% of those showing significant gain modulations (black histograms) were found to have their RF closer to the straight-ahead direction in the condition of

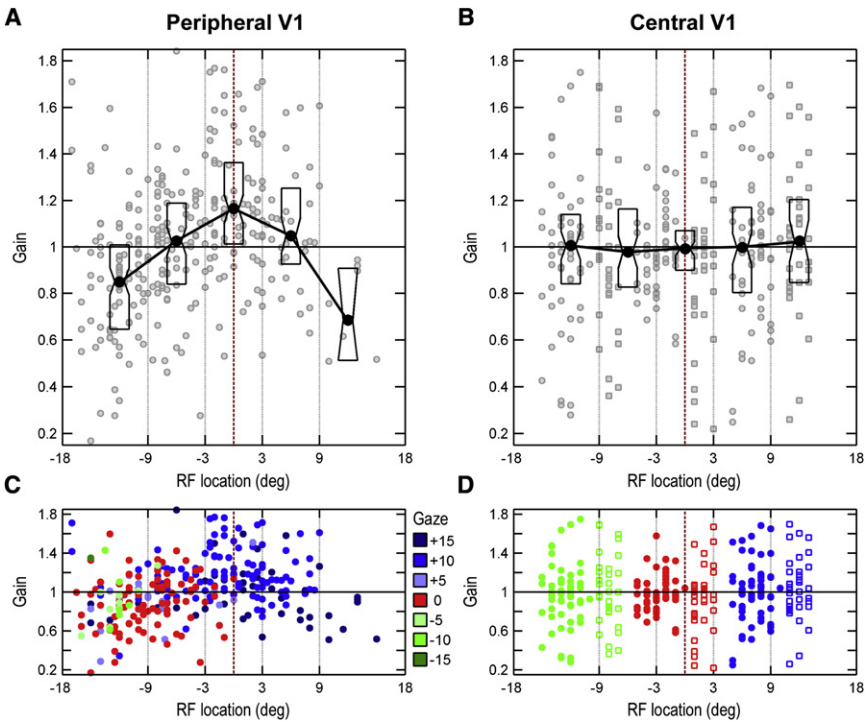

Figure 3. Population Gain Profiles (Single Units)

(A and B) Scatter plots of all the gain values as a function of RF egocentric location (relative to the straight-ahead direction) in peripheral and central V1 neurons. The superimposed box-plots indicate the median gain levels and interquartile ranges for central (<±3°), intermediate (±3° to ±9°), and eccentric (>±9°) RF locations. Notches in the box-plots signal the 95% confidence intervals for the median gain values (see also Table 1).

(C and D) Same scatter plots as those shown in (A) and (B) with a color code indicating leftward (green), central (red), and rightward (blue) gaze directions. Dashed vertical lines indicate the straight-ahead direction. In central V1, circular and square symbols are for neurons from the left and right visual hemi-fields respectively.

See also Figure S1.

maximum gain than in the condition of minimum gain, in close agreement with the 50% expected by chance ($p < 0.84$ for all the cells, $p = 0.70$ for cells showing significant gain modulations).

We also derived "population gain profiles" by computing the median and interquartile range of all the gain values across the central, intermediate, and eccentric intervals. In peripheral V1 (Figure 3A), the population gain profile was "bell-shaped" and centered on the straight-ahead direction (brown dashed line), with a highly significant relationship between gain level and RF location (Kruskall-Wallis ANOVA, $\chi^2 = 67.7$, $p < 10^{-14}$). Note that the lower and upper parts of the box-plots indicate respectively the 25th and 75th percentiles of the gain distributions. Thus, it appears that more than 75% of the gain values sampled in the central interval are above unity, against only 25% of the gain values sampled in the eccentric intervals. Median gain values (±95% confidence intervals) for the different intervals are given in Table 1, considering all the cells or only those significantly modulated by the direction of gaze. Once again, results differed radically in central V1 (Figure 3B and Table 1), where the population gain profile as a function of RF location was flat ($\chi^2 = 0.65$, $p = 0.96$).

In Figure 3C, it can be seen that in peripheral V1, RF located at intermediate and eccentric distances from the straight-ahead direction are associated to rightward fixations (in blue) on the right side of the head and mainly to central (in red) or leftward (in green) fixations on the left side of the head. By considering only the interval in which central, leftward and rightward gaze directions occur (i.e., for RF locations between ±[6°–18°]), we found no statistical difference in median gain values between central, leftward and rightward gaze directions (Kruskall-Wallis ANOVA, $\chi^2 = 3.41$, $p = 0.19$). This result was confirmed by a partial correlation analysis, which allows estimating what the

Table 1. Median Gain Values (and 95% Confidence Intervals) for the Three Egocentric Eccentricities of RF Considered in the First Experiment (Single Units) and Second Experiments (Multiunits)

			Central	Intermediate	Eccentric
			±[0°–3°]	±[3°–9°]	±[9°–18°]
Single units	Periph. V1	All	1.17 (1.09–1.19)	1.03 (1.00–1.07)	0.84 (0.80–0.89)
		G.M.	1.20 (1.13–1.36)	1.04 (0.98–1.10)	0.82 (0.70–0.86)
	Central V1	All	1.02 (0.87–1.09)	1.00 (0.94–1.05)	1.01 (0.95–1.05)
		G.M.	0.98 (0.75–1.08)	1.03 (0.96–1.13)	0.99 (0.88–1.09)
			0°	±5°	±10°
Multiunits	Periph. V1	All	1.08 (1.03–1.20)	1.02 (0.99–1.05)	0.94 (0.91–0.97)
		G.M.	1.15 (1.08–1.25)	1.05 (0.99–1.12)	0.91 (0.76–0.95)
	Central V1	All	0.99 (0.92–1.01)	0.98 (0.94–1.02)	1.02 (0.97–1.05)
		G.M.	0.98 (0.92–1.08)	0.97 (0.88–1.03)	1.02 (0.96–1.08)

Gain values in peripheral V1 and central V1 were calculated either by considering all the cells (All) or only those showing significant gain modulations (G.M.).

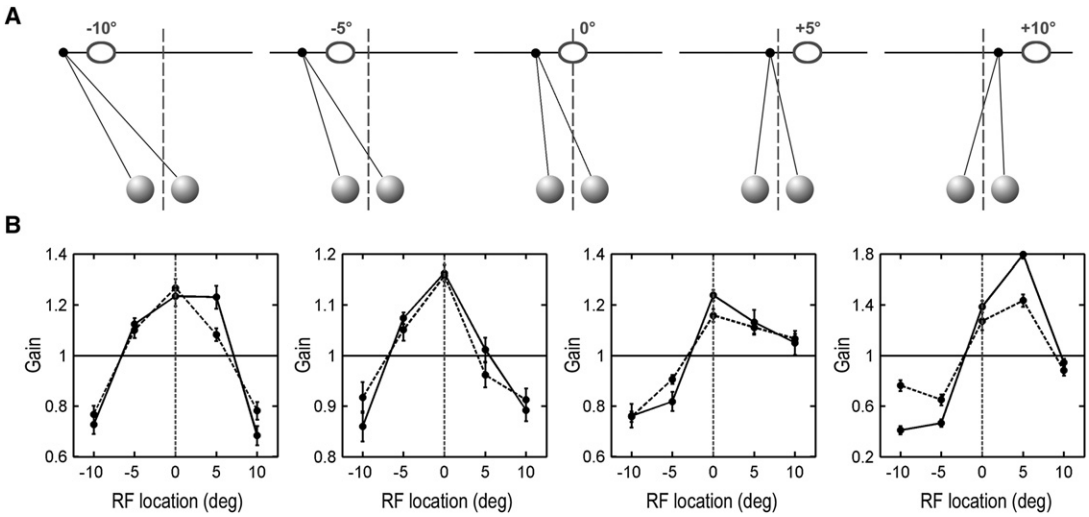

Figure 4. Examples of Straight-Ahead Tunings in Multiunit Recordings

(A) Illustration of the experimental conditions tested during multiunit recordings. Five gaze directions were tested in an interleaved fashion, adjusted for each recording sites in order to bring the RF at 0°, ± 5°, and ± 10° relative to the straight-ahead direction (dashed vertical line).

(B) Gain profiles for four multiunit recording sites in peripheral V1. Plain and dashed profiles show the results obtained during binocular and monocular stimulations respectively. The dashed vertical lines indicate the straight-ahead direction. Error bars indicate standard errors of the mean.

correlation between two variables (e.g., gain level and RF location) would be if a third variable (e.g., gaze direction) was held constant. Interestingly, the correlation between gain and RF location is highly significant after correction for the effect of gaze direction ($r = -0.34$, $p < 10^{-5}$). By contrast, there is no correlation between gain and gaze direction after correction for the effect of RF location ($r = 0.09$, $p = 0.10$). Thus, these results indicate that at constant eccentricity of the RF, there is no preference for central, leftward or rightward gaze directions. The same was true in central V1 (Figure 3D), where preference for a particular gaze direction was encountered neither for neurons coding the left visual hemi-field (Figure 3D, filled circular symbols; $\chi^2 = 0.21$, $p = 0.90$) nor for neurons coding the right visual hemi-field (Figure 3D, open square symbols; $\chi^2 = 1.15$, $p = 0.56$).

Unwanted variations in the quality of fixation as a function of gaze direction should lead to a direct relationship between gaze direction and overall gain levels, independently of RF location and comparable between central and peripheral V1. However, the facts that the straight-ahead tuning we have evidenced is restricted to peripheral V1 and depends on both gaze direction and retinal RF location, argues against an explanation based on variations in the quality of fixation. Nevertheless, we assessed the influence of gaze direction on the trial-to-trial variability of the visual responses, which represents an indirect measure of the quality of fixation (Gur et al., 1997). The absence of relationship between response variability and gaze direction in both central and peripheral V1 (see Figures S1A and S1B available online), indicates that fixation quality is likely to be constant within the range of investigated gaze angles (±15°). Note also that eye calibration was checked carefully at the beginning of each recording session and that stimulus size (6°) was large enough to ensure that the totality of the RF would be stimulated even with a slight miscalibration.

Gaze-Related Gain Modulations and the Influence of RF Location in Central and Peripheral V1: Multiunit Recordings

The second experiment was designed to test more specifically, through multiunit recordings, the existence of a systematic preference for the straight-ahead direction across peripheral V1 neurons. To do so, we recorded multiunit activity elicited by dynamic random dots in the central (n = 20) and peripheral (n = 20) representations of the right visual hemifield in a third animal involved in a fixation task. The random dot stimuli were identical to those used in the first experiment. Five directions of gaze were systematically tested in an interleaved sequence. They were adjusted for each site in order to bring the RF at 0°, ± 5°, and ± 10° relative to the straight-ahead direction (Figure 4A). Symmetrical sampling around the straight-ahead direction, combined to multiunit recordings, allows testing unambiguously, and in each recording site, whether an overall tuning for the straight-ahead direction emerges from the gain modulations recorded in neuronal populations with overlapping RF.

The percentage of sites showing significant gain modulations was slightly larger in peripheral than in central V1 (70% against 50%; $\chi^2 = 1.67$, $p = 0.20$). Among these sites, the median increase of activity level between the preferred and worst gaze directions was higher in peripheral than in central V1 (181% against 139%; Wilcoxon rank-sum test, $p < 0.01$). Moreover, there was also a marked difference in the dispersion of gain values across the neuronal populations in central (standard deviation = 0.14, 95% confidence interval: 0.12–0.16) and peripheral V1 (SD = 0.21, 95% CI: 0.19–0.25; F test, $F = 2.42$, $p < 10^{-4}$). Note that in the first experiment, the dispersion of gain values was similar in central (SD = 0.32; 95% CI: 0.30–0.34) and peripheral V1 (SD = 0.31, 95% CI: 0.29–0.34; $F = 1.04$, $p = 0.76$), suggesting that averaging the activity of nearby

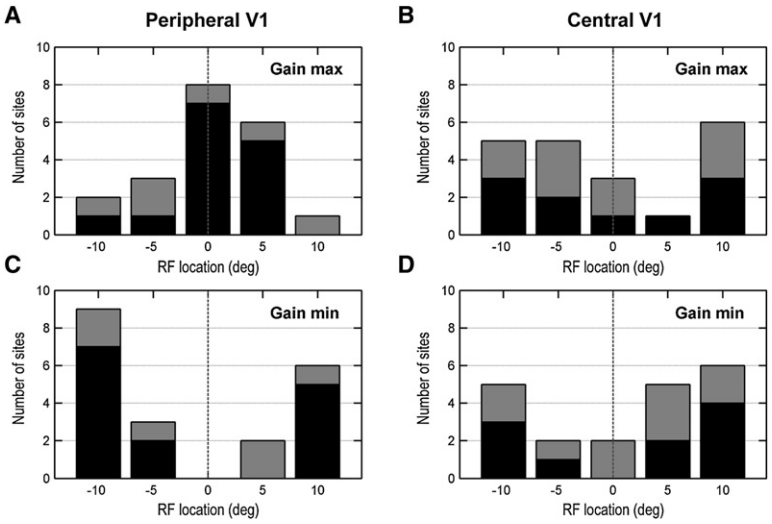

Figure 5. Distributions of RF Egocentric Locations Associated to Maximum and Minimum Gains (Multiunits)

Distributions of receptive field (RF) egocentric locations (relative to the straight-ahead direction) associated to the highest (A and B) and lowest (C and D) gain values for the recording sites in peripheral and central V1. Dark gray histograms represent all the sites and black histograms only those showing significant gain modulations. Dashed vertical lines indicate the straight-ahead direction.

neurons has a different impact on the gain modulations recorded in both regions. A likely explanation, based on the results of the first experiment, is that nearby neurons in central V1 exhibit a greater diversity of gain profiles which are balanced out in the multiunit activity.

Four examples of multiunit gain profiles recorded in peripheral V1 are shown in Figure 4B. They are all "bell-shaped," with a peak aligned, or close, to the straight-ahead direction (dashed lines).

This trend was confirmed at the population level when considering the distributions of RF locations associated to the maximum and minimum gain values for all the recording sites in peripheral V1. As shown in Figure 5A, the maximum gains were found mainly for RF located in the vicinity of the straight-ahead direction (dashed lines; dark gray and black histograms represent all recording sites and those showing significant gain modulations, respectively). By contrast, the minimum gains were encountered mainly for RF located 10° away, either on the left or right side of the straight-ahead direction (Figure 5C). For a majority of sites (70%), the RF was closer to the straight-ahead direction for the condition evoking maximum gain than for the condition evoking minimum gain. This percentage was significantly higher than the 32% expected by chance (binomial test; $p < 10^{-3}$; note that chance expectation was less than 50% because maximum and minimum gains could also be encountered for RF locations at equal distance from the straight-ahead direction, e.g., −5° and +5°, or −10° and +10°). In central V1, no obvious relationship between RF location and maximum/minimum gains was found, in line with the first experiment (Figures 5B and 5D). The RF were closer to the straight-ahead direction for the condition evoking maximum gain for only 25% of the sites, in good agreement with chance expectation (32%; $p = 0.50$).

As shown in Figure 6, the population gain profiles obtained by considering all gain values were in excellent agreement with those constructed from the populations of single cells in central

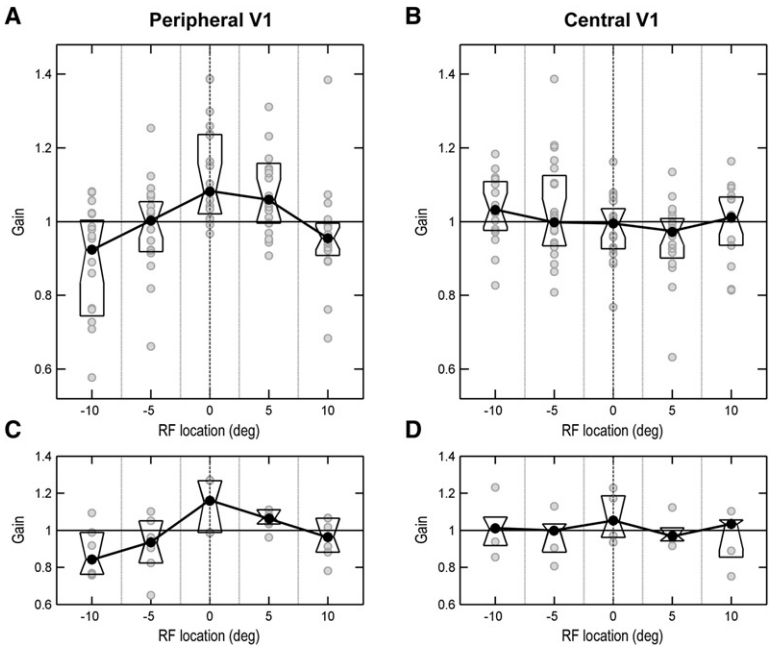

Figure 6. Population Gain Profiles (Multiunits)

(A and B) Scatter plots of all the gain values as a function of RF egocentric location (relative to the straight-ahead direction) in peripheral and central V1 recording sites. The superimposed box-plots indicate the median gain levels and interquartile ranges for central (0°), intermediate (±5°), and eccentric (±10°) RF locations. Notches in the box plots signal the 95% confidence intervals for the median gain values (see also Table 1).

(C and D) Same as (A) and (B) for the monocular controls recorded in peripheral and central V1. See also Figure S3.

See also Figure S1.

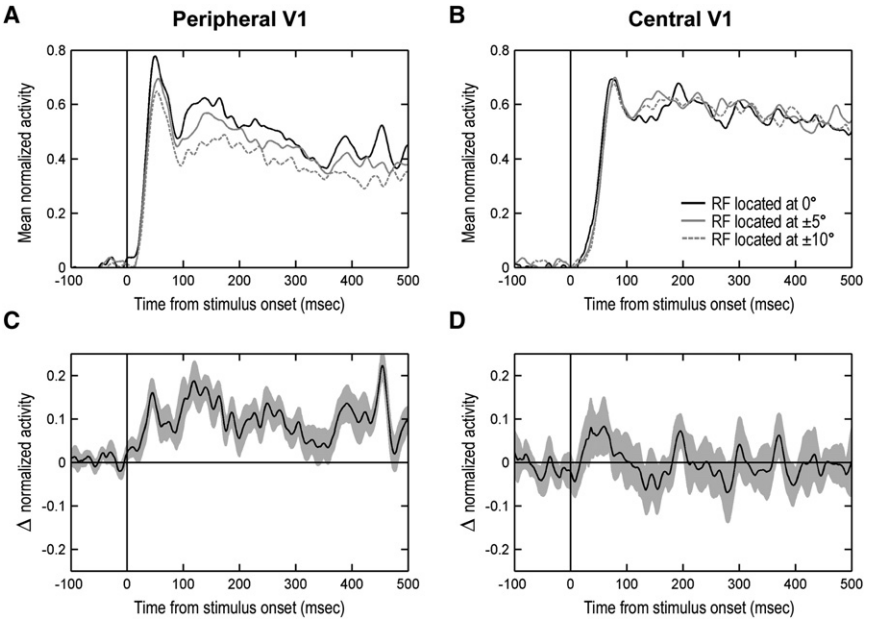

Figure 7. Time Course of the Straight-Ahead Effect (Multiunits)

(A and B) Mean temporal response profiles computed for central (0°), intermediate (±5°), and eccentric (±10°) RF egocentric locations (relative to the straight-ahead direction) in peripheral and central V1 (bins of 1 ms, smoothed with a Gaussian kernel, σ = 3ms). Response profiles were normalized for each recording site and then averaged across sites.

(C and D) Differential activity between the temporal response profiles for central (0°) and eccentric (±10°) RF locations. Dark gray areas indicate the 95% confidence intervals.

See also Figure S2.

and peripheral V1 (cf. Figures 3A and 3B). Indeed, the population gain profile was "bell-shaped" and centered on the straight-ahead direction in peripheral V1 (Figure 6A; Kruskall-Wallis ANOVA, $\chi^2 = 33.31$, $p < 10^{-5}$) and basically flat in central V1 (Figure 6B; $\chi^2 = 7.89$, $p = 0.10$). Note, however, that the "bell-shaped" profile in peripheral V1 was slightly "flatten" compared to that of the first experiment (Table 1). A likely explanation is the more restricted range of eccentric RF positions that were explored (±10°) in order to sample symmetrically on both sides of the straight-ahead direction. As in the first experiment, there was no systematic preference for rightward (>3°), leftward (<−3°), or central [−3°, 3°] gaze directions, neither in central V1 ($\chi^2 = 3.58$, $p = 0.17$) nor in peripheral V1 ($\chi^2 = 3.18$, $p = 0.20$). Thus, gain modulations for the different directions of gaze average out at the population level in both regions.

In this second experiment, fixation quality was also assessed indirectly by response variability and was found to be constant within the range of investigated gaze angles (±20°; Figures S1C and S1D).

Does the preference for the straight-ahead direction in peripheral V1 leads to an overall increase in both signal and noise or to a better signal-to-noise ratio (SNR) for that particular direction? To address this issue, we computed a measure of the SNR by dividing the mean visual responses (signal) by their standard deviations (noise) and we compared the gain values derived from the SNR to those derived from the mean responses. There was a good correlation between these measures for most of the recording sites in both experiments (median correlation coefficient = 0.69, median regression slope = 0.65), which was confirmed at the population level (correlation coefficient = 0.78 [$p < 10^{-5}$]; regression slope = 0.67 [95% CI: 0.63-0.72]). In line with these results, the straight-ahead tuning evidenced in peripheral V1 was significant when the population gain profiles were derived from the SNR, both in the first experiment (Kruskall-Wallis ANOVA, $\chi^2 = 27.51$, $p < 10^{-4}$) and second experiment ($\chi^2 = 18.23$, $p < 0.01$). Thus, the preference for the straight-ahead direction in peripheral V1 leads to an overall increase in SNR for that particular direction.

Finally, we studied the temporal dynamic of the influence exerted by RF location on visual responses in peripheral V1 by computing mean normalized temporal response profiles from all the central and peripheral recording sites and for the three eccentricities of RF location (0°, ± 5°, and ± 10°).

As shown in Figure 7A, distinct mean temporal response profiles were obtained in peripheral V1 when identical visual stimuli were presented in the RF, depending on their central, intermediate, or eccentric location relative to the straight-ahead direction. The overall level of activity decreases with increasing distance between the RF and the straight-ahead direction. Figure 7C shows the mean differential activity and its 95% confidence interval (gray area) between the central (0°) and eccentric (±10°) RF locations. It can be seen that the influence of RF location is already statistically significant at the beginning of the visual response and remains more or less constant during the whole duration of the visual response. In central V1, not such influence of RF location was found (Figure 7B), and the differential activity between central (0°) and eccentric (±10°) RF locations was not significant (Figure 7D). As shown in Figure S2, similar conclusions were reached by performing a related analysis on the single-cell results of the first experiment.

Control Experiments

Control experiments were performed in order to assess whether the straight-ahead tuning evidenced in peripheral V1 might be due to eccentricity-dependent visual factors rather than to a specific organization of the gaze-related gain modulations. Notably, changing the direction of gaze can affect the binocular disparity naturally occurring within the RF. We thus performed monocular controls for five sites in central V1 and six sites in peripheral V1 to assess the potential influence of this factor. In Figure 4B, the gain profiles obtained during monocular stimulation (dashed curves) are superimposed on those measured during binocular stimulation. It is clear that "bell-shaped" profiles are still observed in the absence of binocular disparity. Overall, the correlation between gain values measured during

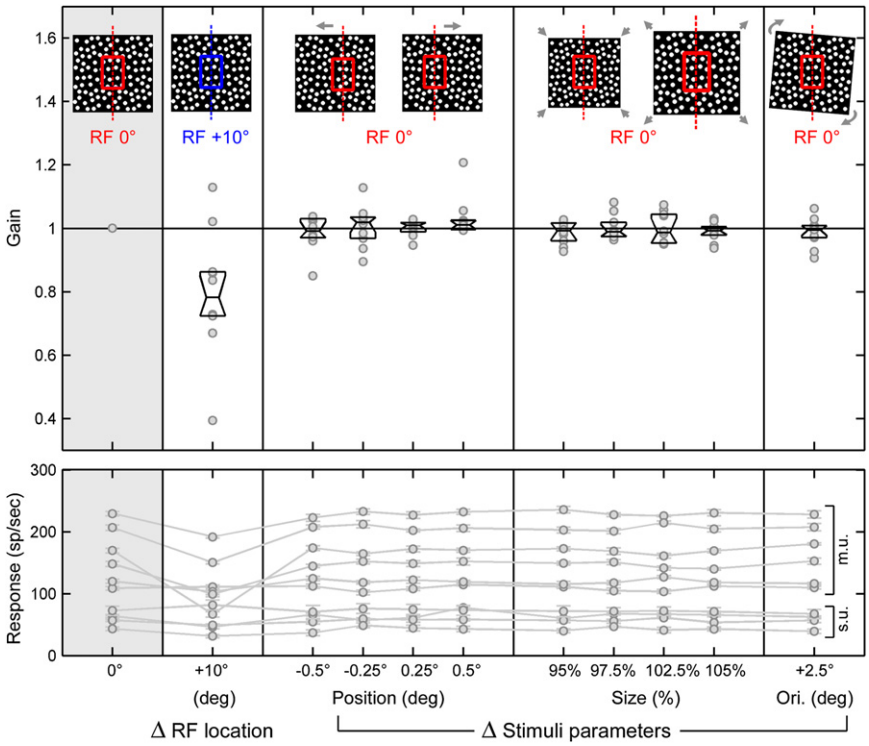

Figure 8. Control Experiments for Slight Variations in Stimuli Parameters

Lower plot shows the mean responses (±standard error) evoked by dynamic random dots for 10 recording sites in peripheral V1 (six multiunits [m.u.] and four single units [s.u.]). In the leftmost column (in gray), the stimuli parameters were identical to those of the main experiment and the RF were located straight ahead (0°, in red). In the second column, the stimuli parameters were unchanged but the RF were shifted 10° to the right (+10°, in blue). In the following columns, RF location was unchanged (0°) but stimuli parameters were varied (in position, size, or orientation). Conditions were interleaved, and ten responses were recorded for each condition. The upper plot shows the gain values derived from the mean responses. They were computed by dividing all the mean responses by those obtained with the native stimuli parameters when the RF were located straight ahead (leftmost column, in gray). The superimposed box plots indicate the median gain values and interquartile ranges. See also Figure S4.

binocular and monocular stimulation was very high ($r = 0.84$; $p < 10^{-5}$), and the "population gain profiles" drawn from these monocular controls (Figures 6C and 6D) were close to those obtained during binocular stimulation (Figures 6A and 6B). Statistically, the relationship between gain and RF location was still significant in peripheral V1 ($\chi^2 = 11.09$, $p < 0.05$) and not significant in central V1 (Kruskall-Wallis ANOVA, $\chi^2 = 1.92$, $p = 0.75$). These results, together with an analysis restricted to the disparity unselective cells in the first experiment (Figure S3), allow ruling out a significant contribution of binocular disparity in the relationship evidenced between gain level and RF location.

Another alternative explanation could be that the visual RF in peripheral V1 are partially spatiotopic, so that when a gaze shift is supposed to bring the RF away from the straight-ahead direction, those latter follow only partially and remain somehow anchored to the straight-ahead direction. This would lead to suboptimal visual stimulation at non-straight-ahead RF directions and could thus produce a straight-ahead tuning similar to that reported here. To test this hypothesis, the visual RF of 10 recording sites in peripheral V1 (6 multiunits and 4 single units) were mapped with a bright bar while gaze direction was precisely adjusted to bring the RF centers in the straight-ahead direction. The RF were mapped again after a 10° gaze shift to the right. All the RF centers showed a shift in RF location no statistically different from the 10° shift predicted by retinotopy (mean ± SD: 9.94° ± 0.14°). Since a significant preference for the straight-ahead direction was also encountered in this population (Figure 8; Wilcoxon signed-rank test, $p < 0.01$), we can rule out an explanation based on spatiotopic properties of the RF in peripheral V1 neurons.

In the second experiment, the five directions of gaze were tested in an interleaved manner, preventing manual correction of the screen orientation to bring it perpendicular to the direction of gaze. Since the screen remained frontoparallel, the stimuli could be slightly shifted with respect to the RF center (<0.2°), and their angular size slightly reduced (<2%), as they were moved away from the straight-ahead direction. Nevertheless, recordings from the ten sites for which the RF were mapped indicate that even larger variations in the stimuli parameters (positional shifts of ±0.5°; size variations of ±5%; and even rotations of 2.5°) do not affect significantly the response level of peripheral V1 neurons (Figure 8). Thus, slight variations in stimuli parameters cannot account for the gain decrease measured as the RF are moved away from the straight-ahead direction. Additional recordings from eight sites indicate that the level of activity elicited by our random dot stimuli are unaffected by slight variations in the luminance of the white dots (from 24 to 30 cd/m^2) displayed on the black background (<0.01 cd/m^2). This last control allows excluding that the luminance inhomogeneity inherent to CRT monitors contributes significantly to the straight-ahead tuning of peripheral V1 neurons (Figure S4).

Together, the results of these control experiments strongly argue against a significant influence of eccentricity-dependent visual factors, and they rather indicate that the straight-ahead tuning of peripheral V1 neurons emerges from a specific organization of the gaze-related gain modulations.

DISCUSSION

In the present study, we found that gain modulations related to the direction of gaze are encountered in area V1 across a large

range of retinal eccentricities but are differently organized in the central and peripheral portions of the visual field. In peripheral V1, the gain of most neurons increases as their receptive fields (RF) are brought closer to the head-body mid-sagittal plane (i.e., the straight-ahead direction) by changing the direction of gaze. No such tendency is observed in central V1, although the influence of gaze direction is similar in term of strength.

These results were evidenced through single-unit recordings and fully confirmed with multiunit recordings in another animal. Importantly, the straight-ahead tuning found in peripheral V1 relates gain level to the combined influence of gaze direction and RF retinal location. Thus, parameters that can vary with the direction of gaze but are independent of RF location, such as the quality of fixation or the calibration of the eye signal, cannot account for this tuning and for the fact that it is confined to peripheral V1 neurons. Moreover, an analysis of response variability provides indirect evidences (Gur et al., 1997) that the quality of fixation was constant across the range of investigated gaze directions in both experiments. Changes in the visual context surrounding the RF as the direction of gaze is varied could have contributed to these results (Andersen et al., 1985; Angelucci et al., 2002; Zipser et al., 1996). However, the set up was in darkness during the experiments, greatly reducing the visibility of surrounding elements. Moreover, all the multiunit recording sites were tested with stimuli presented at the same five horizontal eccentricities on the screen, so that a similar relationship between gain and RF location would be expected in central and peripheral V1 if an effect of screen border was to be involved. Furthermore, control experiments indicate that the slight variations of stimuli parameters induced by shifting the stimuli away from the straight-ahead direction (binocular disparity, stimulus size, location, and luminance) do not play a significant role in the preference of peripheral V1 neurons for that particular direction.

In central V1, the absence of systematic relationship between gaze-related gain modulations and RF location is illustrated by the flat shape of the population gain profiles obtained in both experiments. There was also no systematic relationship between gain modulations and gaze direction per se. These results are in line with previous reports in the same area (Rosenbluth and Allman, 2002) and in higher-order visual areas (Andersen and Mountcastle, 1983; Bremmer, 2000; Bremmer et al., 1997a, 1997b; Galletti et al., 1995; Nowicka and Ringo, 2000; Rosenbluth and Allman, 2002). Thus, in central V1, populations of gain-modulated neurons might support the spatial localization of visual elements, as previously suggested (Pouget et al., 1993), but this mechanism does not impact the visual processing per se.

However, the picture differs markedly in peripheral V1, where we found a clear-cut relationship between the gain modulations measured in individual neurons and the location of their RF, giving rise to ''bell-shaped'' gain profiles centered on the straight-ahead direction. This egocentric tuning implies that gaze-related gain modulations do not average out in peripheral V1 and are rather organized to highlight the visual processing of objects located straight ahead. To appreciate the strength of this effect, note that the response level of peripheral V1 neurons shows a median increase of 20% to 40% as their RF is moved from ±10° to 0° relative to the straight-ahead direction. For comparison, visual attention has been shown to produce increases of 30% or less on the response level of V1 neurons (Haenny and Schiller, 1988; Luck et al., 1997; Marcus and Van Essen, 2002; McAdams and Maunsell, 1999; Moran and Desimone, 1985; Roelfsema et al., 1998). The fact that this straight-ahead tuning is restricted to the peripheral visual field representation explains why it has not been evidenced in earlier studies in area V1, since they did not explore such eccentric retinal locations (Guo and Li, 1997; Rosenbluth and Allman, 2002; Trotter and Celebrini, 1999).

One of these studies (Guo and Li, 1997) suggested another type of organization in area V1, which would lead to highlight the processing of the visual hemifield ipsilateral to the direction of gaze during asymmetric fixations to the right or to the left. However, this finding was not confirmed by further studies (Rosenbluth and Allman, 2002; Trotter and Celebrini, 1999), and the functional advantages that such a mechanism may confer are puzzling. By contrast, the straight-ahead tuning in peripheral V1 seems to have a straightforward explanation, related to one of the important role of peripheral vision: the detection of visual elements that are potentially relevant behaviorally. Our proposal is that elements located straight ahead are more likely to be behaviorally relevant than elements more eccentric in the surrounding space, notably because they represent potential obstacles during navigation. When the gaze is directed straight ahead, these elements are efficiently processed by central vision. However, during visual exploration of the surrounding space, the gaze can be eccentric and the same elements are then processed by peripheral vision. The organization of the gain modulations we have described in peripheral V1 insures that these elements still receive a privileged processing in area V1.

This straight-ahead tuning may be supported by either bottom-up or top-down mechanisms. It has been proposed that gaze-related gain modulations in area V1 arise through the bottom-up integration of proprioceptive signals (Buisseret and Maffei, 1977) and/or efference copy of motor signals, fed either directly or indirectly through the lateral geniculate nucleus (Lal and Friedlander, 1989). A related bottom-up mechanism may be at work in peripheral V1, although it would have to follow specific rules for the emergence of an egocentric tuning at the population level. Alternatively, this egocentric tuning may be governed by the top-down influence of higher-order areas, sending back spatial information for highlighting the processing of visual elements located straight ahead. This top-down influence may notably emanate from areas involved in spatial vision and spatial attention (Andersen and Buneo, 2002; Colby and Goldberg, 1999; Goodale and Milner, 1992; Ungerleider and Mishkin, 1982). Future experiments in which animals are involved in a demanding attentional task directed toward the fixation target may help to distinguish between these alternative explanations (Fang et al., 2008). Note that whatever the mechanism involved, the emergence of the straight-ahead tuning is fast enough (from the very beginning of the visual response) and strong enough (a modulation of the response level of 2% to 4% per degree) to allow an immediate and privileged processing of objects located straight ahead.

As in most previous studies in the field, the animals were head fixed and they moved their eyes in order to bring the gaze at different directions. However, in natural conditions, changing the direction of gaze can involve a combination of both eye and head movements. It will be the aim of future studies to assess whether visual neurons in area V1 are also influenced by head position signals, as those in the posterior parietal cortex (Brotchie et al., 1995). A combination of eye and head position signals may contribute in anchoring the straight-ahead tuning to the mid-sagittal plane of the body or, alternatively, to some external and ecologically meaningful reference point (Snyder et al., 1998), such as the screen center. Future studies will also have to assess how this tuning is expressed along the vertical dimension of space and in the peripheral representation of subsequent visual areas. Since recent functional imaging studies have already reported an influence of gaze direction on visually driven activations in humans (Andersson et al., 2007; DeSouza et al., 2002; Deutschländer et al., 2005), another important issue will be to determine whether a privileged processing of the straight-ahead direction can also be evidenced in the human visual cortex and what the consequences of this egocentric tuning are at the perceptual and motor levels.

To conclude, our results show that part of the gaze-related gain modulations recorded in the visual cortex are not directly, or uniquely, linked to spatial localization processes. Rather, they reflect a previously unknown mechanism for highlighting the visual processing of a behaviorally relevant region of the surrounding space: the straight-ahead direction.

EXPERIMENTAL PROCEDURES

A detailed description of the general methods has been reported elsewhere (Durand et al., 2007; Trotter and Celebrini, 1999). All experimental protocols, including care, surgery, and training of animals were performed according to the Public Health Service policy on the use of laboratory animals. The data reported here were obtained from recordings in four hemispheres in three rhesus monkeys (*Macaca mulatta*) trained to perform a visual fixation task. Most cells recorded from central V1 for the first experiment have already been included in a previous paper (Trotter and Celebrini, 1999) and are reanalyzed here for comparison purpose. Position of both eyes was monitored with the scleral search coil technique (Robinson, 1963) (C-N-C engineering). The REX software (Hays et al., 1982) system (Real Time Experiment) was used to manage the experiment in real time.

Behavioral Task

The monkeys were trained to fixate a small bright target (12 min of arc) that appeared on a video monitor screen at different possible directions along the horizontal meridian of the visual field. They were required to maintain stable binocular fixation, within a window of ±1° centered on the fixation target, for random periods of time between 1 and 2 s in order to be rewarded by a drop of fruit juice or water.

Visual Stimuli

In the initial experiment, the stimuli were square-wave luminance gratings (spatial frequency, 2 cycles/°) displayed in a circular window (diameter, 6°), and dynamic random-dots (white dots on a black background, dot density, 20%; dot size, 0.09°; refresh rate of the random-dots pattern, 30 Hz) displayed in a square window (6° × 6°). The gratings and dynamic random dot stimuli were used respectively to test the selectivity of neurons for orientation (8 orientations tested between 0 and 157.5°, by steps of 22.5°) and binocular disparity (7 values of horizontal disparity, between −0.6° and +0.6°, by steps of 0.2°), respectively. These stimuli were generated by the Vision Works software (Vision Research Graphics) and presented on a CRT monitor (resolution, 1024 × 512; refresh rate, 120 Hz) at a viewing distance of 53 cm. The stimuli were displayed with a maximum luminance contrast between the white and black pixels (respective luminance of 30.8 and ~0.01 cd/m^2 at the screen center). In the present analysis, responses to all the visual conditions were used to assess recording stability, but only those to optimally oriented gratings and to zero-disparity dynamic random dots were considered for quantifying the effects of gaze direction, allowing a direct comparison of the results obtained from the same number of responses to both types of stimuli. Because the first experiment indicated that both types of stimulus lead to similar results regarding the effect of gaze direction, only zero-disparity dynamic random dot stimuli were kept in the second experiment. They were generated by the same software and their parameters were identical to those used in the first experiment.

Electrophysiological Recordings

Recordings were made using insulated tungsten microelectrodes in both dorsal V1 and calcarine V1, where neurons code the central and peripheral parts of the visual field, respectively (Daniel and Whitteridge, 1961). Note that beyond this initial study, calcarine V1 has been investigated by only a few electrophysiological studies (Battaglini et al., 1993; Durand et al., 2002, 2007; Orban et al., 1986). The receptive field (RF) of recorded neurons was localized manually with a bright bar that was moved on the screen. The stimuli were presented for 500 ms, centered on the RF. Spontaneous activity was recorded for 300 ms during the fixation period preceding visual stimulation, and visual activity was recorded for 500 ms during the visual stimulation.

In the first experiment, single-cell recordings were performed in two animals (monkeys A and B). Responses evoked by dynamic random dots (46% of the cells), luminance gratings (40% of the cells,) or both types of stimuli (14% of the cells) were recorded for different directions of gaze ranging from –15° to +15° (5 repetitions for each stimulus condition). Most of the cells were tested for 3 directions of gaze (65%), but some were also tested for 4 (19%), 5 (11%), or 6 (5%) directions of gaze. For each cell, the different gaze directions were tested one after each other in a random order, and the first tested direction was repeated at the end to assess the stability of the electrophysiological signal. In cells for which both dynamic random dots and gratings were used, the different gaze directions were tested first with one type of stimulus and then with the second type of stimulus. The sequence order of tested gaze directions was varied between both types of stimuli. When changing the direction of gaze, the monitor screen was rotated in order to maintain the viewing distance constant at 50 cm (Trotter and Celebrini, 1999). In the second experiment, multiunit recordings were performed in a third animal (monkey C) at regularly spaced intervals of 300 μm. We tested 5 gaze directions, which were adjusted for each recording site according to the retinal location of the RF, so as to bring the RF −10°, −5°, 0°, +5°, and +10° relative to the straight-ahead direction. By contrast with the first experiment, gaze directions were tested in an interleaved fashion, alleviating the need for a control of recording stability, but preventing a manual correction of screen orientation. Ten responses to the dynamic random dots (similar to those used in the first experiment) were collected for each direction of gaze.

Analysis

All the analyses were performed on both the raw activity and the net visual responses (obtained by subtracting the spontaneous activity). The level of spontaneous activity being low (on average 5.3 sp/s) and unaffected by the direction of gaze for a majority of single cells (>90%), analyses on the raw activity and net visual responses yielded qualitatively similar results. All the significant effects reported here with the net responses were also significant on the raw activity. However, subtracting the spontaneous activity remove a constant term to the level of activity measured for different gaze directions. Thus, quantitatively larger gaze-related modulations were obtained on the net visual responses.

In the first experiment, recording stability was assessed by a two-way ANOVA with visual conditions and stability between the initial and control gaze conditions as factors. Only cells showing no instability effect ($p > 0.05$) were kept for further analysis. On this basis, 18% of the recorded cells were discarded from the analysis. For the remaining cells, standard deviation (and 95% confidence interval) of the gain values computed between the initial

and control conditions was 0.06 (0.04–0.08). Since the standard deviation of the gain values between gaze directions was 0.32 (0.30–0.34), it appears that recording instability does not play a significant role in the gaze-related gain modulations recorded in the present study. Note that although all recorded responses (including those to nonoptimally oriented gratings and to dynamic random dots containing disparity) were used to assess the stability of the electrophysiological signal (n = 35 for dynamic random dots, n = 40 for gratings), only those to zero-disparity dynamic random-dots and/or optimally-oriented gratings (n = 5) were used to compute these gain values. However, similar results (not shown) were obtained when grouping the responses to all visual conditions, for both dynamic random dots and gratings.

At the level of each single- or multiunit recording site, the effect of gaze on the amplitude of the visual responses was assessed by a one-way ANOVA with response levels and gaze directions as dependant and independent variables respectively. Visual gain for the different gaze directions was computed by dividing the mean visual response for each gaze direction by the overall mean response across all the tested directions (this was done separately for dynamic random dots and for gratings when both were tested). At the population level, the strength of gaze effects was assessed (1) by the percentage of neurons showing significant gaze-related gain modulations, (2) by the median increase in activity level between the preferred and worst gaze direction, expressed as a percentage, and (3) by the standard deviation of the distributions of gain values. In all the statistical tests, significance threshold was set at $p < 0.05$.

SUPPLEMENTAL INFORMATION

Supplemental Information includes four figures and can be found with this article online at doi:10.1016/j.neuron.2010.03.014.

ACKNOWLEDGMENTS

We would like to thank Dr. Simon Thorpe for helpful comments and English proofing of an earlier version of this article. This work was supported by grants from the Centre National de la Recherche Scientifique (CNRS), the Human Frontier Science Program (HFSP), and the Fondation de France (B. Fouassier) (J.-B.D.).

Accepted: March 3, 2010
Published: April 14, 2010

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