

Tadashi Ogawa · Hidehiko Komatsu

Neuronal dynamics of bottom-up and top-down processes in area V4 of macaque monkeys performing a visual search

Received: 30 September 2005 / Accepted: 9 January 2006 / Published online: 28 February 2006
© Springer-Verlag 2006

Abstract Visual selection is thought to be guided by both bottom-up intrinsic visual saliency and top-down visual attention. We examined how the relative importance of each of these processes dynamically changes over the course of a visual search in area V4 of two macaque monkeys. The animals were trained to perform a multidimensional visual search task in which a search array that consisted of two singleton stimuli, unique in shape and color, and four nonsingleton stimuli was presented. The task was to select one of the singletons as the saccade target, depending on the instructed search dimension, which was switched between shape and color. The strengths of the neural modulations caused by the bottom-up and top-down factors were, respectively, evaluated by assessing the dependence of the visual responses on the singleton type and the behavioral significance of the receptive field stimulus. We found that the initial visual responses of V4 neurons predominantly specified the singleton type of the receptive field stimulus, while the late presaccadic response primarily specified its behavioral significance. For comparison, recordings were also made from the frontal eye field (FEF) of one monkey and we found that the predominant activity of FEF neurons signaled the behavioral significance of the receptive field stimulus over time. These findings suggest that area V4 might function as an intermediate stage where both sensory- and behavior-based signals are dynamically represented, depending on their online requirements during a visual search, whereas the FEF predominantly represents behavior-based signals for upcoming saccade responses.

Keywords Attention · Dynamics · Visual search · Eye movement · Primate

Introduction

Evidence from psychophysical studies suggests that two basic mechanisms are involved in the control of attention for visual search (Yarbus 1967; Egeth and Yantis 1997). First, a bottom-up mechanism that occurs in a parallel manner across the entire visual field and is based on stimulus configuration highlights intrinsically conspicuous objects in a scene. A stimulus that is locally unique in any of the basic visual feature dimensions [i.e. a feature singleton] (Pashler 1988) tends to be salient and can be efficiently detected in a visual search (Treisman and Gelade 1980; Bergen and Julesz 1983; Nothdurft 1993). Second, a top-down mechanism based on the observer's knowledge and intention controls attention to a spatial location or to stimulus features for further visual processing (Posner et al. 1980; Folk et al. 1992). Recent psychophysical studies have provided evidence that these two processes have different temporal profiles during visual searches: the bottom-up influence emerges soon after presentation of a search array, but is overridden by top-down attentional influence later (Kim and Cave 1999; Lamy and Egeth 2003; van Zoest et al. 2004; see also Connor et al. 2004).

Extrastriate area V4 is thought to play a key role in visual search and attention. Influences of both bottom-up and top-down factors have been found. The activity of V4 neurons is selective for the feature contrast between stimuli (Desimone and Schein 1987; Schein and Desimone 1990), so it can identify the locations of the salient singleton stimuli in a visual scene in a bottom-up manner. Top-down attention specific to a spatial location or stimulus features can modulate the activity of V4 neurons (Moran and Desimone 1985; Haenny et al. 1988; Spitzer et al. 1988; Maunsell et al. 1991; Motter 1994; Connor et al. 1997; Luck et al. 1997; McAdams and Maunsell 1999; Reynolds et al.

T. Ogawa (✉) · H. Komatsu
National Institute for Physiological Sciences,
Okazaki, 444-8585, Aichi, Japan
E-mail: ogawat@nips.ac.jp
Tel.: +81-564-557864
Fax: +81-564-557865

T. Ogawa · H. Komatsu
The Graduate University for Advanced Studies (Sokendai),
Okazaki, 444-8585, Aichi, Japan

1999). Previous studies of visual searches in area V4 have demonstrated the response enhancement for the target stimulus over time (Chelazzi et al. 2001; Mazer and Gallant 2003), and a recent study reported that multiple top-down processes caused by feature- and space-based attention influence the activity of V4 neurons during a free-viewing search task (Bichot et al. 2005). In these studies, however, no salient singleton stimuli were presented in a search array; therefore, bottom-up influences were not explicitly examined. Although the top-down and bottom-up influences were separately detected previously (Ogawa and Komatsu 2004), the dynamic aspects of these two processes during a visual search were not studied.

In the present study, we tested whether the relative strengths of the bottom-up and top-down influences in the activity of V4 neurons are constant or change dynamically over the course of a visual search. We found that the dominant factor in neural modulations in area V4 dynamically changed from the bottom-up influences to the top-down influences. For comparison, we also examined the activity of the frontal eye field (FEF) neurons but we did not find this dynamic change in neural modulation. Our findings suggest that area V4 might function as an intermediate stage where both sensory- and behavior-based signals are dynamically represented depending on their online requirements, whereas the FEF predominantly represents behavior-based signals for upcoming saccade responses.

Materials and methods

Subjects and surgery

All procedures for animal care and the experimental protocols were in accordance with the National Institutes of Health Guide for the Care and Use of Laboratory Animals (1996) and were approved by the animal experimentation committee of the Okazaki National Research Institutes. Two monkeys (*Macaca fuscata*), each weighting 5.0–6.0 kg, were used in this study. Surgical procedures were conducted while the animal was under deep anesthesia (intravenous sodium pentobarbital). An eye coil, a head holder and two recording chambers were implanted using sterile techniques. Using magnetic resonance imaging (MRI) prior to surgery, the recording chambers were placed at the stereotaxic coordinates over the V4 and the FEF cortices.

Visual stimulus and behavioral tasks

Visual stimuli were generated by a video signal generator (VSG 2/3; Cambridge Research Systems, Cambridge, UK) and presented on a video monitor at 120 Hz in 800×600 resolution (GDM-2000TD; SONY, Japan), which was viewed binocularly from a distance of 65 cm in a dark room and subtended a visual angle of 30×24°. The

background was uniformly dark gray with a luminance of 0.1 cd/m². The fixation spot was a small spot subtending 0.1°. As described below, the six stimuli in each array had the same luminance (10 cd/m²) and size. The square root of the stimulus size was changed linearly depending on its distance from the fixation point (e.g. 0.26 deg² and 1.04 deg² at 5° and 10° eccentricity, respectively).

The monkeys were trained to perform a multidimensional visual search task. After fixation on a central spot for 800–2,500 ms, a circular stimulus search array containing six isoeccentric stimuli was presented (Fig. 1). Two singleton stimuli, one unique in color (color singleton), the other in shape (shape singleton), were presented with four other identical (nonsingleton) stimuli. One of the singletons served as the target, the other a distractor, depending on the ongoing search dimension. The monkeys needed to distinguish the feature contrast in the relevant search dimension to detect

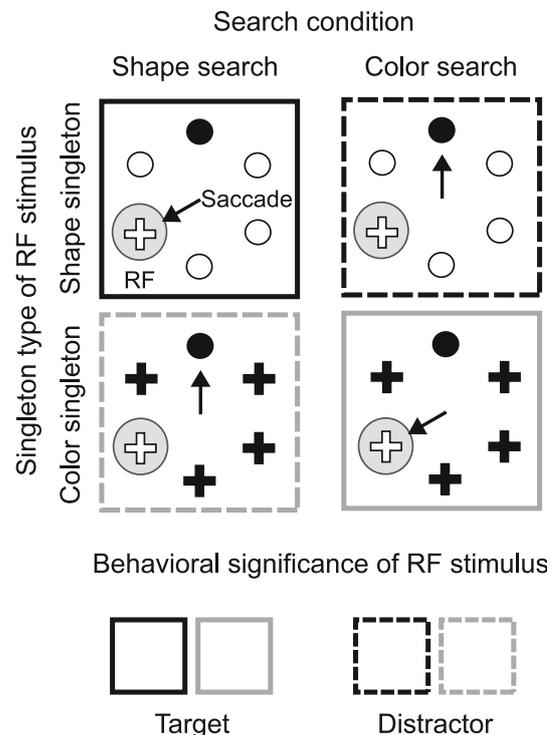


Fig. 1 Design of the multidimensional search task stimulus conditions for the experiment. Two singleton stimuli, one unique in color dimension, the other unique in the shape dimension, were presented simultaneously with four other identical stimuli. The stimulus in the receptive field (RF, gray circles) was of three singleton types: shape (black rectangle frames, top row), color (gray frames, middle row) or nonsingleton (not shown). Monkeys had to make a saccade (arrows) to one of the singleton stimuli, depending on the search dimension; i.e., to the shape singleton in the shape search (left column), or to the color singleton in the color search (right column). Examination of the two search conditions was conducted in separate blocks, and the search dimension was instructed by the color of the fixation spot. Note that when the relevant search dimension was switched, the behavioral significance of the two singleton stimuli, target (thick solid frames) or distractor (thick dashed frames), were exchanged. None of the nonsingleton stimuli ever became the target under either search condition

the target. In the shape search (left column in Fig. 1), the shape singleton was the target and the color singleton was the distractor; this was vice versa in the color search (right column in Fig. 1). A nonsingleton stimulus never became the target under either search condition (this stimulus condition will be referred to as nontarget to contrast with the target and distractor conditions). The monkeys were required to make a saccade to the target. Similar stimulus configurations were used previously in human psychophysical experiments (e.g. Theeuwes 1991; Bacon and Egeth 1994).

Identical sets of 13 different visual stimulus arrays were used under both search conditions. One array was utilized in a catch trial in which all six stimuli had the same color and shape, and the monkeys were given a reward when they held fixation throughout the trial. The remaining 12 arrays included a combination of various stimulus conditions of the receptive field stimulus (two shapes \times two colors \times three singleton types). Stimulus shape and color were randomly selected from two shapes and two colors determined in advance, and were presented with the same frequency at all six possible positions. Consequently, the monkeys could not use any bias for a specific shape, color or position to select the target. With monkey 1, two shapes and two colors were used throughout the training and recording experiments. With monkey 2, the shapes and colors were chosen from among five candidate shapes and colors for each neuron so that the responses to two shapes/colors were as different as possible.

The shape search and color search conditions were applied sequentially in separate trial blocks (typically 50–100 trials). The search dimension was instructed by the color of the fixation spot (shape search, red; color search, blue). In most of the neurons studied, the color cue was given only for the first 5–10 trials of each block, and a white spot was presented in the rest of trials. Data from both cued and non-cued trials were used in the present analysis. The search dimension in the initial block was randomly selected.

Data collection and data analysis

Neural activities were recorded from V4 of two monkeys. In addition, for comparison, recordings were also made from FEF of one monkey. With monkey 1, V4 and FEF recordings were carried out in series but during separate recording sessions. Recordings were made first from V4 and then from the FEF. With monkey 2, recordings were carried out only in V4. Neuronal recording was not begun until the monkeys were highly trained to perform the multidimensional visual search task (more than 1 year), and no systematic changes in the neuronal or behavioral response properties were detected during recording sessions from each area of each monkey. Still, because the FEF recordings were made about 1 year after the V4 recordings, the animal (monkey 1) had more training and, therefore, the

saccade reaction times were shorter in the FEF recordings than the V4 recordings (see Results).

Eye position was monitored using the scleral search coil technique (MEL-250UD; Enzansi Kogyo, Tokyo, Japan) (Fuchs and Robinson 1966; Judge et al. 1980) and recorded at 1 kHz. Regions of V4 and FEF were localized based on their physiological properties and anatomical landmarks. FEF was also localized using a stimulator (SEN-7203; Nihon Kohden, Tokyo, Japan) as the site where a 60 ms train of biphasic current pulses (amplitude, $< 50 \mu\text{A}$; width 0.2 ms; frequency 333 Hz) evoked fixed-vector, saccadic eye movements during fixation (Bruce and Goldberg 1985; Bruce et al. 1985). Single microelectrodes (Frederick Haer & Co, Bowdoinham, ME) were passed through the dura using a set of grids with 0.5 mm precision and advanced into the brain with a hydraulic microdrive (MO-95; Narishige, Tokyo, Japan). Extracellular activity was amplified by a multi-channel amplifier (SS-202J; Nihon Kohden, Tokyo, Japan) and stored on a Windows 2000-based computer equipped with a multichannel analog-to-digital board (PCI-416L2A; Datel Japan, Tokyo, Japan) at sampling rates of 25 kHz. Single units were discriminated according to spike amplitude using a simple threshold method to construct online peristimulus time histograms. Precise spike discrimination was done offline using a template-matching method.

During recording sessions, we searched for a single neuron while the monkey performed the multidimensional search task in which the radius and orientation of the stimulus array were randomly changed from trial to trial. Once a neuron was isolated, we first assessed the visual responsiveness and the receptive field size in a passive visual fixation task. For those neurons that had receptive fields located within an area extending from 4° to 10° from the fovea and did not include the fixation point, we tried to adjust the radius and orientation of the stimulus array so that only one stimulus was presented in a neuron's receptive field in the search task. The appropriateness of the stimulus configuration was then confirmed by examining the visual response obtained when the stimulus in the receptive field was removed and only the remaining five stimuli were presented. If the response to the five-stimulus array was larger than 20% of the response to the single stimulus in the receptive field, the data from that neuron was excluded from the analysis. Usually, each of the shape- and color-search conditions was repeated so that more than 10 repetitions of each trial type were carried out for each neuron; the minimum accepted for analysis was seven. We also recorded some visually nonresponsive neurons in the experiment, but they were not examined in this study.

With the task design described above (Fig. 1), the monkeys had to combine information about the singleton type and the relevant search dimension to identify the location of the target singleton. Under these conditions, the neural mechanisms underlying visual selection should convert stimulus-based signals (singleton type)

into goal-based signals (behavioral significance), depending on the ongoing behavioral context (search dimension). We, therefore, focused on those neurons that conveyed signals encoding information about the singleton type (bottom-up process) and/or the behavioral significance (top-down process) of the receptive-field stimulus and analyzed the way in which the relative importance of these factors dynamically changed in V4 and FEF over the course of visual saccade selection. To identify neurons that showed differential visual responses to the three types of singleton in the receptive field (shape singleton, color singleton, and nonsingleton), we performed a three-way ANOVA (two shapes \times two colors \times three singleton types) for each search condition, analyzing only data obtained in correct trials. Further analysis was then conducted with those neurons in which the main effect of singleton type was significant under at least one search condition (significance was assigned at $P < 0.05$). A square root transformation of the firing rates was carried out to convert neural activity with a Poisson distribution to a normal distribution before the ANOVA. It should be noted that, because each of the three singleton types corresponded to one of the different behavioral significance conditions (target, distractor, and nontarget) mentioned above, this ANOVA also detected the dependence of the receptive field stimulus on the behavioral significance. We distinguished the neuronal modulation correlating with singleton type from that correlating with behavioral significance by comparing the responses recorded under the two search conditions. This is described in more detail in the [Results](#) section. For the ANOVA, we examined neural activities occurring in a post-stimulus period, from the shortest visual latency (70 ms for V4 data, 50 ms for FEF data) (Schmolecky et al. 1998) to times around the minimum onset latency of the saccades (monkey 1, 240 ms for V4 data and 200 ms for FEF data; monkey 2, 180 ms), and those occurring during a 50 ms period immediately before saccade initiation in both monkeys. A few trials in which saccades occurred in the former period were excluded from the data analysis (monkey 1, 0.6% for V4 data 0.5% for FEF data; monkey 2, 1.8%).

The effects of the receptive field stimulus condition (singleton type or behavioral significance) and search dimension on neuronal activity were isolated for each neuron by averaging the firing rates across the stimulus features—i.e., the shape and color of the stimulus in the receptive field—under each search condition. As a result of this averaging, we obtained six responses (two search dimensions \times three singleton types). Then, to compare neural activities across the population of recorded neurons, cell-to-cell differences in response magnitude were normalized by the peak activity across the six stimulus conditions of each neuron. Significant differences between normalized responses were determined using a permutation test (Efron and Tibshirani 1993). In each permutation, trial data were randomly shuffled across the responses to two different singleton stimuli. To avoid

the mixing of responses to different shapes or colors, the shuffling was separately conducted in individual shape and color. This procedure was repeated to produce 100 total permutations. In each permutation, values of the normalized responses were computed in the same way as for the actual data, and the two normalized responses were compared. If the magnitude of the difference in the actual data was larger than the permuted differences in more than 95 iterations, it was deemed that these two responses were significantly different (at the $P < 0.05$ level).

Results

In a multidimensional visual search task (Fig. 1), a search array containing two singleton stimuli, shape and color singletons, was presented after fixation. One singleton that was salient in the instructed search dimension served as the saccade target, while the relevant search dimension was switched between shape and color. By switching the search dimension, the behavioral significance of the two singleton stimuli was exchanged. This enabled us to dissociate the respective influences of the bottom-up (singleton type) and top-down (behavioral significance) factors on neural activity.

Behavioral performance

The monkeys' behavioral performances during the search task were well above the chance level ($1/6 = 16.7\%$). The average scores in the shape and color searches were, respectively, 82.8 and 85.6 correct for monkey 1 and 87.0 and 91.0% correct for monkey 2 during recordings from the V4 neurons studied, and were 84.6 and 88.1% for monkey 1 during recordings from the FEF neurons studied. The performances of both monkeys were thus slightly better in the color search than in the shape search. The average saccade reaction times in the shape and color searches were, respectively, 369 and 359 ms for monkey 1 and 276 and 260 ms for monkey 2 during V4 recording sessions, and were 295 and 292 ms for monkey 1 during FEF recording sessions. There were no significant differences among the six trial conditions (three singleton types \times two search dimensions) used for each area in each monkey (two-factor ANOVA using singleton type and search dimension as main factors), except for the average reaction times in the two search dimensions for monkey 2 ($P < 0.05$).

Neuronal database

One hundred and thirty-two visually responsive neurons were recorded in area V4 of the two monkeys. The neural samples from area V4 were identical with those

analyzed in our previous study (Ogawa and Komatsu 2004). Although only neural data recorded from the initial interval in individual trials were studied in our previous study, whole neural data throughout individual trials were used in this study. Thirty-five of the 132 neurons recorded were excluded from our analysis because their responses in the control experiment did not fulfill the criterion that only one stimulus was presented in their receptive field (see [Materials and methods](#)). Of the remaining 97 neurons, 41 (42%; 29 from monkey 1 and 12 from monkey 2) showed significant dependence on the receptive-field stimulus condition (singleton type and/or behavioral significance) during at least one of the early or late periods analyzed under either search condition ($P < 0.05$, three-factor ANOVA) (see [Materials and methods](#)) and were, therefore, analyzed further. Eighty-eight neurons were recorded from the FEF of monkey 1 and 50 of them were visually responsive. The control experiment confirmed that 31 of these 50 neurons had a receptive field of appropriate size for the present study. Twenty-six of these remaining 31 neurons showed significant dependence on the stimulus condition during at least one of the four analyzed periods ($P < 0.05$, three-factor ANOVA) and were analyzed further. The mean number of trial repetitions for each stimulus condition was 17.0 for the V4 neurons and 17.8 for the FEF neurons. [Table 1](#) summarizes the numbers of V4 and FEF neurons showing a dependence on the stimulus condition of the receptive field stimulus.

Responses in single V4 neurons

We found that the activity of V4 neurons signaled information about both the singleton type (bottom-up factor) and the behavioral significance (top-down factor) of the receptive-field stimulus, and that within the population of V4 neurons there were systematic tendencies in the temporal patterns of the evolution of these neural modulations (as shown later in [Figs. 3, 4](#)), though their

Table 1 Numbers of neurons showing significant dependence on the singleton type and/or behavioral significance of the receptive field stimulus

Area	Time	Search condition		Total
		Shape search	Color search	
V4	Early	22	22 (10)	34
	Late	20	19 (13)	26
FEF	Early	7	11 (5)	13
	Late	21	23 (18)	26

Numbers of neurons showing significant dependence on stimulus condition in shape search, color search or both during the early and late periods are indicated separately. Ninety-seven V4 neurons and 31 FEF neurons were examined. The significance of effect on neural activity was evaluated by three-way ANOVA using the shape, color and singleton type (behavioral significance) of the receptive-field stimulus as factors. Values of $P < 0.05$ were considered significant. The numbers in parenthesis indicate the number of neurons showing significant effects under both search conditions

manifestation varied among individual neurons. [Figure 2](#) shows the activities of two representative V4 neurons that clearly illustrate the neuron-to-neuron variation. One of these neurons exhibited visual responses of relatively short duration and showed a significant dependence on the singleton type of the receptive-field stimulus ([Fig. 2a–d](#)). Following initial phasic visual responses under both search conditions (left column in [Fig. 2a, b](#)), this neuron was most strongly activated when the color singleton stimulus appeared in its receptive field (gray lines). Thus, the initial visual responses (around 120 ms–180 ms after search array presentation) of this neuron were determined mainly by the singleton type of the receptive-field stimulus. However, this bottom-up information about singleton type was no longer available at later times because of the lack of activity during the period extending from 100 ms to 0 ms before saccade initiation (right column in [Fig. 2a, b](#)).

To quantify the dynamics of this response modulation over the course of the search task, we evaluated the magnitude of the difference between the responses to the shape and color singletons at different times by moving a 50-ms time window for analysis in 20-ms steps. [Figure 2c](#) and [d](#) show the normalized responses to the shape (black circles) and color (gray circles) singletons in the shape and color searches, respectively. These normalized responses were obtained by dividing the responses of each neuron by its peak activity. For clarity, the differences in values from the average across the three normalized responses under each search condition were plotted at each step. The heights of the connected black and gray circles at each step indicate the magnitudes of the differences in the responses between the two singleton stimuli. After presentation of the search array (left column in [Fig. 2c](#) and [d](#)), the early visual responses to the color singleton were significantly larger than those to the shape singleton under both search conditions (asterisk, permutation test, $P < 0.05$). On the other hand, during the late presaccadic period (right column), there was no such difference between the two singleton stimuli, which is consistent with the lack of response seen in [Fig. 2a](#) and [b](#) (permutation test, $P > 0.05$).

[Figure 2e–h](#) shows the activity of another single V4 neuron; in this case, the cell showed a strong dependence on the behavioral significance of the receptive-field stimulus. During the late presaccadic period (right column in [Fig. 2e, f](#)), the response to the target stimulus (thick solid lines) was much larger than to the distractor (thick dashed lines) or the nontarget (thin dotted lines) stimuli under both search conditions. However, this increment in the response to the target stimulus was not seen in the initial visual responses recorded around 120 ms to 140 ms after search array presentation (left column in [Fig. 2e, f](#)). Instead, the response to the color singleton (gray lines) was the largest under either search condition, reflecting selectivity for singleton type, which was confirmed by the quantitative analysis shown in [Fig. 2g](#) and [h](#).

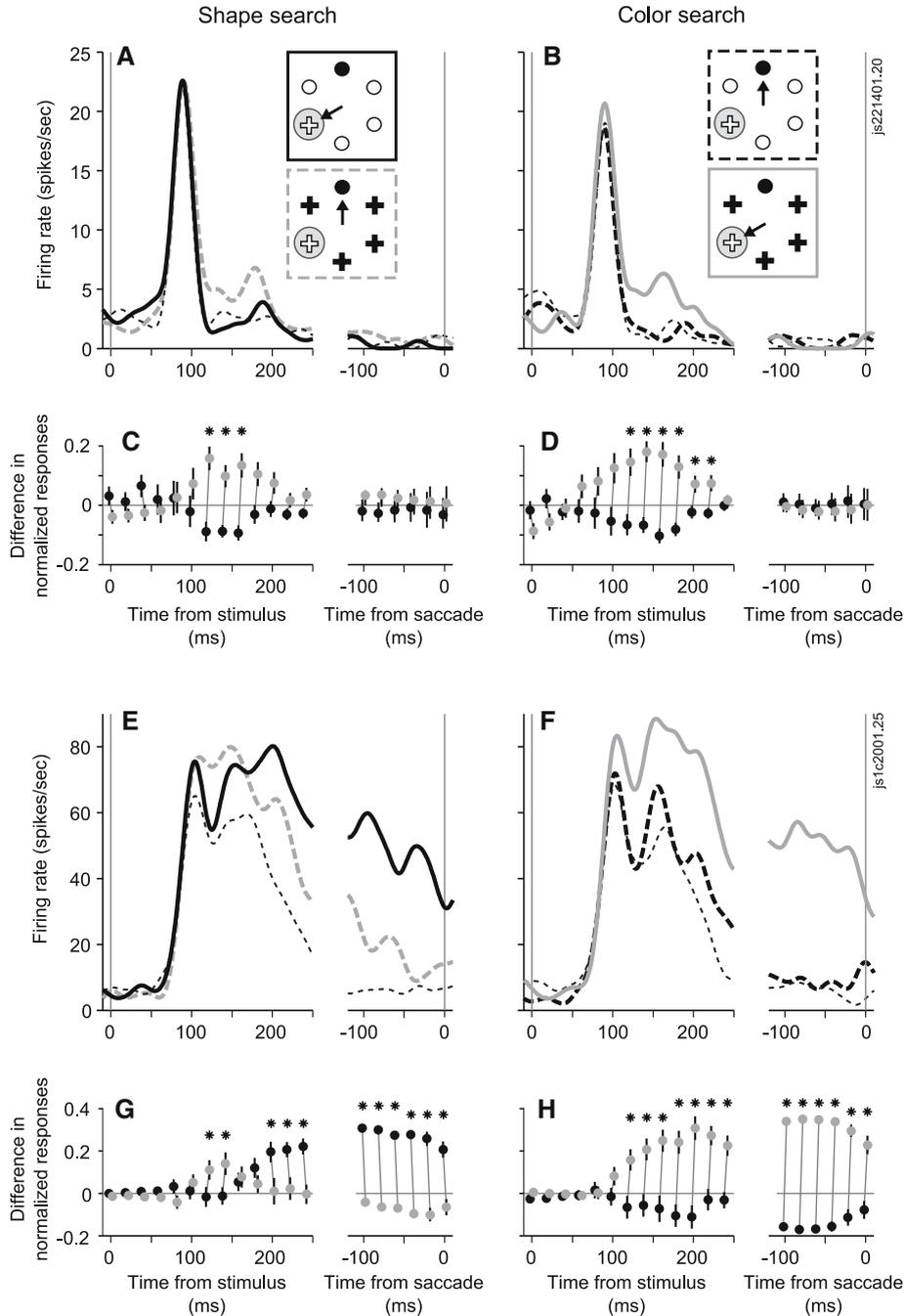


Fig. 2 Activity of single V4 neurons (**a–d**) Activity of a representative V4 neuron showing dependence on the singleton type of the receptive-field stimulus. **a** Spike density functions obtained in the shape search. To see only the effects of singleton type (behavioral significance) and search dimension on neural activity, the responses were averaged across the receptive-field stimulus features (*two shapes* \times *two colors*) for each singleton type in each search dimension. *Left* and *right* columns indicate the stimulus- and saccade-aligned functions. *Thick black*, *thick gray* and *thin black lines*, respectively, indicate the responses when the shape singleton, color singleton or nonsingleton stimulus was presented within the receptive field. The *thick solid*, *thick dashed* and *thin dashed lines*, respectively, indicate that the stimulus in the receptive field was the target, distractor or nontarget. The spike density functions were

smoothed with a Gaussian function ($SD = 10$ ms). **b** Spike density functions in the color search. **c** Normalized responses obtained in the shape search. *Black* and *gray circles* represent the normalized responses to the shape and color singletons, respectively. Each value of the normalized response was calculated from the neural data within a 50-ms window centered at each time step. For clarity, each point is depicted as the difference in value from the average across the three normalized responses at each time step under each search condition. Asterisks indicate significant differences between the two corresponding mean values (permutation test, $P < 0.05$). **d** Normalized responses obtained in the color search. **e–h** Another V4 neuron showing dependence on the behavioral significance of the receptive-field stimulus. Conventions are the same as in (**a–d**)

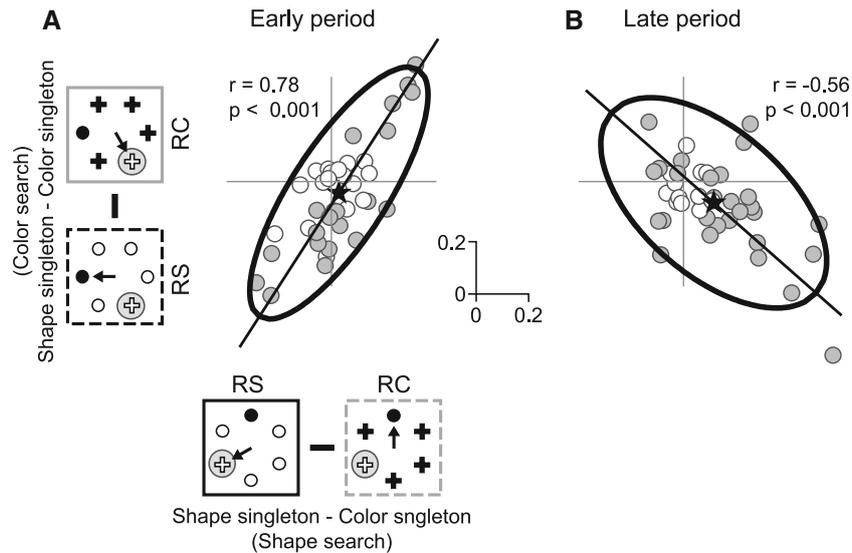


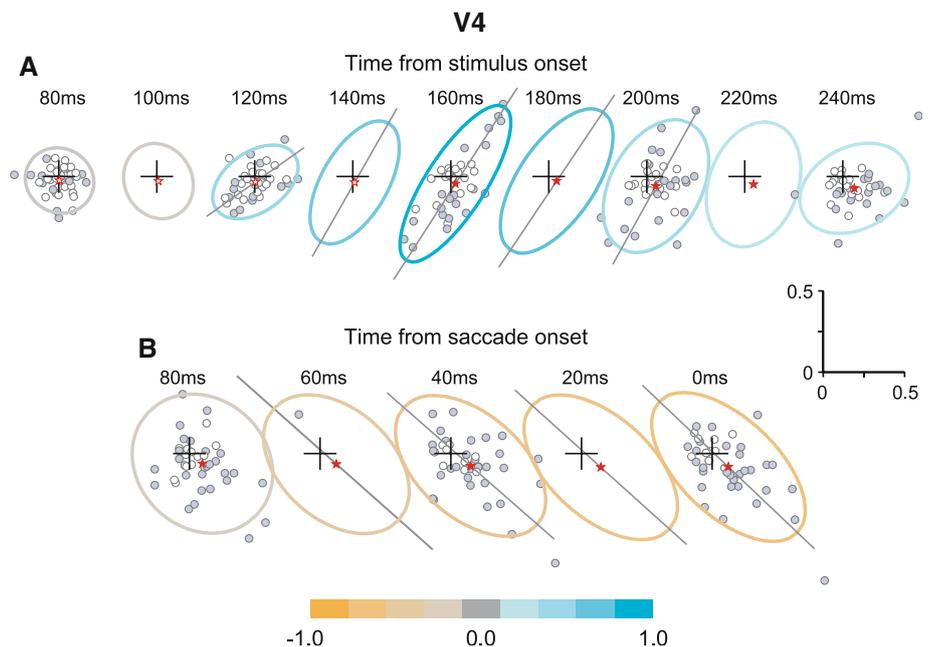
Fig. 3 Sensory and behavioral components of V4 activity (**a**, **b**) Dependence of neural modulation on singleton type and behavioral significance assessed in a population of V4 neurons ($n = 41$). **a** Early period activity (during a 50-ms time window centered at 160-ms after stimulus onset). For each neuron, the difference in the normalized responses to the shape and color singletons (RS-RC) under the shape search conditions was compared with that under the color search conditions. Each data point represents a pair of difference in values obtained from one neuron. A positive (negative) value on each axis indicates that the shape singleton elicited a stronger (weaker) response than the color singleton. There

is a significant positive correlation between these two values ($r = 0.78$, $P < 0.001$). An *ellipse* and a *solid line* indicate the 95% confidence interval for the data points and the main axis of the ellipse, respectively. *Filled circles* indicate neurons in which response modulation was significantly different from zero (a permutation test, $P < 0.05$). A *star* indicates the center of gravity of the distribution. **b** Late period activity (during the 50 ms immediately prior to saccade initiation). There is a significant negative correlation between these two values ($r = -0.56$, $P < 0.001$). Conventions are the same as in (**a**)

It thus appears that the responses of individual V4 neurons can be influenced by both bottom-up and top-down factors, and that the manifestation of these two modulatory factors influencing neural activity varies

from one neuron to another. In the analyses described below, we attempted to determine whether the modulations by these two factors exhibit any systematic patterns in their temporal dynamics in a population of V4

Fig. 4 Dynamics of the response modulation in V4 The dynamics of the response modulation in a population of V4 neurons ($n = 41$) were examined over the course of visual selection. A 50 ms time window for analysis was moved along the time axis in 20 ms steps, and the same analysis depicted in Fig. 3 was conducted at each time step. The middle of the time window was moved stepwise from 80 to 240 ms after search array presentation in (**a**) and from 80 to 0 ms before saccade initiation in (**b**). The color of each ellipse corresponds to the color scale at the bottom and indicates the correlation coefficient at each time. For clarity, the data points were omitted from every other ellipse. Other conventions are the same as in Fig. 3



neurons. To do this, we evaluated the relative strengths of the response modulations that correlated with the singleton type and behavioral significance of the receptive field stimulus. We will refer to the values obtained as the *sensory component* and *behavioral component*, respectively.

Bottom-up and top-down influences on the activities of V4 neurons

To roughly determine the temporal aspects of the dependence on singleton type and behavioral significance in a population of V4 neurons, we divided the recorded neural activity into early-period activity (a 50-ms time window centered at 160 ms after search array presentation) and late-period activity (a 50-ms time window immediately before saccade initiation), and conducted an analysis similar to the one used in our previous study (Ogawa and Komatsu 2004). We computed the average magnitudes of the normalized responses to the shape singleton (RS) and the color singleton (RC) during the analyzed periods and plotted the difference in values (RS-RC) obtained under the shape search conditions versus those obtained under the color search conditions (Fig. 3). If the sensory component was dominant, neurons should maintain a preference for one of the singleton types across the two search conditions, and there should be a positive correlation between the difference in values, with data points clustering along a diagonal line with a positive slope ($y = x$). On the other hand, if the behavioral component is dominant, there should be a negative correlation, and the data points should cluster along another diagonal line with a negative slope ($y = -x$).

We found that for early period activity (Fig. 3a), there was a significant positive correlation in the distribution of the data points (correlation coefficient, $r = 0.78$; $P < 0.001$). This indicated that the sensory component was dominant across the V4 neurons studied, although a weak but consistent behavioral component could also be seen as a significant deviation of the center of gravity (star) from zero toward the lower right (permutation test, $P < 0.05$). That is, despite the dominance of the sensory component in individual V4 neurons, the averaged V4 population response significantly signaled the behavioral significance of the receptive field stimulus. In contrast to the early period, the behavioral component dominated in the activity recorded during the late presaccadic period (Fig. 3b), as indicated by the significant negative correlation (correlation coefficient, $r = -0.56$; $P < 0.001$). In this case, the distribution expanded toward the lower right, with about half of the V4 neurons studied ($n = 18$) and the center of gravity of the distribution significantly deviated from zero in that direction (permutation test, $P < 0.05$). Thus, for both the individual responses and the averaged population response, the late presaccadic activity of V4 neurons pre-

dominantly encoded the behavioral significance of the receptive field stimulus.

These response properties were consistently observed in the individual monkeys. When the same analysis was conducted on the data from each monkey, the values of the correlation coefficient in the early and late periods were respectively 0.81 and -0.60 for monkey 1 ($n = 29$) and 0.77 and -0.31 for monkey 2 ($n = 12$). Although the correlation in the late period for monkey 2 was not significant ($P > 0.05$), it did have a negative value. All other correlations were significant ($P < 0.05$). Thus, both monkeys showed sensory-component dominance during the early period and behavioral-component dominance during the late period of the visual search.

Dynamics of response modulation of V4 neurons

Figure 3 shows that the dominant modulating factor affecting neural activity in area V4 changed from the singleton type to behavioral significance over the course of visual selection. To examine the dynamics of this transition in more detail, we next analyzed the response modulations within a 50 ms time window that was shifted in 20 ms steps during the course of visual selection. Figure 4a shows the time course of neural modulations locked at the search array presentation: the center of the time window was moved stepwise from 80 to 240 ms after stimulus presentation. Initially, the distribution was isotropic. Development of the anisotropic distribution started around 120 ms after search array presentation and reached an extreme at around 160–180 ms, after which the anisotropy diminished. Throughout this process, the distribution was consistently elongated toward the upper right and lower left and showed significant positive correlation (correlation coefficient, $r = 0.37$ to 0.78 from 120 to 200 ms after stimulus presentation, $P < 0.05$), indicating the predominance of the sensory component in the early population activity of V4 neurons. Figure 4b shows the time course of neural modulations locked at saccade initiation: the center of the time window was moved stepwise from 80 to 0 ms before saccade initiation. In this case, the anisotropic distribution gradually developed as saccade initiation approached. The distribution of the data points elongated toward the lower right and showed significant negative correlations ($r = -0.58$ to -0.39 from 60 to 0 ms before saccade, $P < 0.05$), indicating the predominance of the behavioral component in the late presaccadic population activity. In sum, the results presented so far demonstrate that in area V4 of monkeys performing a multidimensional visual search task, the bottom-up and top-down factors tend to operate within different time domains, with the evolution of the sensory component coming first after search array presentation and followed by the behavioral component toward saccade initiation.

The results in Fig. 4 were also confirmed by the analysis at the level of unnormalized response. When we

did the same analysis as in Fig. 4 on the raw activity of individual neurons, we still found sensory-component dominance in the early period (correlation coefficient, $r=0.11$ to 0.34 from 120 to 180 ms after stimulus presentation) and behavioral-component dominance in the late period ($r=-0.79$ to -0.60 from 100 to 0 ms before saccade initiation). The correlation in the early period became significant ($P<0.05$) at 140 ms after stimulus onset, and that of the late period was significant ($P<0.001$) through the 100 ms period before saccade initiation.

One might argue that the difference between the modulations shown in Fig. 4a and b might be due to the difference in the timing at which each response was aligned, as responses in a are aligned at the stimulus onset, whereas those in b are aligned at the saccade onset. To test this, we did the same analysis using a common temporal frame of reference. The analysis was conducted only on the responses of monkey 1 with a larger amount of neuron data, because the considerable difference in the average saccade reaction times between the two monkeys obscured the neural modulation at later times, when their data were combined. We still found that sensory-component dominance occurred first (correlation coefficient, $r=0.33$ to 0.81 from 120 to 220 ms after stimulus presentation) and was followed by behavioral-component dominance ($r=-0.61$ to -0.12 from 240 to 360 ms after stimulus presentation). This confirms that the present results in V4 did not arise from methodological artifacts. An additional experiment on FEF neurons lends further support to this conclusion (see below).

Dynamics of response modulation of FEF neurons

The response properties in visual search have been extensively examined in the FEF (see reviews, Schall and

Thompson 1999; Thompson and Bichot 2005). It seems that the FEF would be a good reference site to understand qualitative differences in the visual selection dynamics between visual areas (area V4) and visual-motor areas. Although the influences of bottom-up and top-down factors have been detected in the FEF, the relative strengths of these two factors differed across previous studies (e.g. Thompson et al. 1997, 2005; Bichot et al. 2001; Murthy et al. 2001). In order to directly compare the response properties between area V4 and the FEF, we also recorded the activity of FEF neurons from one monkey (monkey 1) performing the same multidimensional visual search task.

In contrast to V4 neurons, visually responsive FEF neurons exhibited a stereotyped pattern of activity in which there was no apparent early neural modulation reflecting the sensory component. The response of a representative FEF neuron is shown in Fig. 5. At around 140 – 160 ms after search array presentation, the responses started to differentiate under both search conditions: the responses to the target stimulus became larger while those to the other stimuli became smaller (left column in Fig. 5a, b). This response differentiation gradually increased and was sustained until initiation of the saccade (right column in Fig. 5a, b). Quantitative analyses of the normalized responses (Fig. 5c, d) confirmed that the behavioral component was predominantly signaled in the FEF, and it was especially evident in the late presaccadic period.

To determine the visual selection dynamics of the activity of FEF neurons, we next examined the temporal patterns of the evolution of the sensory and behavioral components over the course of a visual selection in a population of FEF neurons ($n=26$). The same analysis depicted in Fig. 4 was used to evaluate the activity of FEF neurons. Figure 6a shows the time course of the response modulations locked at search array

Fig. 5 Neural activity of a single FEF neuron. The conventions are the same as in Fig. 2

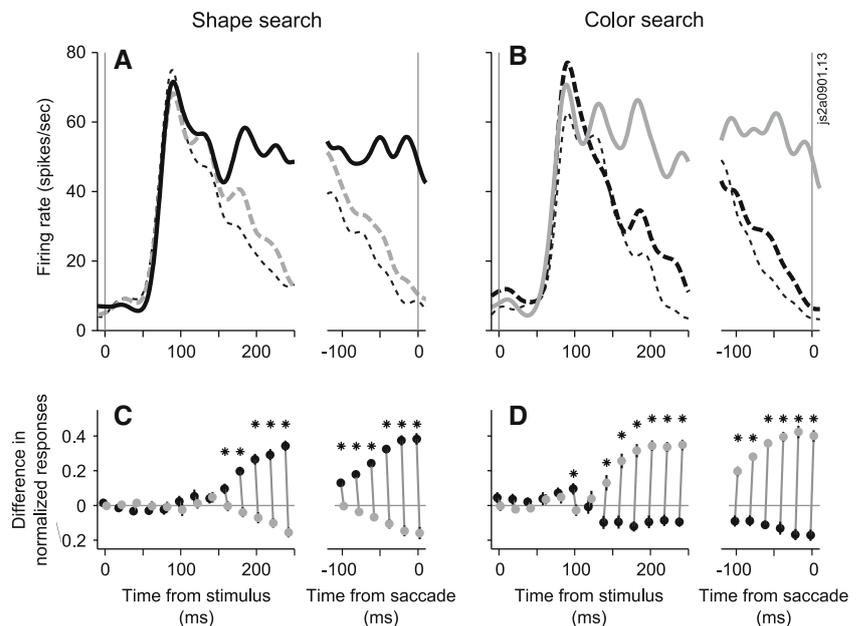
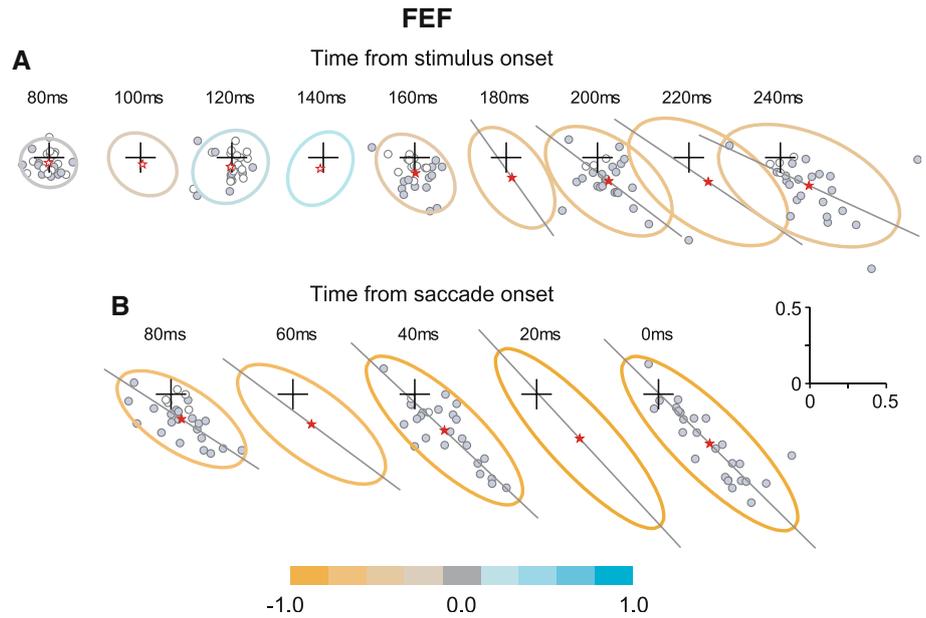


Fig. 6 Dynamics of response modulation in the FEF. The dynamics of the response modulation in a population of FEF neurons ($n=26$) were examined over the course of the visual selection. The conventions are the same as in Fig. 4



presentation. There was no systematic tendency reflecting the sensory component. Earlier than 140 ms after search array presentation, the data points clustered near the origin, and the distribution was isotropic. However, after that time, most of the data points were shifted toward the lower right and showed significant negative correlation ($r = -0.54$ to -0.47 from 180 to 240 ms after stimulus onset, $P < 0.05$). This tendency in the response modulation developed gradually and was sustained until saccade initiation ($r = -0.86$ to -0.64 from 80 to 0 ms before saccade, $P < 0.001$) (Fig. 6b). Except for two neurons, the largest activity was induced by the target singleton stimulus. FEF neurons thus predominantly signaled the behavioral component, particularly at late presaccadic times.

The results in Fig 6 were also confirmed by the analysis at the level of the unnormalized raw activity of individual neurons. We only found behavioral-component dominance in the early period ($r = -0.85$ to -0.41 later than 160 ms after stimulus presentation, $P < 0.01$) and in the late period ($r = -0.94$ to -0.70 from 100 to 0 ms before saccade initiation, $P < 0.001$).

The present results from the FEF are essentially the same as those previously reported (Schall and Thompson 1999; Thompson and Bichot 2005). We also found reflectance of visual saliency in the activity of FEF neurons (Thompson et al. 1997; Murthy et al. 2001); the response to the distractor singleton was slightly larger than to a nonsingleton stimulus during the period extending from 180 ms after search array presentation to saccade initiation (permutation test, $P < 0.05$). However, as shown above, the tendency was that most FEF neurons continuously exhibited the largest activity when the receptive field stimulus was the target stimulus (Bichot et al. 2001; Thompson et al. 2005). This was clearly

different from the present results we observed in area V4. Because both areas were examined in the same visual search task, we can conclude that the presently observed properties of V4 responses are not due to methodological artifacts, but are due to the inherent characteristics of V4 neurons.

Discussion

To examine the dynamics of bottom-up and top-down neuronal processing in visual search, we examined the activity of V4 neurons using the multidimensional visual search task. This task design allowed us to clearly dissociate the two factors in neural modulation, and this advantage makes the present study different from other previous studies of visual search in visual cortical areas (Chelazzi et al. 2001; Sheinberg and Logothetis 2001; Lee et al. 2002; Mazer and Gallant 2003; Bichot et al. 2005). The results showed that whereas the early period neural modulation in V4 primarily signaled the singleton type of the receptive field stimulus (bottom-up factor), the late period neural modulation signaled its behavioral significance (top-down factor). Although the latter behavioral component was not significant in one monkey (monkey 2), the significant manifestation of the former sensory component was temporally limited in the early period in both monkeys, indicating that the relative strengths of the bottom-up and top-down influences dynamically changed over the course of a visual search task. In contrast, the largest activity of most FEF neurons continuously signaled the behavioral component during visual search. Thus, the present results demonstrate that the contribution of the bottom-up and top-down signals differs between two areas and that the

modulatory factors influencing on the activity of V4 neurons dynamically changed over the course of the visual search.

Sensory-based and behavior-based signals in area V4

In the early period, around 120–200 ms after array presentation, the dominant factor modulating individual V4 neurons' responses were the singleton type of the receptive field stimulus (the distribution of the data points shows a significant positive correlation, Fig. 4a). However, the averaged population response significantly discriminated the target around 160 ms after search array presentation (the center of gravity is significantly deviated toward the lower right, Fig. 4a). This suggests that, even during the early period, the neurons downstream of area V4 could detect the target by receiving the pooled response of V4 neurons, and that the downstream individual neurons may be able to discriminate the target earlier than individual V4 neurons. Even so, it should be realized that the target discrimination process at the downstream visual-motor areas cannot start without the contributions of visual areas such as area V4. In this sense, area V4 should be regarded as one of the key elements for the converting process from sensory-based signals into behavior-based signals in visual searches.

In the late period before saccade initiation, both the population average response and the individual neurons' response came to signal the behavioral significance of the receptive field stimulus (Fig. 4b). Previous studies of visual search in area V4 showed a neural modulation that predicts the location of the selected stimulus (Chelazzi et al. 2001; Mazer and Gallant 2003; Bichot et al. 2005). When a visual search ultimately selects only one object as the saccade target, top-down attention might be spatially allocated to the target location. Psychophysical studies provided evidence that supports this view (Hoffman and Subramaniam 1995; Kowler et al. 1995; Deubel and Schneider 1996). On the other hand, the behavioral significance dependency observed in the late period may be partially due to motor-related signals to trigger saccade initiation. However, previous neurophysiological studies showed that presaccadic activation observed in V4 (Fischer and Boch 1981a, b) depends primarily on the visual target and has orientation selectivity (Moore et al. 1998; Moore 1999). Considering these results, it is unlikely that area V4 plays a direct role in triggering saccade responses (Moore 1999).

Behavior-based signals in the FEF

The neural mechanisms underlying visual search have been extensively studied in visual-motor areas such as the FEF (Schall et al. 1995a; Hanes and Schall 1996; Thompson et al. 1996), the posterior parietal cortex (PPC) (Gottlieb et al. 1998; Constantinidis and

Steinmetz 2001), and the superior colliculus (Basso and Wurtz 1997; McPeck and Keller 2002). In these visual-motor areas, the responses to the target stimulus are enhanced over time when the receptive field stimulus was the target in the visual search.

In this study, we found that behavioral component was dominant in the activity of FEF neurons throughout visual search, contrasting with the response profiles of V4 neurons. Although the response profiles of FEF neurons and the comparison with those of V4 neurons were based on one monkey (monkey 1), this limitation might be complemented by the evidences from previous studies of visual search. Although bottom-up sensory information about stimulus saliency is reflected in neural modulation of the FEF and PPC (Thompson et al. 1997; Bichot et al. 2001; Constantinidis and Steinmetz 2001; Murthy et al. 2001), its strength in neural modulations appears to be different from that of V4 neurons. A recent study of the FEF showed that when monkeys erroneously perform saccades to one of the non-salient background stimuli, the largest activity did not reflect the location of the salient singleton stimulus, but rather the end point of the forthcoming saccade (Thompson et al. 2005). Furthermore, even when correctly performing a search task for a less-salient singleton target with a salient distractor singleton, FEF neurons exhibited the highest activation for the less-salient target singleton (Bichot et al. 2001). In the present study, we also found that most FEF neurons exhibited the largest response when the receptive field stimulus was the target (Fig. 6). These results suggest that behavior-based signals predominate throughout the trial in the FEF (but see Thompson et al. 1997; Murthy et al. 2001). This clearly contrasts with the early period predominance of sensory signals we observed in area V4. In neural networks underlying visual search, area V4 might provide visual-motor areas with relevant sensory evidences, while visual-motor areas might be more closely related to the target selection process and functions as a winner-take-all filter (Koch and Ullman 1985; Itti and Koch 2000).

Functional role of area V4 in visual search

In daily life, we often search for behaviorally relevant objects using prior knowledge about the objects. During this type of search, our attention might be directed to the stimulus features of the target object (Chelazzi et al. 2001; Bichot et al. 2005). Even in such conditions, information about intrinsic visual saliency might play an important role. We do not search over the entire visual field but tend to direct our vision to visually salient locations (Yarbus 1967). Identification of singleton stimuli based on bottom-up signals could limit the number of locations to be inspected. At least during the early phase of the visual search, particularly when there are many potential targets in a scene, the top-down process based on the prior knowledge and the

bottom-up process based on visual saliency might cooperate to detect the target. On the other hand, when the visual selection process proceeds and one of the objects becomes a potential target, the essential information is the location of that object to which we will make a saccade. At the late phase of the visual search, therefore, bottom-up information about visual saliency is no longer useful and top-down attention might be allocated to the upcoming saccade location (Hoffman and Subramaniam 1995; Kowler et al. 1995; Deubel and Schneider 1996). Our present results and previous neurophysiological findings are in line with this scenario.

Recordings from area V4 showed that even in the early phase, the averaged population response of V4 neurons signaled behavioral significance of the receptive field stimulus. This response enhancement for the target stimulus is evoked by attention specific to search dimension. As V4 neurons directly connect to neurons in the FEF (Schall et al. 1995b; Stanton et al. 1995) and the PPC (Baizer et al. 1991), V4 activity could be a source of enhancement of activity at the target location in visual-motor areas. Increasing activity in the FEF could in turn enhance V4 activity at the location of the behaviorally relevant stimulus (Moore and Armstrong 2003). This feedback from the FEF can be an origin for spatial attention (Moore and Fallah 2004), and it might be one of the origins producing the behavioral-significance dependency during the late presaccadic period. The dynamics of these neural modulations has been well simulated by a recent visual search model (Hamker 2004) that extends the original feature-specific biased competition model (Desimone and Duncan 1995; Chelazzi et al. 1998; Reynolds et al. 1999) by adding a secondary location-based bias from the FEF. It predicts that the location-based bias from the FEF, which dominates later, overwrites the initially dominant feature-specific bias from the prefrontal cortex. Thus, even in a short interval of a visual search, there might be more than one process and bottom-up and top-down processes should dynamically and effectively function when they are needed. The present findings suggest that area V4 might be an intermediate stage where both sensory- and behavior-based signals are dynamically represented depending on their online requirements during a visual search.

Acknowledgements We thank M. Togawa for technical assistance. Supported by Grants-in-Aid for Scientific Research for Young Scientists (B) from the Ministry of ECSST and Biological Information Technology Grant for Top Priority Research and Development to Be Focused from the Ministry of PMHAPT.

References

- Bacon WF, Egeth HE (1994) Overriding stimulus-driven attentional capture. *Percept Psychophys* 55:485–496
- Baizer JS, Ungerleider LG, Desimone R (1991) Organization of visual inputs to the inferior temporal and posterior parietal cortex in macaques. *J Neurosci* 11:168–190
- Basso MA, Wurtz RH (1997) Modulation of neuronal activity by target uncertainty. *Nature* 389:66–69
- Bergen JR, Julesz B (1983) Parallel versus serial processing in rapid pattern discrimination. *Nature* 303:696–698
- Bichot NP, Chenchal Rao S, Schall JD (2001) Continuous processing in macaque frontal cortex during visual search. *Neuropsychologia* 39:972–982
- Bichot NP, Rossi AF, Desimone R (2005) Parallel and serial neural mechanisms for visual search in macaque area V4. *Science* 308:529–534
- Bruce CJ, Goldberg ME (1985) Primate frontal eye fields. I. Single neurons discharging before saccades. *J Neurophysiol* 53:603–635
- Bruce CJ, Goldberg ME, Bushnell MC, Stanton GB (1985) Primate frontal eye fields. II. Physiological and anatomical correlates of electrically evoked eye movements. *J Neurophysiol* 54:714–734
- Chelazzi L, Duncan J, Miller EK, Desimone R (1998) Responses of neurons in inferior temporal cortex during memory-guided visual search. *J Neurophysiol* 80:2918–2940
- Chelazzi L, Miller EK, Duncan J, Desimone R (2001) Responses of neurons in macaque area V4 during memory-guided visual search. *Cereb Cortex* 11:761–772
- Connor CE, Egeth HE, Yantis S (2004) Visual attention: bottom-up versus top-down. *Curr Biol* 14:R850–R852
- Connor CE, Preddie DC, Gallant JL, Van Essen DC (1997) Spatial attention effects in macaque area V4. *J Neurosci* 17:3201–3214
- Contantini C, Steinmetz MA, (2001) Neuronal responses in area 7a to multiple stimulus displays: I. Neurons encode the location of the salient stimulus. *Cereb Cortex* 11:581–591
- Desimone R, Duncan J (1995) Neural mechanisms of selective visual attention. *Annu Rev Neurosci* 18:193–222
- Desimone R, Schein SJ (1987) Visual properties of neurons in area V4 of the macaque: sensitivity to stimulus form. *J Neurophysiol* 57:835–868
- Deubel H, Schneider WX (1996) Saccade target selection and object recognition: evidence for a common attentional mechanism. *Vision Res* 36:1827–1837
- Efron B, Tibshirani R (1993) An introduction to the bootstrap. Chapman & Hall, New York
- Egeth HE, Yantis S (1997) Visual attention: control, representation, and time course. *Annu Rev Psychol* 48:269–297
- Fischer B, Boch R (1981a) Enhanced activation of neurons in prelunate cortex before visually guided saccades of trained rhesus monkeys. *Exp Brain Res* 44:129–137
- Fischer B, Boch R (1981b) Selection of visual targets activates prelunate cortical cells in trained rhesus monkey. *Exp Brain Res* 41:431–433
- Folk CL, Remington RW, Johnston JC (1992) Involuntary covert orienting is contingent on attentional control settings. *J Exp Psychol Hum Percept Perform* 18:1030–1044
- Fuchs AF, Robinson DA (1966) A method for measuring horizontal and vertical eye movement chronically in the monkey. *J Appl Physiol* 21:1068–1070
- Gottlieb JP, Kusunoki M, Goldberg ME (1998) The representation of visual salience in monkey parietal cortex. *Nature* 391:481–484
- Haenny PE, Maunsell JH, Schiller PH (1988) State dependent activity in monkey visual cortex. II. Retinal and extraretinal factors in V4. *Exp Brain Res* 69:245–259
- Hamker FH (2004) A dynamic model of how feature cues guide spatial attention. *Vision Res* 44:501–521
- Hanes DP, Schall JD (1996) Neural control of voluntary movement initiation. *Science* 274:427–430
- Hoffman JE, Subramaniam B (1995) The role of visual attention in saccadic eye movements. *Percept Psychophys* 57:787–795
- Itti L, Koch C (2000) A saliency-based search mechanism for overt and covert shifts of visual attention. *Vision Res* 40:1489–1506
- Judge SJ, Richmond BJ, Chu FC (1980) Implantation of magnetic search coils for measurement of eye position: an improved method. *Vision Res* 20:535–538
- Kim MS, Cave KR (1999) Top-down and bottom-up attentional control: on the nature of interference from a salient distractor. *Percept Psychophys* 61:1009–1023

- Koch C, Ullman S (1985) Shifts in selective visual attention: towards the underlying neural circuitry. *Hum Neurobiol* 4:219–227
- Kowler E, Anderson E, Doshier B, Blaser E (1995) The role of attention in the programming of saccades. *Vision Res* 35:1897–1916
- Lamy D, Egeth HE (2003) Attentional capture in singleton-detection and feature-search modes. *J Exp Psychol Hum Percept Perform* 29:1003–1020
- Lee TS, Yang CF, Romero RD, Mumford D (2002) Neural activity in early visual cortex reflects behavioral experience and higher-order perceptual saliency. *Nat Neurosci* 5:589–597
- Luck SJ, Chelazzi L, Hillyard SA, Desimone R (1997) Neural mechanisms of spatial selective attention in areas V1, V2, and V4 of macaque visual cortex. *J Neurophysiol* 77:24–42
- Maunsell JH, Sclar G, Nealey TA, DePriest DD (1991) Extraretinal representations in area V4 in the macaque monkey. *Vis Neurosci* 7:561–573
- Mazer JA, Gallant JL (2003) Goal-related activity in V4 during free viewing visual search. Evidence for a ventral stream visual salience map. *Neuron* 40:1241–1250
- McAdams CJ, Maunsell JH (1999) Effects of attention on orientation-tuning functions of single neurons in macaque cortical area V4. *J Neurosci* 19:431–441
- McPeck RM, Keller EL (2002) Saccade target selection in the superior colliculus during a visual search task. *J Neurophysiol* 88:2019–2034
- Moore T (1999) Shape representations and visual guidance of saccadic eye movements. *Science* 285:1914–1917
- Moore T, Armstrong KM (2003) Selective gating of visual signals by microstimulation of frontal cortex. *Nature* 421:370–373
- Moore T, Fallah M (2004) Microstimulation of the frontal eye field and its effects on covert spatial attention. *J Neurophysiol* 91:152–162
- Moore T, Tolias AS, Schiller PH (1998) Visual representations during saccadic eye movements. *Proc Natl Acad Sci USA* 95:8981–8984
- Moran J, Desimone R (1985) Selective attention gates visual processing in the extrastriate cortex. *Science* 229:782–784
- Motter BC (1994) Neural correlates of attentive selection for color or luminance in extrastriate area V4. *J Neurosci* 14:2178–2189
- Murthy A, Thompson KG, Schall JD (2001) Dynamic dissociation of visual selection from saccade programming in frontal eye field. *J Neurophysiol* 86:2634–2637
- Nothdurft HC (1993) The role of features in preattentive vision: comparison of orientation, motion and color cues. *Vision Res* 33:1937–1958
- Ogawa T, Komatsu H (2004) Target selection in area V4 during a multidimensional visual search task. *J Neurosci* 24:6371–6382
- Pashler H (1988) Cross-dimensional interaction and texture segregation. *Percept Psychophys* 43:307–318
- Posner MI, Snyder CR, Davidson BJ (1980) Attention and the detection of signals. *J Exp Psychol* 109:160–174
- Reynolds JH, Chelazzi L, Desimone R (1999) Competitive mechanisms subserve attention in macaque areas V2 and V4. *J Neurosci* 19:1736–1753
- Schall JD, Hanes DP, Thompson KG, King DJ (1995a) Saccade target selection in frontal eye field of macaque. I. Visual and premovement activation. *J Neurosci* 15:6905–6918
- Schall JD, Morel A, King DJ, Bullier J (1995b) Topography of visual cortex connections with frontal eye field in macaque: convergence and segregation of processing streams. *J Neurosci* 15:4464–4487
- Schall JD, Thompson KG (1999) Neural selection and control of visually guided eye movements. *Annu Rev Neurosci* 22:241–259
- Schein SJ, Desimone R (1990) Spectral properties of V4 neurons in the macaque. *J Neurosci* 10:3369–3389
- Schmolesky MT, Wang Y, Hanes DP, Thompson KG, Leutgeb S, Schall JD, Leventhal AG (1998) Signal timing across the macaque visual system. *J Neurophysiol* 79:3272–3278
- Sheinberg DL, Logothetis NK (2001) Noticing familiar objects in real world scenes: the role of temporal cortical neurons in natural vision. *J Neurosci* 21:1340–1350
- Spitzer H, Desimone R, Moran J (1988) Increased attention enhances both behavioral and neuronal performance. *Science* 240:338–340
- Stanton GB, Bruce CJ, Goldberg ME (1995) Topography of projections to posterior cortical areas from the macaque frontal eye fields. *J Comp Neurol* 353:291–305
- Theeuwes J (1991) Cross-dimensional perceptual selectivity. *Percept Psychophys* 50:184–193
- Thompson KG, Bichot NP (2005) A visual salience map in the primate frontal eye field. *Prog Brain Res* 147:251–262
- Thompson KG, Bichot NP, Sato TR (2005) Frontal eye field activity before visual search errors reveals the integration of bottom-up and top-down salience. *J Neurophysiol* 93:337–351
- Thompson KG, Bichot NP, Schall JD (1997) Dissociation of visual discrimination from saccade programming in macaque frontal eye field. *J Neurophysiol* 77:1046–1050
- Thompson KG, Hanes DP, Bichot NP, Schall JD (1996) Perceptual and motor processing stages identified in the activity of macaque frontal eye field neurons during visual search. *J Neurophysiol* 76:4040–4055
- Treisman AM, Gelade G (1980) A feature-integration theory of attention. *Cogn Psychol* 12:97–136
- van Zoest W, Donk M, Theeuwes J (2004) The role of stimulus-driven and goal-driven control in saccadic visual selection. *J Exp Psychol Hum Percept Perform* 30:746–759
- Yarbus AL (1967) *Eye movements and vision*. Plenum, New York