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Neurons in Area V4 of the Macaque Translate Attended Visual Features into Behaviorally Relevant Categories

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SUMMARY

Neural processing at most stages of the primate visual system is modulated by selective attention, such that behaviorally relevant information is emphasized at the expenses of irrelevant, potentially distracting information. The form of attention best understood at the cellular level is when stimuli at a given location in the visual field must be selected (space-based attention). In contrast, fewer single-unit recording studies have so far explored the cellular mechanisms of attention operating on individual stimulus features, specifically when one feature (e.g., color) of an object must guide behavioral responses while a second feature (e.g., shape) of the same object is potentially interfering and therefore must be ignored. Here we show that activity of neurons in macaque area V4 can underlie the selection of elemental object features and their "translation" into a categorical format that can directly contribute to the control of the animal's behavior.

INTRODUCTION

Performing a visual task requires that the brain select relevant information from the scene for privileged perceptual analysis and ultimately use this information to control behavior (Desimone and Duncan, 1995; Maunsell and Cook, 2002; Reynolds and Chelazzi, 2004). A separate decision stage, linking sensory-perceptual to motor processes, is also implicated (Glimcher, 2003; Gold and Shadlen, 2001; Schall, 2003). Current views assign analysis of the visual input to different neural substrates from those responsible for decision mechanisms and motor control (Glimcher, 2003; Gold and Shadlen, 2001; Schall, 2003), although some evidence suggests at least partial anatomical overlap between perceptual and decision mechanisms (e.g., Dodd et al., 2001). Visual area V4 in the primate brain is no exception to this principle of segregation. From its original discovery (Zeki, 1971), area V4 has been associated with the encoding of stimulus hue (Schein and Desimone, 1990; Zeki, 1980), orientation, length, width, spatial frequency, texture (Desimone and Schein, 1987), and, more recently, contour shape (Pasupathy and Connor, 2001), surface slant (Hinkle and Connor, 2002), and binocular disparity (Hinkle and Connor, 2005)—the general notion being that area V4 is part of the neural machinery underlying visual object recognition.

In addition, over 20 years of research have demonstrated that responses of V4 neurons to a receptive field (RF) stimulus are gated by selective attention, so that attended stimuli will elicit greater responses and will exert greater control on the cells' firing, compared to unattended stimuli (Maunsell and Cook, 2002; Reynolds and Chelazzi, 2004). These effects have been observed with a variety of paradigms, including ones in which the animal is cued to attend to stimuli at a single visual field location (Connor et al., 1997; Luck et al., 1997; McAdams and Maunsell, 2000; Moran and Desimone, 1985; Motter, 1993; Reynolds et al., 1999) or else is cued to search for a target object defined by its feature composition and presented anywhere in the field (Bichot et al., 2005; Chelazzi et al., 2001). In contrast, few studies so far have tested whether neurons in area V4 are also modulated by selective attention to individual object features.

Two forms of feature-based attention have been distinguished. In one form, feature information guides selection of *whole* objects, for instance when an observer selects one or multiple items in an array whose color matches a predefined value, e.g., the red items (Saenz et al., 2003; Wolfe et al., 1989). Using paradigms of this sort, it has been shown that objects in the visual field characterized by a relevant feature value (e.g., the red ones) are preferentially encoded by neurons in macaque area V4

(Bichot et al., 2005; Motter, 1994). A different form of feature-selective processing is engaged any time an observer is to attend to one feature of an object, such as its color, while ignoring other features of the same object, such as its shape and texture (Fanini et al., 2006; Nobre et al., 2006). The ability to let a specific object feature guide behavior while other features of the object are disregarded is essential in many real-life situations and is also tapped by several cognitive tests, including the Stroop task (Stroop, 1935) and the Wisconsin card-sorting task (Milner, 1963). To our knowledge, the cellular correlates of the latter form of feature-selective attention have been investigated in only two prior studies of V4 neurons (Maunsell and Hochstein, 1991; McClurkin and Optican, 1996), and the results were only preliminary (Maunsell and Hochstein, 1991) or mostly negative (McClurkin and Optican, 1996). The main goal of these studies was to test whether the tuning properties of V4 neurons for a given stimulus feature would change depending on its relevance for the current task. In particular, V4 neurons might become more sharply tuned for the property of the stimulus that is to be discriminated, compared to when the same property is irrelevant. In the present study, we have reinvestigated this possibility by recording the responses of area V4 neurons in two macague monkeys while the animals performed a task specifically designed to tap feature-selective processing.

We accomplished this by training the animals to discriminate either the color or the orientation of a bar stimulus presented inside the RF of the recorded neuron, while maintaining central fixation. Four colors and four orientations were used, resulting in 16 total stimuli (Figure 1A). Two colors and two orientations were associated to one behavioral response-the turning of a response lever to the right-while the remaining two colors and two orientations were associated to the alternative response-the turning of the lever to the left. Given these associations. half of the stimuli were defined as "congruent," since both their constituent features required the same response, while the remaining half of the stimuli were defined as "incongruent," since their two constituent features required opposite and conflicting responses (Figure 1A). Incongruent stimuli were critical to ensure that the animal would have to select one feature or the other to produce the correct behavioral response. In addition, they gave us the opportunity to dissociate neural activity due to the stimulus itself from neural activity related to the behavioral response, since the same incongruent stimulus required opposite responses depending on the task being performed. Prior to any RF stimulus, a cue was presented at the center of gaze (either a circle or a triangle, respectively), indicating that the stimulus color or orientation was relevant in the current trial, followed by a delay interval (Figure 1B).

RESULTS

Table 1 summarizes behavioral performance of the two monkeys. After excluding trials in which central fixation



Figure 1. Visual Stimuli, Behavioral Tasks, and Location of Recording Sites

(A) The stimuli used in the experiment consisted of all combinations of four orientations and four colors. The bars were 0.4° wide and 2.0° long. CIE x and y coordinates were 0.598 and 0.349 for red, 0.152 and 0.079 for blue, 0.285 and 0.586 for green, 0.430 and 0.476 for yellow. Colors were matched for luminance (10.64 cd/m²). Stimuli were presented against a dark background (CIE x and y coordinates were 0.285 and 0.330, respectively; luminance was 0.66 cd/m²). The behavioral response required for each feature value is indicated with "RIGHT" and "LEFT." Shaded cells correspond to incongruent stimuli, unshaded ones to congruent stimuli.

(B) Task sequence for a representative trial in the Orientation task. In the Color task, the cue was represented by a circle. FP is the fixation point; RF indicates the classical receptive field. In the final stimulus display, the task-relevant bar is surrounded by a crown of distracting bars, whose purpose was to increase difficulty of the task.

(C) Location where recordings were obtained in the two monkeys (shaded region), based on MRI scans. All recording sites lie in dorsal area V4. STs, superior temporal sulcus; Ls, lunate sulcus; IOs, inferior occipital sulcus.

was not maintained (38.3%), percentage of correct responses was high in both animals, indicating that they were able to respond only on the basis of the relevant stimulus feature. However, accuracy was reliably higher in response to congruent rather than incongruent stimuli, indicating that the irrelevant feature of incongruent stimuli caused some interference. This was confirmed by faster reaction times (RTs) for congruent than incongruent stimuli in both animals. Finally, overall RTs were much shorter in monkey "F" than monkey "B," and overall accuracy was higher in monkey "B" than monkey "F."

Table 1. Behavioral Performance of the Two Monkeys during the Recording Sessions					
		MONKEY "B"		MONKEY "F"	
		Accuracy (%)	RT (ms)	Accuracy (%)	RT (ms)
Color TASK	Congruent	98.87	692.3	89.53	456.2
	Incongruent	84.93	848.5	78.11	480.4
	p	<0.001	<0.001	<0.001	<0.001
Orientation TASK	Congruent	98.77	687.5	93.54	427.3
	Incongruent	83.48	813.6	79.72	446.0
	p	<0.001	<0.001	<0.001	<0.001

Average accuracy and reaction time (RT) are reported separately for the color and the orientation discrimination tasks and for the congruent and incongruent stimuli. Differences in accuracy and in RT between congruent and incongruent stimuli were evaluated by means of paired t-tests.

A total of 185 individual neurons were recorded from two hemispheres in the two animals (116 and 69 neurons from monkey "B" and "F," respectively). Of these, 152 (90 and 62 cells from monkey "B" and "F," respectively) were classified as visually responsive, as they gave significant responses to at least one of the 16 stimuli, based on a paired t test comparing baseline activity with activity during a visual response epoch (p < 0.05, Bonferroni corrected). The latter covered between 50 and 200 ms after stimulus onset, and the baseline epoch covered 150 ms just prior to stimulus onset. These visually responsive cells will be the focus of the present report.

Recordings were all obtained from dorsal area V4 on the exposed surface of the prelunate gyrus (Figure 1C). Location and size of the RFs were compatible with known topography of dorsal area V4. RFs were $4^{\circ}-8^{\circ}$ of visual angle in size, and they were centered at $4^{\circ}-8^{\circ}$ of eccentricity. In the following sections, only spiking data from correctly performed trials will be considered, unless otherwise stated.

The task allowed us to compare neural responses to identical RF stimuli when color versus orientation was the relevant feature. Figure 2A illustrates the activity of an example cell whose responses were modulated by feature-selective attention. Raster plots and spike-density plots are shown for two representative stimuli, along with the average spike-density plot computed across all 16 stimuli. Responses of this cell were enhanced during color versus orientation discrimination, and the effect was similar across all 16 stimuli. For this cell, the modulation began 100–120 ms post-stimulus onset.

To explore effects of feature-selective attention across the neural population, for each cell we performed an analysis of variance (ANOVA) with stimulus color (4), stimulus orientation (4), and task (2) as the main factors. The time window over which we computed average firing rates for this analysis (150–500 ms post-stimulus onset for cells from monkey "B," and 100–300 ms post-stimulus onset for cells from monkey "F") was adjusted separately for each animal in order to cover until the behavioral response (500 ms and 300 ms were roughly the shortest RT in monkey "B" and "F," respectively) and to exclude at least part of the transient response to the stimulus onset, which usually was not modulated by the task.

The results of this analysis showed that across animals 136 neurons (89.5%) were significantly (p < 0.05) selective for the stimulus orientation, while 95 (62.5%) were selective for the stimulus color. In 60 cases (39.5%), selectivity for the two stimulus attributes interacted significantly with one another. Of major relevance, 42 neurons (27.6%) showed a main effect of task. Of these, 23 had overall higher firing rates in the color versus orientation task, while the remaining 19 cells displayed the opposite pattern. In addition, other neurons showed a significant two-way interaction between task and stimulus color (10, or 6.6%), between task and stimulus orientation (13, or 8.6%), or finally both between task and stimulus color and between task and stimulus orientation (5, or 3.3%). Six neurons (3.9%) showed a significant triple interaction. Overall, 50.0% of the recorded neurons were thus reliably modulated by the task being performed, and the incidence of task-dependent effects was highly similar between animals (Figure 2B). To explore the time course of taskdependent modulations, we performed the same ANOVA on firing rates computed in a sliding 100 ms time window (50 ms overlap) spanning roughly the entire interval between stimulus onset and behavioral response in each animal (Figure 2B). Whereas significant main effects of task occurred with a similar frequency throughout the interval, the incidence of significant interactions between task and one or the other stimulus attribute, or both, increased considerably toward the end of the trial in each animal. The functional implication of this late increase in the rate of significant interactions involving the task factor will be unveiled in later sections.

Figure 2C shows population average spike-density plots comparing responses to the various feature values during the task yielding the higher versus lower firing rates. Only cells with a significant main effect of task (n = 42) were included. The plots indicate that the modulatory effect of feature selection was similar for all feature values and that it started some time after the latency of the visual



Figure 2. Task-Dependent Modulation of Visual Responses

(A) Responses of an example cell to two individual stimuli (left and middle panel), and the response of the same cell averaged across all 16 stimuli (right panel), are compared between the two tasks. Firing rates are plotted as spike-density functions (Gaussian kernel width 50 ms). Only correct trials were included. For the two single stimuli, neural activity is also illustrated with raster displays. Each row in the raster corresponds to an individual trial. Vertical tick-marks indicate single spikes. Blue and red rasters illustrate neural discharges during the orientation and the color task, respectively. (B) Incidence of cells significantly (p < 0.05) modulated by the task, according to a series of ANOVAs on average firing rates computed over a 100 ms sliding window roughly covering until the behavioral response in the two animals. Significant main effects of task (black) and significant interactions involving the factor task (pale gray), as well as their co-occurrence (dark gray), are shown. The panel also reports the percentage of significantly task-modulated cells resulting from a single ANOVA on firing rates computed over a larger time window in the two monkeys (see text for details).

response. A time-series statistical analysis of the population average responses (Figure 2C) revealed that activity in the two tasks started to diverge 100–150 ms poststimulus onset. Across the population, the average percent change in firing rate in the preferred versus nonpreferred task was 21% \pm 6.0% (SE).

Changes in activity related to the task were also explored in the time interval before RF stimulus onset. To this aim, we used a t test comparing activity of individual cells in the 250 ms before RF stimulus onset in color versus orientation discrimination trials. The analysis revealed that a significant task-related difference in pre-stimulus activity was present in 27 out of 152 cells (17.8%), with 11 of them showing greater activity in color discrimination trials and the remaining 16 cells showing the opposite pattern. For 11/27 cells in this group, the task preference in the pre-stimulus epoch was significantly maintained during the subsequent visual response epoch, while for 4/ 27 additional cells there was a significant but opposite task preference during the visual response epoch. Finally, 12/27 cells were not significantly modulated by the task during the visual response epoch. Across the 27 neurons, the average difference in firing rate between the preferred and nonpreferred task was 1.52 spikes/s (±0.28 SE, or 26.15% ± 2.92% SE). Further analyses demonstrated that these task-dependent changes in delay activity did not reflect persisting responses to the cues (see Supplemental Data Section 1, available online).

Having established that activity of many cells was modulated by the task being performed, we tested the obvious possibility that feature-selective attention might change neural selectivity for the stimulus features. In particular, one might predict that selectivity for color would increase during the color task and, conversely, that selectivity for orientation would increase during the orientation task. To estimate the degree of neural selectivity for color and orientation as a function of task, we computed the amount of mutual information for each stimulus feature transmitted in the firing pattern of neurons in the population, separately for each task. First, we computed transmitted information in the same time epochs as for the previous ANOVAs (150-500 ms post-stimulus onset for monkey "B" and 100-300 ms post-stimulus onset for monkey "F"). Results of this analysis showed that both across the entire population of recorded cells (n = 152) and across the subpopulation of cells significantly modulated by the task (n = 76), selectivity for neither stimulus feature was reliably modified depending on which feature was to be discriminated. For example, the cells significantly modulated by task (n = 76) did not become more selective for the stimulus color during the color task (average information

per cell for stimulus color, 0.072 bits \pm 0.01, SE) compared to the orientation task (0.077 bits \pm 0.02, SE, p = 0.40). Similarly, the same cells did not become more selective for the stimulus orientation during the orientation task (average information per cell for stimulus orientation, 0.2 bits \pm 0.03, SE) compared to the color task (0.177 bits \pm 0.02, SE, p = 0.21). On average, the same cells conveyed more information about the orientation than the color of the stimuli (p < 0.001). Thus, it appears that feature-selective attention did not produce consistent changes in tuning across the population of V4 cells, in agreement with prior reports (Maunsell and Hochstein, 1991; McClurkin and Optican, 1996; see Supplemental Data Section 2).

Given that the need to engage feature-selective attention may be greater for incongruent than congruent stimuli, as only incongruent stimuli force selection of the relevant feature, in subsequent analyses we tested whether effects of feature-selective attention might differ between incongruent and congruent stimuli. Moreover, since the need to counteract potential response conflict in the case of an incongruent stimulus must arise some time after stimulus onset (after each feature is mapped onto the corresponding behavioral response), it might be that effects of feature-selective attention become more robust in a time epoch approaching the behavioral response. Two series of two-way ANOVAs on the activity of individual cells were thus performed on successive 100 ms time epochs, one for congruent and one for incongruent stimuli. One factor in the ANOVA was the stimulus (the eight congruent or eight incongruent stimuli), and the other factor was task (Color versus Orientation). Here we will report the results obtained in an early versus a late time window. While the early time window (50-150 ms post-stimulus onset) was the same for both animals, the late time window was tailored separately for each animal, since average RT was much shorter in monkey "F" than monkey "B"; it covered between 400 and 500 ms after stimulus onset in monkey "B" and between 200 and 300 ms after stimulus onset in monkey "F."

In line with our predictions, different results were obtained for congruent and incongruent stimuli. For congruent stimuli, the results were similar between early and late epochs after stimulus onset. In the early epoch, 105 (69.1%) cells responded differently depending on the stimulus, and 19 (12.5%) cells were significantly modulated by the task, with 13 (8.5%) cells showing a significant interaction. In the late epoch, 112 (73.7%) cells were significantly selective for the stimulus and the activity of 21 (13.8%) cells was significantly modulated by the task, with 8 (5.3%) cells showing a significant interaction. In

⁽C) Population average (n = 42) spike-density plots comparing neural responses during the task yielding the higher versus lower firing rates (Gaussian kernel width 50 ms). Each plot shows the response to an individual feature value (colors above, orientations below), from most preferred to least preferred. Task preference was determined in the time windows 150–500 ms and 100–300 ms post-stimulus onset, respectively, for monkey "B" and "F." Only neurons with a significant main effect of task were included. For each feature value, a paired t test was used to determine when the population average response differed significantly between the two tasks (50 ms bins). t values are plotted below each graph. The dotted horizontal line indicates the threshold value of t where differences become statistically significant (p = 0.05).



Figure 3. V4 Neurons Encode the Behavioral Response Associated to the Relevant Feature of the (Incongruent) Stimulus in a Time Epoch Approaching the Behavioral Response

(A) Example neuron whose activity modulates according to the impending behavioral response. For each of the eight incongruent stimuli, the firing rate during one task and the other is averaged across 16 correct trials and is represented as the spike-density function (Gaussian kernel width 50 ms).

(B) Mean firing rates of the neuron shown in (A) computed in the 100 ms time window preceding the behavioral response for each of the eight incongruent stimuli, separately during the color and the orientation discrimination task. Error bars are ± 1 SE.

contrast, for incongruent stimuli, results differed considerably between early and late epochs. In the early epoch, 91 (59.9%) cells responded differently depending on the stimulus, and 19 (12.5%) cells were significantly modulated by the task, with 6 (3.9%) cells showing a significant interaction. In the late epoch, a similar number of cells (109, or 71.7%) was significantly selective for the stimulus, and a similar number of cells (20, or 13.2%) showed a significant main effect of task. However, there was 6-fold increase in the number of significant interactions in the late epoch (38, or 25.0%) compared to the early one. It thus appears that effects of feature-selective attention were more prominent in the case of incongruent stimuli, especially in a late phase after stimulus onset, and they predominantly took the form of significant interactions between stimulus and task. In the remainder of the Results, we will concentrate on the changes in neural activity following incongruent stimuli. The nature of these changes is revealed in Figures 3 and 4.

Responses of an example neuron to the eight incongruent stimuli during the color versus orientation discrimination task are shown in Figure 3A. Graphs in the upper row illustrate responses to the four stimuli that required a right turning of the response lever during the color task and a left turning of the lever during the orientation task, while graphs in the lower row illustrate responses to the four stimuli for which the opposite response assignment applied. As noted previously, modulation of activity depending on task was negligible during the initial response to the stimulus, whereas activity after this transient peak was robustly modulated. Specifically, in a late phase after stimulus onset, activity was higher during the color task for all stimuli shown in the top panels of Figure 3A and during the orientation task for all stimuli shown in the bottom panels. Activity of this example neuron thus clarifies the nature of the significant interaction between (incongruent) stimuli and task. In this epoch, the neuron appears to modulate depending on the required behavioral response, in that activity is higher for all conditions in which the animal is about to deliver a right versus left lever response. Figure 3B further illustrates this result by showing the average firing rate of the same neuron in response to the eight incongruent stimuli computed in a 100 ms time window preceding the behavioral response in each trial, separately for the two tasks. The neuron displays a clear preference for all stimulus-task combinations requiring a right turning of the response lever.

In order to directly test whether the activity of V4 neurons may be modulated by the alternative behavioral response that is being planned, we performed an ANOVA on individual cells with stimulus (the eight incongruent stimuli) and response category (two, left or right) as the main factors. Thus, here we disregarded whether a specific combination between stimulus and response category pertained to one or the other task. Like for the previous ANOVAs, we performed this analysis on data from early versus late epochs following stimulus onset. While the early epoch covered between 50 and 150 ms post-stimulus onset for all cells, the late 100 ms epoch was tailored separately for each cell, so that it would terminate at the minimum RT recorded during the corresponding experimental session (excluding trials with congruent stimuli). On average, across cells from monkey "B," the late window spanned between 471 and 571 ms after stimulus onset, while it spanned between 231 and 331 ms after stimulus onset across cells recorded in monkey "F." In the early epoch, only 7 cells (4.6%) showed a significant main effect of response category, while for 9 more cells (5.9%) there was a significant interaction between stimulus and response category (94 cells, or 61.8%, showed a main effect of the stimulus). In contrast, in the late epoch, the number of cells reliably modulated by response category increased to 44 (28.9%), with 11 more cells (7.2%) showing a significant interaction (108 cells, or 71.1%, showed a main effect of the stimulus). Among the cells with a significant effect of response category in the late epoch (n = 44), 25 showed a preference for the right response, while 19 cells showed the opposite preference. Importantly, we did not fully rely on analyses time-locked to the behavioral response on a trial-by-trial basis, since in both monkeys average RT differed between right and left responses (left responses being faster than right responses by an average of 70 ms in monkey "B" and 32 ms in Monkey "F"), although results obtained with this approach were highly consistent with what is reported above.

To quantify the magnitude of the effect across the population of neurons significantly modulated by response category in the late epoch (n = 44), for each cell we computed an index of normalized preference for response category. The index had the form:

Response Category Index (RCI) = (PR - NP)/(PR + NP), where PR and NP represent the average activity in trials requiring, respectively, the preferred and the nonpreferred response.

The index can take a value between zero, corresponding to no preference for one or the other response category, and one, indicating an "all-or-none" preference for one category over the other. The average RCI across the 44 neurons was 0.25 (\pm 0.02, SE), corresponding to a 35.5% change in response (\pm 2.38, SE). In comparison, the average index value across the same cells in the early epoch (50–150 ms after stimulus onset) was 0.10 (\pm 0.01, SE), corresponding to a 16.63% change (\pm 1.1, SE), and the difference between epochs was highly significant (p < 0.001).

Figure 4A illustrates the population average activity of cells significantly modulated by response category, separately for the two animals. Responses to the eight incongruent stimuli were averaged together. A time-series analysis of the difference in activity between preferred and nonpreferred response trials across the cell population revealed that the two conditions started to diverge around 225–250 ms post-stimulus onset in monkey "B" and around 200–225 ms post-stimulus onset in monkey "F." Careful analyses ruled out the possibility that the above modulation might be due to small but consistent differences in eye position across conditions (see Supplemental Data Section 3).

In order to provide an alternative measure of the ability of the same neurons to discriminate between competing behavioral responses, we next performed a Receiver Operating Characteristics (ROC) analysis of firing rates from trials with a right versus left motor response, separately in the early and late time windows (Dayan and Abbott, 2001). Results from this approach for an example neuron are illustrated in Figure 4B, while results for the 44 neurons significantly modulated by response category are illustrated in Figure 4C. Across the population, the average choice probability in the early epoch was 0.53 ± 0.003 (SE), while in the late epoch this value rose to $0.59 \pm$ 0.008 (SE), a highly significant difference (p < 0.001).

It appears from previous analyses that, while neural activity in an early-to-intermediate phase after RF stimulus onset mainly encoded the features of the stimulus (see Supplemental Data Section 2) and was often modulated by the task being performed, activity in a later phase tended to also encode the behavioral response associated to the relevant feature of the stimulus. To provide more direct support for this notion, we assessed changes over time in the amount of information for the response category transmitted by the neurons that were significantly modulated by this variable (n = 44). Figure 4D illustrates the results, separately for the two animals. As shown in the graph, information for the response category was virtually null until well after stimulus onset and then increased substantially in the time period preceding the behavioral response. Interestingly, the rate of rise was similar in the two animals, except that in monkey "F" the rise of information for response category was truncated much sooner than in monkey "B," reflecting shorter RTs in monkey "F" than monkey "B" and perhaps also accounting for higher error rates in monkey "F" relative to monkey "B" (see Table 1). For comparison, the same figure shows the time course of the average choice probability for the behavioral response estimated across the same group of neurons, separately for the two monkeys. As shown, remarkably similar time courses were obtained with the two approaches. Finally, Figure 4E illustrates the time course of transmitted information for the stimulus color and orientation, computed across the same cells. Direct comparison of panels D and E shows that, although these neurons retained their selectivity for the stimulus features in a late phase following stimulus onset, in the same phase they displayed increasing selectivity for the impending motor response. This conclusion was further supported by a multiple linear regression analysis (Kleinbaum et al., 1988; Takeda et al., 2005; see Supplemental Data Section 4). In summary, the above results suggest that a large fraction of neurons in area V4 may participate in the process by which the relevant feature of the current stimulus is converted into the required motor response.

If this neural effect were indeed related to the mechanisms that allow the animal to select one or the other of

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Figure 4. Encoding of the Behavioral Response Category Associated to the Relevant Feature of the (Incongruent) Stimulus at the Population Level

(A) Population average spike-density plots comparing activity elicited by the eight incongruent stimuli when the preferred versus nonpreferred behavioral response for each individual neuron was required (Gaussian kernel width 25 ms). Plots on the left show average activity across 29 cells recorded in monkey "B," which were significantly modulated by response category. Plots on the right show the same for the 15 cells significantly modulated by response category in monkey "F." A paired t test was used to determine when firing rates were significantly modulated according to the behavioral response (25 ms bins).

(B) Results of the ROC analysis for an example neuron showing robust selectivity for the behavioral response only late after stimulus onset (choice probability for this neuron was 0.53 in the early epoch and 0.75 in the late epoch).

(C) Scatter plot comparing the choice probability for the behavioral response between an early versus late time epoch after stimulus onset for each of the 44 neurons significantly modulated by response category.

(D) Time course of transmitted information (black) and choice probability (gray) for the behavioral response, computed from trials with an incongruent stimulus, across the population of cells significantly modulated by response category in monkey "B" (solid line; n = 29) and monkey "F" (dotted line; n = 15). Firing rates were measured in overlapping 100 ms time windows. Data points are plotted at the center of the corresponding time window. See Experimental Procedures for details.

(E) Time course of transmitted information for the color and the orientation of the stimulus,

computed across the same neurons as in (D). Firing rates were measured in overlapping 100 ms time windows. Data points are plotted at the center of the corresponding time window. Notice that, while information for the motor response was computed only from trials with an incongruent stimulus, information for the stimulus color and orientation was computed from trials with either a congruent or an incongruent stimulus. In (D) and (E), error bars represent one SE.

the two alternative behavioral responses, one would expect that its time of occurrence be linked to the RT of the animal on a trial-by-trial basis. To test this, for each individual neuron, we first subdivided the total trials collected in any given condition (e.g., trials in which a red horizontal bar was presented and the animal had to discriminate its color) into three equal groups: one comprising the 1/3 of the trials with the faster RTs, one comprising the 1/3 of the trials with the slower RTs, and finally one comprising the 1/3 of the trials with intermediate RTs. Then we assessed the time at which neurons would start to encode the response category, separately for the fast and slow trials (the intermediate group was excluded for this analysis). Figure 5A compares the activity of an example neuron significantly modulated by response category during fast versus slow trials. During fast trials (average RT = 620 ms), activity of the neuron began to diverge significantly as a function of the impending behavioral response already at 150–200 ms poststimulus, while divergence occurred only at 450–500 ms poststimulus during slow trials (average RT = 756 ms).

Across all sessions in which cells with a significant main effect of the behavioral response were recorded (n = 44), this resulted in one group of "fast" trials with an average RT of 539 ms for monkey "B" and an average RT of 309 ms for monkey "F," and one group of "slow" trials with an average RT of 711 ms for monkey "B" and an average RT of 393 ms for monkey "F" (again, the 1/3 of the trials with intermediate RTs were excluded). The corresponding population spike-density plots averaged across all incongruent stimuli are shown in Figure 5B. A time-series analysis of the difference between the activity in the preferred versus nonpreferred response trials showed that in the case of fast trials the difference became first significant 250–300 ms post-stimulus onset in monkey "F," while in



Figure 5. Comparing the Time Course of the Response-Related Effect between Trials with Relatively Short versus Long RTs

For this analysis, trials were sorted according to the required behavioral response and by reaction time. For each individual incongruent stimulus, two groups of trials were created: one comprising the 1/3 of the total trials with the shortest reaction times and one comprising the 1/3 of the total trials with the longest reaction times. Neuronal activity is represented by spike-density functions (Gaussian kernel width 50 ms). A paired t test was used to assess the time at which neural activity differentiates significantly between alternative response categories (50 ms bins).

(A) Discharges of an example neuron during trials when a right versus left behavioral response was required, separately for the fast (left panel) and slow (right panel) third of the trials.

(B) Panels in the top row show population average spike-density plots of the activity elicited by incongruent stimuli computed across those cells recorded in monkey "B" significantly modulated by response category, separately for the fast (left panel) and slow (right panel) third of the trials. In the bottom row, the same population average spike-density plots are shown for cells recorded in monkey "F," which were significantly modulated by response category.

the case of slow trials it became first significant only 350– 400 ms post-stimulus onset in monkey "B" and 250–300 ms post-stimulus onset in monkey "F." Interestingly, the difference in the time of onset of these neural effects between fast and slow trials (100 ms and 50 ms, respectively, in the two animals) parallels rather closely the difference in average RT between slow and fast trials (172 ms and 84 ms, respectively, in the two animals).

These results were confirmed at the single-cell level. For each cell, we performed two separate ANOVAs comparing firing rates in the preferred versus nonpreferred response trials: a first ANOVA on data from the one-half of the total trials with slower behavioral responses and a second ANOVA on data from the one-half of the total trials with faster behavioral responses (dividing the total trials into three equal groups would have reduced too much the statistical power of this analysis). When the analysis was performed on the 100 ms epoch terminating with the minimum RT for the fast trials (on average, between 471 and 571 ms poststimulus in monkey "B" and between 231 and 331 ms poststimulus in monkey "F"), only 20 cells (13.2%) showed a significant effect of response category in the slow trials, whereas this number rose to 37 (24.3%) in the fast trials, i.e., trials in which firing rates were computed during an epoch closer in time to the behavioral response. However, when data from slow trials were analyzed using firing rates in a 100 ms time window terminating with the minimum RT in these trials (on average, between 601 and 701 ms poststimulus in monkey "B" and between 309 and 409 ms poststimulus in monkey "F"), then 38 cells (25.0%) reliably encoded the response category.

To further assess whether these effects are related to behavioral performance, we also analyzed neural activity

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Figure 6. Comparison between Correct and Error Trials

In the top row, population average spikedensity plots (Gaussian kernel width 50 ms) comparing the response-related effect between correct (left panel) and error trials (right panel) across cells (n = 29) significantly modulated by response category in monkey "B." Trials were selected in such a way that both the number of trials and the stimuli were equally represented across the two panels. Each curve represents the neuronal activity averaged across 253 trials. In the case of error trials, preferred and nonpreferred response trials were defined based on the preference expressed during correct trials. A paired t test was used to assess the time at which neural activity differentiates significantly between alternative response categories (50 ms bins). In the bottom row, population average spike-density plots are shown for cells (n = 15) significantly modulated by response category in monkey "F." Each curve represents neuronal activity averaged across 229 trials.

recorded during error trials. Since the error rate in most recording sessions was low, it was not possible to perform statistical analyses on data from individual cells. However, we could construct population average spike-density plots of neural activity from error trials and then compare these plots to those similarly constructed from correct trials. Again at the population level, we could also compare the results of time-series statistical analyses (t tests) performed on error versus correct trials. As shown in Figure 6, separately for each animal, activity recorded during error trials did not show any sign of significant modulation as a function of response category during the late phase of the trial, unlike for correct trials. This indicates that the animals were more likely to make an error when neural activity in V4 failed to differentially encode the two response categories.

Interpreting results from error trials is problematic, however, since incorrect performance may originate for different reasons and at different processing levels. Therefore, the possibility remains that what we have described as response-related categorical representation of the attended stimulus feature could instead reflect the mere reverberation at the level of area V4 of a (pre)motor signal coding the direction of the impending lever response. In order to directly test this possibility, we have carried out a series of control experiments. In these experiments, we recorded the activity of 40 visually responsive neurons from 29 sessions in monkey "F" while the animal performed two new tasks, besides the standard one. In one task, while maintaining central fixation, the monkey had to detect the brief (500 ms duration) luminance increase or decrease of a gray square presented in the visual quadrant diametrically opposite the RF of the recorded neuron. Luminance increases and decreases required opposite lever responses. In the second task, while the animal had to detect luminance changes in the same manner as above, irrelevant visual stimuli were shown inside the RF of the neuron in order to provide visual drive to the neuron. For each unit, four stimuli were used, which were obtained by pairing two shapes (annulus and pentagon) with two colors (orange and cyan, or magenta and lime). The animal performed these new tasks with a good level of accuracy (81.5% on average).

In the standard task, 15 out of 40 cells (37.5%) showed reliably different firing rates related to the motor response following incongruent stimuli in a 200 ms time window preceding the motor response. In sharp contrast, in the luminance detection task without visual stimulation of the RF, only one cell (2.5%) showed a significant difference related to the motor response in the same time window, and similarly in the luminance detection task with visual stimulation only two cells (5.0%) showed such significant difference. Therefore, activity modulations in area V4 related to an impending motor response seem to occur only when the recorded neuron is directly engaged in the process of converting sensory evidence about taskrelevant stimulus features into a behavioral response code that can be used to control behavior. Further evidence supporting this claim was obtained by means of two additional control conditions in which the animal produced right and left lever responses at random (see Supplemental Data Section 5). Additional, detailed characterization of





Figure 7. Encoding the Behavioral Response Category in Trials with Congruent Stimuli

(A) Responses of an example cell to each of the eight congruent stimuli. Firing rates are represented as spike-density functions (Gaussian kernel width 50 ms). Only correct trials were included.

(B) Scatterplot showing the relationship between preference for one or the other behavioral response for incongruent versus congruent stimuli. Each dot represents an individual neuron. Only cells significantly modulated by response category following incongruent stimuli in the two monkeys were included (n = 44). The dashed line indicates the best-fitting linear regression through the data (slope = 0.38; intercept = 0.03; r = 0.33; p = 0.026).

(C) Pairs of congruent stimuli used to compute the within-category (pairs of stimuli inside each circle) and between-category (pairs of stimuli connected by each arrow) index of selectivity. (D) Scatter plot comparing the within-category and between-category index across the entire population of recorded cells (n = 152). Both index values were computed during a 100 ms time window preceding the behavioral response. The best-fitting regression line (dashed) is shown (slope = 0.58; intercept = 0.08; r = 0.677; p < 0.001). Numbers in italics at the top right of the plot indicate the number of points above and below the diagonal.

(E) Same as in (D) for index values computed in the time window 50–150 ms after stimulus onset. The best-fitting regression line (dashed) is shown (slope = 0.54; intercept = 0.06; r = 0.524; p < 0.001).

the response-related modulation of neuronal activity is provided in Supplemental Data Section 6.

As already emphasized, incongruent stimuli enabled us to explore the influence on V4 neurons' activity of factors related to the behavioral response, independently from the stimulus itself. In contrast, factors related to the stimulus features and to the behavioral response are confounded in the analysis of neuronal responses to congruent stimuli, since each congruent stimulus was always associated with the same behavioral response, regardless of task. It is nonetheless plausible that activity evoked by congruent stimuli was similarly modulated by response category.

Figure 7A illustrates the responses of an example neuron to each of the eight congruent stimuli. For this neuron,

and several others in the sample, responses elicited by the eight congruent stimuli appeared to "cluster" depending on the behavioral response associated to each stimulus. In the example, firing rates following the four congruent stimuli associated to a right behavioral response were consistently higher than firing rates following the four congruent stimuli associated to a left response. While this pattern might be indicative of a categorical representation of stimuli, it is equally plausible that the pattern was entirely due to feature selectivity per se and happened to match categorical boundaries by chance. In order to address these possibilities, we have followed several approaches.

First, for each of the 44 cells significantly modulated by response category in trials with an incongruent stimulus, we compared the preference for one versus the other

category between responses to incongruent and congruent stimuli. The 100 ms time window of the neural responses to congruent stimuli was adjusted for individual cells to terminate at the shortest RT in the corresponding session (on average, between 444 and 544 ms after stimulus onset in monkey "B," and between 230 and 330 ms after stimulus onset in monkey "F"). If the level of neural activity elicited by the two groups of congruent stimuli (those requiring a right lever response and those requiring a left lever response) were solely determined by the features of the stimuli, regardless of response category, then one would expect that the apparent preference for one or the other response category computed for congruent stimuli should be unrelated to that computed for incongruent stimuli. Figure 7B demonstrates that this was not the case. The graph is a scatter plot showing the relationship between preference of individual cells for one or the other category following congruent versus incongruent stimuli in a late time window preceding the behavioral response. As illustrated in the figure, the majority of cells in the sample (33/44, or 75.0%; p < 0.001, χ^2 test) displayed a consistent preference for response category following congruent and incongruent stimuli. A regression analysis on the preference for response category following the two types of stimuli revealed a significant correlation (slope = 0.38; intercept = 0.03; r = 0.33; p = 0.026;Figure 7B).

We also sought evidence for a categorical representation of congruent stimuli across the entire population of cells (n = 152). For each cell in the sample, we separately calculated a within-category (WC) and a between-category (BC) index of stimulus selectivity and then compared the resulting values across the population. The rationale for this analysis was that neurons encoding the behavioral response category ought to display, on average, greater selectivity for stimuli belonging to different response categories than for stimuli belonging to the same category. The general formula for computing the selectivity index was:

Selectivity Index (SI) = (RS1 - RS2)/(RS1 + RS2), where RS1 and RS2, respectively, represent responses to stimulus 1 and stimulus 2 in the pair.

The scheme in Figure 7C illustrates the stimulus pairs used to compute the WC and BC selectivity index on each cell (stimulus pairs confined within a circle, and stimulus pairs connected by an arrow, respectively). Four index values were computed for each type, which were next rectified and averaged. It is important to note that all selectivity index values were computed between stimuli differing both in color and orientation and that orthogonal orientations or complementary colors were never compared. Figures 7D and 7E illustrate the results of this analysis. In a 100 ms time epoch preceding the behavioral response (on average, between 441 and 541 ms poststimulus in monkey "B" and between 222 and 322 ms poststimulus in monkey "F"; Figure 7D), 92/152 neurons in the population (60.5%) were more selective for stimuli between- than within-category, and the average BC selectivity index calculated across the entire sample of neurons

(0.28 ± 0.02 SE) was significantly greater than the average WC index (0.24 ± 0.01 SE; p = 0.004) calculated across the same neurons. Results were different in an early time epoch between 50 and 150 ms post-stimulus onset (Figure 7E). In this epoch, 81/152 neurons in the population (53.3%) were more selective for stimuli between- than within-category, and the average selectivity index was not significantly different in the two cases (0.18 ± 0.01 SE versus 0.17 ± 0.01 SE, p = 0.12; see also Supplemental Data Section 7). Therefore, it appears that activity in trials with congruent as well as incongruent stimuli was similarly encoding which of the two response categories was required to perform the task.

DISCUSSION

In the present study, we have explored the cellular correlates of feature-selective attention in primate area V4 by using a behavioral paradigm specifically designed to engage selective processing of individual features. Onehalf of the recorded neurons were modulated by featureselective attention. Task-related modulations were mainly evident in the responses driven by RF stimuli, but some neurons varied their activity as a function of task already in the time period preceding RF stimulus onset. The latter effect presumably reflects a task-set signal instantiated by the cue stimulus shown at the start of the trial. These results are in general agreement with prior single-unit recording studies demonstrating an influence of featureselective attention on the visually driven responses of primate V4 neurons (Maunsell and Hochstein, 1991; McClurkin and Optican, 1996), except that changes in baseline activity depending on the task are reported here for the first time (to our knowledge). More generally, previous demonstrations of feature-selective modulation in area V4 (Maunsell and Hochstein, 1991; McClurkin and Optican, 1996), together with the present report, are in keeping with functional brain imaging studies in humans showing changes in activity in extrastriate visual cortical areas, including the putative homolog of area V4, depending on feature-selective attention (Chawla et al., 1999; Corbetta et al., 1991; Giesbrecht et al., 2003). In particular, our observation that feature-selective attention can affect the baseline firing of V4 neurons is consistent with similar effects reported in some prior imaging studies in humans (Chawla et al., 1999; Giesbrecht et al., 2003).

In further agreement with previous reports (Maunsell and Hochstein, 1991; McClurkin and Optican, 1996), we have shown here that, under our task conditions, tuning of V4 neurons for stimulus color and orientation was not modified in a consistent manner depending on the component feature to be discriminated in a given trial. Maunsell and Hochstein (1991) recorded the activity of V4 neurons in one monkey while the animal discriminated either the color or the orientation of grating stimuli presented inside the neurons' RF. For $\sim 1/3$ of the studied cells, the response to one or more color gratings was modulated depending on the attended stimulus feature. More

importantly, a few cells (n = 8) were tested with a complete set of 16 color gratings under both discrimination conditions to assess changes in tuning depending on the required discrimination. Across these cells, there was no evidence for systematic increase in color selectivity when the animal was attending color or in orientation selectivity when the animal was attending orientation. Similar conclusions were reached by McClurkin and Optican (1996), who also tested whether encoding properties of neurons in area V4 (as well as V1 and V2) might change in a taskdependent manner. In their study, monkeys had to make a saccade to a target stimulus in a three-stimulus array that matched a central sample either on the basis of pattern or color. Thus, only one feature of the peripheral stimuli was relevant to perform the task, while the other feature was irrelevant (but never conflicting). Information transmitted by V4 neurons for the color and the pattern of the stimuli was unchanged by whether target selection was based on one or the other feature of the target stimulus (similar results were obtained for the other two areas). However, similar to the study of Maunsell and Hochstein (1991), and to the present report, a relatively large fraction of recorded cells in each of the three areas ($\sim 25\%$ in area V4) was modulated by feature-selective attention. Thus, although our paradigm attempted to maximally engage feature-selective attention by rendering the irrelevant feature of the stimulus potentially interfering for response selection-which was not the case in the prior studieswe failed to reveal changes in neuronal tuning, just like previously reported (Maunsell and Hochstein, 1991; McClurkin and Optican, 1996). Although one may thus be tempted to conclude that the tuning properties of V4 neurons are immune to the influence of feature-selective attention, consistent changes in the tuning of V4 cells might occur under a task paradigm that stresses perceptual aspects of feature analysis (e.g., threshold discrimination of feature values).

In spite of no consistent changes in tuning, the demonstration that selective attention to the component features of a multidimensional object can alter the responses of V4 neurons to an otherwise identical RF stimulus strengthens the notion that cells in area V4 are sensitive to a variety of attentional signals, including forms of feature-based attention. Motter (1994) first demonstrated that V4 neurons produce enhanced responses to stimuli in the visual field matching a cued feature value, e.g., the red stimuli, thus effectively "highlighting" multiple potential targets in parallel across the entire scene (global feature-based attention). Compatible findings have been reported in subsequent studies of V4 neurons (Bichot et al., 2005), and analogous effects based on motion information have been documented in macaque area MT (Treue and Martinez Trujillo, 1999). These effects are different from those explored in the present study. Global feature-based attention allows the visual system to privilege processing of whole objects throughout the scene that match a predefined feature value (Bichot et al., 2005; Motter, 1994), while the feature-selective mechanisms explored in the present

study allow the visual system to privilege processing of one elemental feature of an object while concurrently filtering out other features of the same object (see Supplemental Data Section 8).

The entirely novel finding of this study is that \sim 1/3 of the V4 neurons in the sample encoded the behavioral response category associated with the attended stimulus feature. This effect was more straightforward to document for the incongruent than for the congruent stimuli in the set, and for this reason we mainly focused on data collected with the incongruent stimuli. Nonetheless, the evidence suggests that a similar response-related representation might take place for congruent stimuli as well. Remarkably, the categorical representation revealed here implies that, instead of becoming more finely tuned to the different feature values, V4 neurons tended to "cluster" feature values depending on the behavioral response to which they are associated.

Neural activity reflecting categorical representation of visual stimuli has been demonstrated in lateral prefrontal cortex (Freedman et al., 2002, 2003), parietal area LIP (Freedman and Assad, 2006), and the inferotemporal cortex (Freedman et al., 2003; Kreiman et al., 2000; Thomas et al., 2001), whereas this is the first description (to our knowledge) of a similar encoding property reflected in the activity of area V4 neurons. The categorical encoding of visual objects is thought to represent a fundamental step for the sake of visually guided cognition and action, as it attests the brain's ability to create representations of the visual input that are tailored to the task at hand (Miller et al., 2003). Area V4 neurons appear to contribute to this ability.

The categorical representation of the attended feature of incongruent stimuli was not evident from the beginning of the visual response to the RF stimulus; rather, it began around 200-250 ms after stimulus onset (this was over 300 ms before response time in monkey "B," and over 100 ms before response time in monkey "F"). Afterward, categorical information became progressively stronger approaching the time of the behavioral response. Interestingly, the amount of categorical information transmitted by neurons collected in the two monkeys at a time just preceding the behavioral response was higher in monkey "B" than monkey "F," and this may be related to the greater accuracy and longer RTs in monkey "B" than monkey "F"-a form of speed-accuracy trade-off. Thus it appears that response-related information began to be encoded at roughly the same time-and built-up with a similar time course - in the two animals, but its rise was truncated earlier in monkey "F," perhaps reflecting a lower criterion for response initiation (cf. Reddi et al., 2003).

There are at least two candidate interpretations of the delay with which categorical information following incongruent stimuli began to be encoded by V4 neurons in the present task, and they are not mutually exclusive. One interpretation relates to the nature of the incongruent stimuli. For these stimuli, the categorization process must have followed selection of the task-relevant feature. For this reason, it would be very informative to explore the time course of categorical representations in area V4 in the absence of this intermediate stage of processing, namely feature selection. The second interpretation relates to the possibility that categorical information was relayed to V4 neurons only after it was first encoded in other brain areas, e.g., inferotemporal and/or prefrontal cortex. Inferotemporal neurons have been reported to encode stimulus categories relatively early (~100 ms) after RF stimulus onset (Freedman et al., 2003), but in the context of a behavioral paradigm in which there was no feature-selection component.

A central question that we tackled was whether categorical information in V4 plays a role in task performance. Three lines of evidence favored a positive answer. First, by subdividing trials depending on the speed of the animal's behavioral response on a trial-by-trial basis, we demonstrated that V4 neurons began to encode the required response earlier in trials with short versus long RTs, suggesting a close link between the neural effects and the behavioral output. This view is also supported by the analysis of neural activity during error trials. Response-related information was completely abolished when the animal produced the wrong behavioral response, further suggesting that this information at the level of V4 correlates with the behavioral choice. Importantly, if the responserelated modulation reflected the mere reverberation of (pre)motor signals onto area V4, then one would predict a reverse pattern of activity in error trials relative to correct trials, but this was not observed. Third, and perhaps most crucially, response-related modulation of neuronal firing in a time window approaching the behavioral response was abolished under task conditions in which the recorded neuron was not directly involved in the process of converting sensory evidence presented within its RF into a code specifying the behavioral response. The latter evidence was gathered by means of control experiments in which the animal produced the same lever responses as in the standard task but to signal a luminance change presented outside the RF (or an auditory tone; see Supplemental Data Section 5), while task-irrelevant visual stimuli could be presented inside the neuron's RF. In the face of this evidence, a strictly motor interpretation of the responserelated modulation seems highly unlikely.

In conclusion, the present finding that V4 neurons are capable of encoding the behavioral category to which a stimulus (feature) is associated lends itself to two main interpretations. One interpretation is that V4 neurons directly participate in the process of converting the selected feature of the stimulus into a response-related format that can contribute to behavioral control. The second possibility is that categorical information is first encoded in other brain structures, likely including inferotemporal and prefrontal cortices, and is then fed back to area V4 neurons, perhaps to "shape" the ongoing perceptual analysis of stimulus features in a way that matches the behavioral valence of the features. Either way, these findings cast doubts on a firm distinction between brain areas concerned with perceptual analysis and brain areas concerned with decision making and behavioral control. Instead, the present observation that V4 neurons may play a role beyond visual analysis, effectively bridging between perceptual and motor domains, favors a view of brain function positing a continuous interplay among multiple stages along the chain linking sensation to action.

EXPERIMENTAL PROCEDURES

Surgical Techniques

Two adult male rhesus macaques weighing 9–10 kg were used. Before surgery, structural MRI images of the animals' brains were obtained with a 1.5T scanner, while the anesthetized monkeys were placed in a stereotaxic apparatus. The images (3 mm thick coronal slices) were used to guide placement of the recording chamber over dorsal area V4 on the exposed surface of the prelunate gyrus (Figure 1C). Under aseptic surgical conditions, the recording chamber, a head-hold-ing device, and a scleral eye coil for monitoring eye position (Robinson, 1963) were implanted while the monkeys were under general anesthesia (Domitor medetomidina, 1 mg/ml, Orion Pharma, Espoo, Finland). Antibiotics and analgesics were administered postoperatively. The skull remained intact during the initial surgery, and small holes (~3 mm in diameter) were later drilled within the recording chambers under ketamine anesthesia.

Electrophysiology

Recordings were obtained using tungsten microelectrodes (Frederick Haer & Co, Bowdoinham, ME, impedance ~1 M\Omega at 1 kHz) controlled by a hydraulic microdrive (Micropositioner model 650, Kopf Instruments, Tujunga, CA). Spikes were discriminated using an online spike-sorting system (SPS-8701, Signal Processing Systems, Prospect, Australia) and acquired for offline analysis at 1 kHz on a PC. In most cases, two neurons could be recorded simultaneously and differentiated on the basis of the size and shape of the spike waveform. After one or two responsive cells were isolated, we determined the RF borders (minimum response field method) and stimulus preferences of the neurons by moving and flashing colored bars on the screen under was made to select neurons that were visually responsive and selective for either color or orientation.

All procedures and animal care were conducted according to National Institutes of Health guidelines and were approved by the animal care and use committee of the Italian Ministry of Health.

Behavioral Task

Monkeys were first trained to discriminate among four colors and four orientations by using circular color patches and gray oriented bars, respectively. For one-half of the feature values, the animal was required to turn a response lever to the right, while for the other half it was required to turn the lever to the left (Figure 1A). Once these associations were learned (>90% correct), monkeys were trained to discriminate either the color or the orientation of one of 16 stimuli from a new stimulus set in which the two features were combined (Figure 1A). The task is diagrammed in Figure 1B. Each trial began with the presentation of a fixation target (white square, $0.4^{\circ} \times 0.4^{\circ}$) at the center of the display, a CRT computer monitor placed at a distance of 57 cm from the monkey's eves. Five hundred milliseconds after the animal acquired fixation, an instruction cue, either a gray triangle or circle $(1.3^{\circ} \times 1.3^{\circ})$, was presented at the center of gaze for 700 ms. A circle directed the attention of the monkey to the color of the stimulus, while a triangle directed attention to the stimulus orientation. After a delay of 1000-1200 ms, one bar from the set of 16 was selected at random and presented inside the RF of the neuron(s) under study. In order to earn a drop of juice, the monkey had a maximum of 4 s to respond by turning the response lever to the right or to the left according to the relevant stimulus feature (Figure 1A). For 8 out of 16 stimuli, the requested motor response was the same regardless of which feature was to be discriminated—congruent stimuli. The other half of the stimuli required opposite motor responses depending on the relevant feature—incongruent stimuli. In order to maximally engage attention to the relevant feature of the target stimulus, this was surrounded by a circular array of eight distracting bars varying in color and orientation (Figure 1B). If at any time during the trial the eyes deviated more than 1° from the fixation spot, the trial was aborted, and no reward was delivered. A complete recording session typically consisted of 512 correct trials. These were composed of 256 trials in which the monkey had to discriminate the stimulus orientation (16 repetitions for each stimulus).

Data Analysis

To explore task-related effects both at the single-cell and population level, ANOVAs and t tests were performed. An α level of p < 0.05 was used throughout to evaluate whether a statistical test was significant. Cells were assessed for visual responsiveness by conducting paired t tests on the response to each stimulus presented inside the RF in a time window from 50 to 200 ms post-stimulus onset, compared with the firing rate in a 150 ms prestimulus period. A cell was considered to be visually responsive if at least one of the 16 stimuli elicited an activity significantly greater than the corresponding baseline firing rate. Task effects were evaluated using a three-factor ANOVA with stimulus color (four), stimulus orientation (four), and task (two) as the main factors. This analysis was performed on average firing rates computed over a time window between 150 and 500 ms poststimulus for monkey "B" and between 100 and 300 ms poststimulus for monkey "F" (to accommodate for the different RTs between the two animals), as well as on average firing rates computed in a 100 ms sliding window (50 ms overlap) spanning the period between stimulus onset and behavioral response in each animal. Task effects for congruent and incongruent stimuli were also assessed by separate two-factor ANOVAs, with stimulus (the eight stimuli, either congruent or incongruent) and task (2) as the main factors, in both early and late 100 ms time windows. The effect of the behavioral response category required in a given trial was evaluated by performing a two-factor ANOVA, with stimulus (the eight incongruent stimuli) and response category (two, right or left) as the main factors, in both early and late 100 ms time windows. Attentional effects across a group of cells were also examined by constructing population average spike-density plots, with Gaussian kernel widths of 25 or 50 ms. Since it made no difference whether the population plots were averaged from actual firing rates or from responses normalized to the peak firing rate, all figures show the unnormalized responses so that absolute firing rates can be appreciated. Further analyses of the data were conducted using multiple linear regression (Kleinbaum et al., 1988; Takeda et al., 2005), the Receiver Operating Characteristics (ROC) approach (Dayan and Abbott, 2001), and information theoretic methods (Shannon, 1948; Shannon and Weaver, 1949; Panzeri and Treves, 1996; see Supplemental Data Section 9).

Supplemental Data

The Supplemental Data for this article can be found online at http://www.neuron.org/cgi/content/full/54/2/303/DC1/.

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