Temporal dynamics of neuronal modulation during exogenous and endogenous shifts of visual attention in macaque area MT

Laura Busse*†, Steffen Katzner*†, and Stefan Treue*†‡§

*Cognitive Neuroscience Laboratory, German Primate Center, Kellnerweg 4, 37077 Göttingen, Germany; †Bernstein Center for Computational Neuroscience, Bunsenstrasse 10, 37073 Göttingen, Germany; and ‡Department of Biology, Georg-Elias-Müller Institute for Psychology, University of Göttingen, Gosslerstrasse 14, 37073 Göttingen, Germany

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Dynamically shifting attention between behaviorally relevant stimuli in the environment is a key condition for successful adaptive behavior. Here, we investigated how exogenous (reflexive) and endogenous (voluntary) shifts of visual spatial attention interact to modulate activity of single neurons in extrastriate area MT. We used a double-cueing paradigm, in which the first cue instructed two macaque monkeys to covertly attend to one of three moving random dot patterns until a second cue, whose unpredictable onset exogenously captured attention, either signaled to shift or maintain the current focus of attention. The neuronal activity revealed correlates of both exogenous and endogenous attention, which could be well distinguished by their characteristic temporal dynamics. The earliest effect was a transient interruption of the focus of endogenous attention by the onset of the second cue. The neuronal signature of this exogenous capture of attention was a short-latency decrease of responses to the stimulus attended so far. About 70 ms later, the influence of exogenous attention leveled off, which was reflected in two concurrent processes: responses to the newly cued stimulus continuously increased because of allocation of endogenous attention, while, surprisingly, there was also a gradual rebound of attentional enhancement of the previously relevant stimulus. Only after an additional 110 ms did endogenous disengagement of attention from this previously relevant stimulus become evident. These patterns of attentional modulation can be most parsimoniously explained by assuming two distinct attentional mechanisms drawing on the same capacity-limited system, with exogenous attention having a much faster time course than endogenous attention.

attentional time course | extrastriate cortex | middle temporal area | visual motion

Visual attention selectively modulates the sensory processing of information according to behavioral relevance (1–4). For instance, directing attention to a stimulus placed inside the receptive field (RF) of a visual neuron enhances the firing rate compared with when attention is focused somewhere else (5, 6). With only a few exceptions (7–9), most single-unit recordings in awake-behaving primates have investigated the effects of sustained attention on sensory responses, using paradigms in which the focus of attention constantly remained on a stimulus or a stream of stimuli for up to several seconds (6, 10–12). Although the ability to attend to a stimulus for a prolonged period is of great importance, many real-life situations crucially require flexible shifts of the focus of attention to direct the limited processing capacities to the currently most relevant information.

Behavioral experiments have documented two different modes of attentional orienting. Exogenous, or reflexive, shifting of attention is driven by salient stimuli and occurs largely involuntarily (13), whereas endogenous attention is goal-directed and under voluntary control (14). Although both modes of attentional orienting enhance behavioral performance and neuronal responses, behavioral, neurophysiological, neuroimaging, and neuropsychological experiments have revealed important dissociations between them. According to behavioral studies, the effects of exogenous and endogenous attentional orienting have different temporal dynamics (15). Moreover, endogenous and exogenous attention differentially influence EEG gamma band activity recorded from scalp electrodes (16). Finally, the two modes of orienting are governed by partially segregated control networks (17) and are differentially affected in neuropsychological disorders such as autism spectrum disorder (18) or Alzheimer's disease (19).

These differences between the two modes of attentional orienting support the notion that they are distinct mechanisms that both affect the processing of sensory information. Here, we directly test whether exogenous and endogenous orienting differ in their modulation of single-neuron activity in extra-striate visual cortex.

Results

Two macaque monkeys were trained to fixate and to release a lever as soon as the target, a coherently moving random dot pattern (RDP) presented at a cued peripheral location, briefly changed its direction of motion. They also had to ignore changes in the direction of motion in two other RDPs that were presented simultaneously at other locations (distractors). Target and distractor changes occurred randomly in time. One of the three RDPs was always placed inside the classical RF of the neuron under study, the other two were outside, and each RDP moved either in the preferred or antipreferred direction of the neuron. The experiment consisted of three conditions: In simple cueing trials (Fig. 1*A*), the trial started with the presentation of the cue placed on a virtual line connecting the fixation point to the upcoming target. In shift cueing trials (Fig. 1*B*), a second cue appeared randomly during the trial, making one of the other two stimuli a target and thereby signaling the monkey to shift the spatial focus of attention. From the moment of shift cue onset, the monkey was only rewarded for responding to changes in the newly cued stimulus and had to ignore changes in the other two stimuli, including the previous target stimulus. Finally, in stay cueing trials (Fig. 1*C*) the second cue was presented at the same position as the first cue, instructing the monkey to continue attending to the already attended stimulus.

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§To whom correspondence should be addressed. E-mail: treue@gwdg.de.

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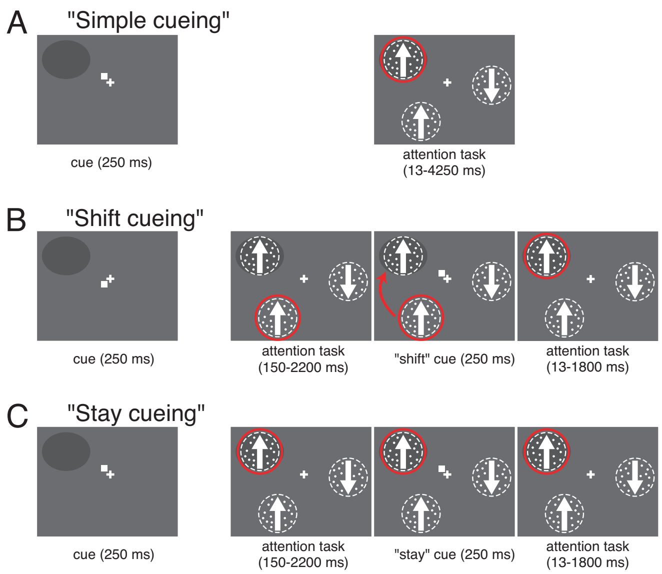

Fig. 1. Schematic trial structure for the three experimental conditions. After the monkey had acquired fixation, a small white square appeared (1.5° eccentricity), serving as the cue. After a short blank period, three RDPs were presented at equal eccentricity, one inside the classical RF (indicated by the dark gray patch), the other two outside. The red circle illustrates the focus of attention and was not shown in the actual experiment. (*A*) In the simple cueing condition, the monkey was rewarded for responding to brief changes in direction of motion of the cued target. (*B*) In shift cueing trials, a second cue appeared at a random time, instructing the monkey to shift attention to the newly cued stimulus. The depicted trial would be an example for the Shift A Out → In condition, because attention is shifted from the stimulus outside to the stimulus inside the RF. (*C*) In stay cueing trials, the second cue was presented at the same position as the first cue, signaling the monkey to stay focused on the already attended stimulus. The depicted trial would be an example for the Stay A In condition, because the cue instructs the monkey to keep attending to the stimulus inside the RF. Note that conditions in *B* and *C* are completely identical in sensory stimulation at the onset of the shift/stay cue.

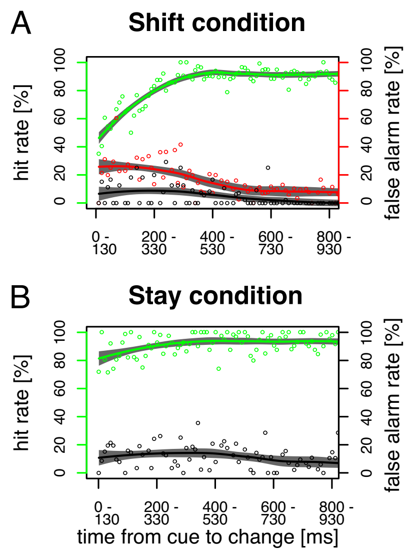

Fig. 2. Behavioral signatures of shifting attention. (*A*) Average hit rates for correctly detected targets (green), false alarm rates for the previously attended stimulus (red), and false alarm rates for the third, completely irrelevant, stimulus (black) plotted as a function of time between shift cue onset and direction change (130-ms duration). Hit rates for newly cued targets are decreased, and false alarm rates to the previously attended stimulus are increased for ≈300 ms after shift cue onset. (*B*) Corresponding data for the stay cueing condition. Here, the slight drop in hit rates for short intervals between cue and target illustrates the automatic attraction of attention by cue onset away from the target stimulus. The decrease in performance is much less pronounced compared with the shift condition. The solid lines depict the local polynomial regression (loess) fit to the data. The shaded areas indicate the 95% confidence interval for the fit. Because behavioral responses to direction changes could be triggered by either change onset or offset, we plot the corresponding change interval for each temporal bin.

Behavioral Performance. The behavioral performance for events occurring after the shift and stay cues provides a first indication that our paradigm induced both endogenous and exogenous shifts of attention. Fig. 2 shows hit rates (green circles) and false alarm rates (red and black circles) averaged across recording sessions as a function of time between shift cue or stay cue onset and the direction change. In the shift cueing condition (Fig. 2*A*), the monkeys achieved hit rates of ≈90% for changes occurring later than 550 ms after cue onset, whereas hit rates strongly declined for shorter delays between cue and target events. In approximately the same period, the monkeys made significantly more false alarms to the stimulus that was relevant before cue-onset (Fig. 2, red circles), while they successfully ignored changes in the third, completely irrelevant stimulus (Fig. 2, black circles). In the stay cueing condition (Fig. 2*B*), a small decrease in hit rates for short delays between the cue and target change is also evident. Considering the almost flat distribution of false alarm rates across time, this drop in performance most likely reflects the exogenous attraction of attention away from the relevant target RDP, triggered by the onset of the cue. This pattern of performance confirms behaviorally that attention was successfully manipulated in our paradigm.

Dynamics of Attentional Modulation. To investigate attentional modulation during shifts of attention we aligned neuronal responses to the random onset of the shift or stay cue. For all subsequent analyses we always compared shift and stay-cueing conditions in which the cue appeared at the same spatial location, but carried the information to either shift attention to a particular stimulus or maintain the current focus of attention (compare Fig. 1 *B* and *C*). In these comparisons, all sensory stimuli (including the cue) are completely identical. Only the starting location of the attentional focus and hence the meaning of the cue differs between conditions. Any modulation of neuronal responses must therefore reflect the effects of shifting the spatial focus of attention.

Fig. 3 shows the attentional modulation before and during shifts of attention. Fig. 3 *A–C* compares neuronal activity when attention is shifted into the RF (Shift A Out → In) against the condition in which the cue confirms the focus of attention inside (Stay A In). Fig. 3 *D–F* contrasts the conditions when attention is shifted out of the RF (Shift A In → Out) vs. stays on the stimulus outside (Stay A Out). In all conditions, attention is only shifted across space and not across stimulus features (i.e., directions of motion), because the attended RDPs inside and outside the RF always move in the preferred direction of the recorded neuron.

Effects of Sustained Attention Before Cue Onset. The neuronal modulations by sustained attention before shift or stay cue onset confirm that the monkeys attended to the designated target before the onset of the second cue. Our task design offers two different comparisons to assess the effects of sustained spatial attention before shift/stay cue onset. Comparison 1 involves attending inside before being cued to stay in vs. attending outside before shifting in (Fig. 3 *A–C*), and comparison 2 involves attending inside before shifting out vs. attending outside before being cued to stay out (Fig. 3 *D–F*). For both comparisons,

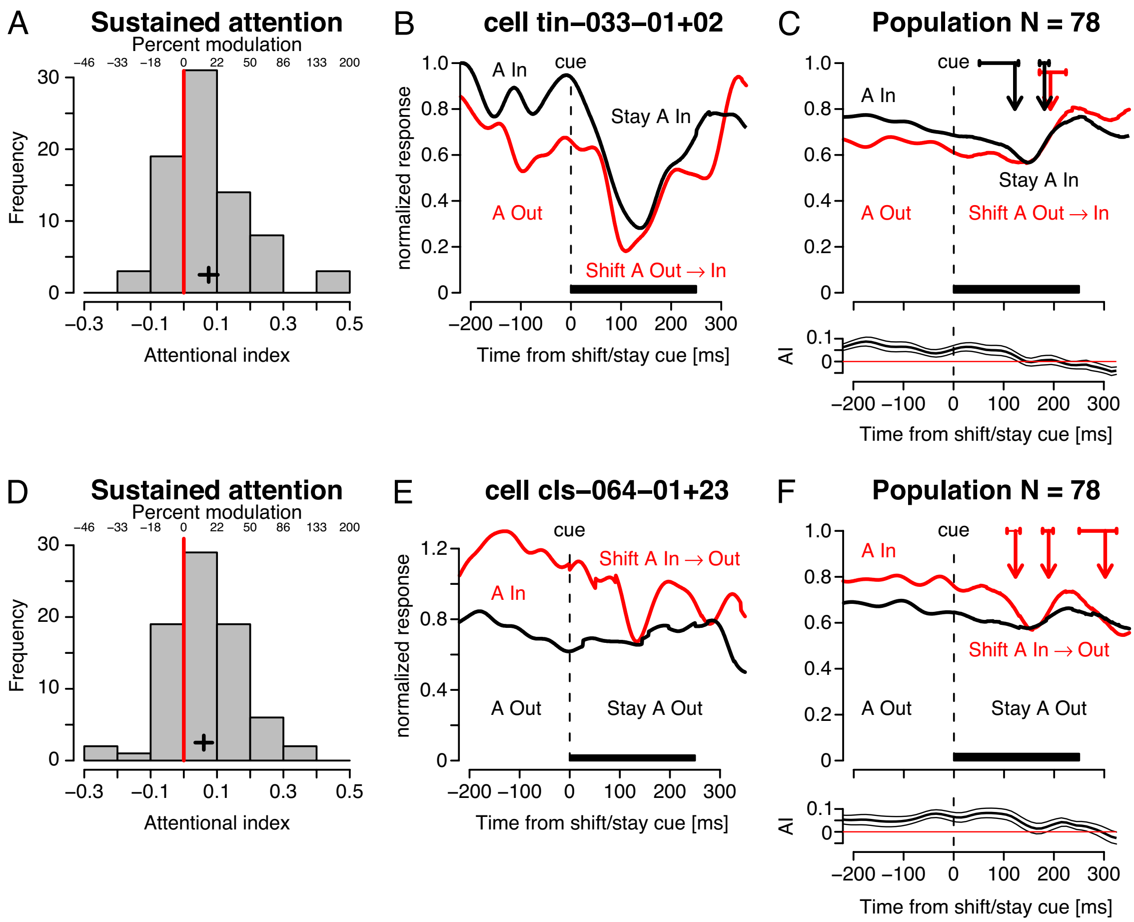

Fig. 3. Dynamics of attentional modulation, time-locked to the onset of the shift/stay cue (time 0). Before the onset of the shift or stay cue, neuronal activity is enhanced when attention is directed to the stimulus inside compared with outside the RF. (*A* and *D*) Distribution of spatial attention effects. The black crosses mark the average attentional modulation for each histogram, and horizontal arms span the 95% confidence interval of the means. (*B* and *C*) Single neuron data and population activity when attention is shifted from outside into the RF (red trace) or is cued to stay focused on the stimulus inside (black trace). (*E* and *F*) Illustration of conditions in which attention is shifted out of the RF (red trace) versus kept focused on the stimulus outside (black trace). The thick black horizontal bar marks the duration of the shift/stay cue; arrows indicate the average latency of the attentional modulation; adjacent horizontal lines cover the time interval corresponding to the 95% confidence interval for the mean. The time course of neuronal responses shows components of exogenous and endogenous attentional orienting. The initial, short-latency decrease of activity (≈120 ms; *C*, black trace; *F*, red trace) reflects the exogenous attraction of attention by the onset of the cue away from the RF because it even interrupts the endogenous focus of attention when the cue instructed the monkey to keep attending to the stimulus inside the RF. This effect of exogenous attention is only transient and levels off after ≈70 ms. Here, we observe both an increase of activity as attention is endogenously shifted into the RF (*C*, red trace, 190 ms) and a rebound of responses to the previously attended stimulus (*F*, red trace, 190 ms). Finally, endogenous disengagement of attention from the RF stimulus consists of a late decrease of responses (*F*, red trace, 300 ms). The time course of the attentional index (AI) is shown below *C* and *F*. See Fig. S3 for the same analyses performed on a selected sample of neurons.

average activity was higher when attention was directed to the stimulus inside versus outside the RF. We evaluated statistical significance of these effects by calculating, for each neuron separately, an attentional index (AI; see *Materials and Methods*) in a time window from 600 to 100 ms before cue onset. Fig. 3 *A* and *D* shows the distribution of AIs for comparison 1 and comparison 2, respectively. Across the recorded population of 78 neurons, the distribution of AIs was centered on positive values in both comparisons. The average AI corresponded to a 15% increase in responses (Fig. 3*A*: 16.2%, t test, $P = 8.34 \times 10^{-7}$; Fig. 3*D*: 12.8%, t test, $P = 1.27 \times 10^{-5}$). These effects replicate previous studies of sustained spatial attention (6, 12). See supporting information (*SI*) *Text* and Figs. S1 and S2 for additional analyses.

Time Course of Attentional Modulation During Shifts of Attention. To analyze the dynamics of attentional modulation we computed the latency at which neuronal activity changed most strongly (see *Materials and Methods*). In Fig. 3, we depict the average latency as an arrow with adjacent horizontal lines showing the time window that corresponds to the 95% confidence interval of the mean.

Fig. 3 *B* (single neuron) and *C* (population) compares neuronal activity when attention shifts into the RF vs. is cued to stay focused inside. In Fig. 3*C*, after the onset of the shift cue (time 0, vertical dashed line), population activity in the Shift A Out → In condition (red trace) increases with a latency of 193 ms (95% confidence interval: 170–222 ms) as attention is endogenously shifted into the RF. Across the recorded population, activity increased in 55 of 78 neurons at this latency, with the average slope of activity being significantly > 0 ($P = 5.6 \times 10^{-6}$, t test). In contrast, in the Stay A In condition (Fig. 3*C*, black trace), activity initially decreased with a latency of 122 ms after the onset of the stay cue (95% confidence interval: 51–129 ms). At this latency, a decrease of activity was evident in 54 of the 78 recorded neurons, and the average slope was significantly < 0 ($P = 0.002$, t test). This decrease of firing was followed by a response enhancement (maximal positive slope occurred at 181

ms, 95% confidence interval: 171–190 ms), which was also present in the majority of the recorded neurons (62 of 78, $P = 1.12 \times 10^{-5}$, t test). This increase brings activity back to approximately its level at the time of cue onset. Interestingly, the enhancement of activity in the Shift A Out → In condition exceeds the increase in the Stay A In condition such that responses to newly attended stimuli are 8.3% stronger than responses to stimuli that have been attended throughout the trial (for all 50-ms time windows betweeen 280 and 350 ms, P between 0.04 and 0.017).

We consider the early decrease of activity at ≈120 ms a signature of the involuntary capture of attention by the sudden onset of the cue (20), because this effect prevailed even though the cue signaled that attention should be kept focused on the already attended stimulus (Fig. 3 *B* and *C*, black trace). The subsequent enhancement of responses ≈70 ms later (Fig. 3 *B* and *C*, red trace), however, can only be attributed to endogenous orienting of attention because the cue only carried symbolic information about the location of the new target. Thus, the dynamics of attentional modulation show that automatic shifts of attention triggered by the onset of the cue occur in a distinct time window with a shorter latency compared with voluntary shifts of attention for which the position of the cue has to be interpreted.

Fig. 3 *E* (single neuron) and *F* (population) contrasts neuronal activity when attention is shifted out of the RF vs. is kept focused on a stimulus outside. After the onset of the shift cue, activity in the Shift A In → Out condition (Fig. 3*F*, red trace) decreased rapidly with a latency of 123 ms (95% confidence interval: 106–132 ms). Across the recorded population, activity decreased in 58 of 78 recorded neurons at this latency, and the average slope was significantly < 0 ($P = 4.49 \times 10^{-5}$, t test). Remarkably, although the cue instructed the monkey to shift attention out of the RF, the initial decrease was followed by a rebound of activity that was most pronounced at 189 ms (95% confidence interval: 177–198 ms). At this latency, firing increased in 52 of 78 recorded neurons ($P = 1.69 \times 10^{-5}$, t test). Only ≈110 ms later activity decreased again (302 ms, 95% confidence interval: 250–324 ms), with this effect being present in 48 of 78 neurons (average slope < 0, $P = 0.028$, t test). Finally, activity in the Shift A In → Out condition reached the level of activity in the Stay A Out condition (time window 220–270 ms, AI not significantly different from 0, $P = 0.09$; for all subsequent 50-ms intervals $P > 0.164$). Throughout, activity in the Stay A Out condition (Fig. 3*F*, black trace) remained stable across time.

The rapid latency of the early response decrease at ≈120 ms (Fig. 3 *E* and *F*, red trace) suggests that the effect can again be attributed to an exogenous pull of attention away from the RF because of the sudden onset of the cue. Interestingly, even though attention has already been automatically directed toward the new target, activity rebounds ≈190 ms, indicating that exogenous orienting has only a transient effect on neuronal firing and levels off after ≈70 ms. Importantly, the endogenous shift of attention is not a simple continuation of the shift induced by the exogenous pull of attention. Instead, the rebound of activity suggests that exogenous and endogenous mechanisms of orienting seem to be two, rather distinct, mechanisms with different time courses drawing on the same capacity-limited system.

Finally, in agreement with two studies in the ventral stream (8, 9), a comparison of latencies during endogenous attention shifts into (Fig. 3 *B* and *C*, red trace) and out of the RF (Fig. 3 *E* and *F*, red trace, final decrease) reveals that the allocation of attention to a new target occurs ≈120 ms earlier than the withdrawal of attention from a previously attended object. The time windows for endogenous allocation and withdrawal of attention do not overlap, indicating two temporally distinct neuronal processes.

Discussion

This study demonstrates that switches in the behavioral relevance of a stimulus are associated with characteristic modulations of sensory single-unit activity whose temporal dynamics depend on the nature of the orienting mechanism. A short-latency decrease of activity reflects the exogenous attraction of attention out of the RF. This exogenous influence is transient and levels off after ≈70 ms, when endogenous attention regains its influence. We observe a simultaneous increase of neuronal activity as attention is endogenously shifted into the RF, and a rebound of responses to the previously relevant stimulus, even when attention was exogenously pulled toward the newly cued target. This pattern of results shows that endogenous attention is interrupted by exogenous attention, and that shifts of endogenous attention out of the RF are not a simple continuation of the exogenous pull.

The observed patterns of attentional modulation can be most parsimoniously explained by assuming two distinct attentional mechanisms with markedly different temporal dynamics. This interpretation matches the findings from other studies of separable exogenous and endogenous attention including a classical behavioral study (21), which observed two distinct time periods in which rapidly streamed items could be identified after an exogenous cue. Trying to account for the pattern of modulation we observed by just a single mechanism of attention would require the assumption that spatial attention first shifts to the cue, then, rather than continuing to the new target, would return to what is now the distractor, only to turn around again ≈70 ms later. Although such a behavior cannot be ruled out it would come at the expense of rewarded behavior (the appropriate response to the new target) without any necessity or apparent benefit.

Investigating the influence of exogenous attentional capture during endogenous attentional control, Bisley *et al.* (7) reported neuronal correlates for both types of attentional allocation in the lateral intraparietal area (LIP). Neurons responded strongly when a distractor was flashed inside their RF while attention was focused elsewhere in the visual field, but their response did not decrease when attention was inside the RF and the flash occurred elsewhere. Hence, the neuronal modulation caused by endogenous effects of attention was not interrupted when attention was exogenously attracted to a different region in visual space. This finding is in contrast to our experiment in which sensory responses strongly decreased when attention was automatically attracted to a region outside the RF of the neuron under study. A likely explanation for this discrepancy is that the distractors used in the former study were task-irrelevant whereas the cue attracting attention in our study carried important information about whether to keep attending or to shift attention. It has been previously shown that exogenous capture of attention of irrelevant stimuli can be overridden by top-down control (22, 23), and that training can improve the resistance to stimulus-driven capture by lowering LIP responses to task-irrelevant distractors (24).

Interactions between endogenous and exogenous attentional influences on sensory and higher-order processing of visual information have recently been investigated by using event-related scalp potentials (ERP) in human subjects (25). Consistent with our single-neuron results, the ERP data support the hypothesis that exogenous and endogenous orienting represent two distinct mechanisms that have different, but partially overlapping, temporal dynamics. Exogenous attraction of attention dominated neural modulation in early stages of processing (120–150 ms), even when the current focus of endogenous attention was directed elsewhere. After a time period in which effects of both exogenous and endogenous attention were present (150–210 ms), endogenous attention dominated later

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(300–400 ms). These findings are in close agreement with our single-neuron results.

Recently, Khayat *et al.* (8) have provided a quantitative investigation of attentional modulations during endogenous shifts of attention using extracellular multiunit recordings in primary visual cortex (V1). Consistent with earlier findings in V4 by Motter (9), this study shows that enhancement of activity during allocation of attention precedes the decrease of activity caused by removal of attention. This temporal sequence of attentional modulations seems incompatible with a serial model postulating subsequent stages of disengagement, shifting, and engagement of attention (26), although the impact of this temporal asymmetry on overt behavior is still unclear. Our data on endogenous modulations are strikingly similar to the results reported by both studies, indicating that the same principle seems to hold for early and intermediate stages of visual processing in both ventral and dorsal pathways. A possible neuronal mechanism underlying this temporal asymmetry might be a shift of RFs toward the newly attended stimulus (27), with the leading edge of the RF shifting faster than the trailing edge. Such a distortion of RF shape has been reported in the context of predictive remapping during saccadic eye movements (28, 29). Here, RFs in LIP shift earlier toward the future saccade goal than away from the current fixation position (29), effectively increasing the RF size in the dimension toward the saccade target.

In conclusion, we show highly dynamic attentional modulations in extrastriate cortex that reflect changes in behavioral relevance on a very rapid time scale. Our data demonstrate the neural correlate of both exogenous and endogenous attentional orienting, which are controlled by two distinct, but interacting, mechanisms with a markedly different time course.

Materials and Methods

We recorded responses of 78 isolated direction-selective neurons in area MT of two macaque monkeys to moving RDPs in conditions of sustained attention and shifts of attention. Standard surgical techniques were used (30). Recordings were made by using a one-channel recording system (David Kopf Instruments) or a five-channel recording system (MiniMatrix; Thomas Recording); single units were isolated by using the Plexon Data Acquisition System. Cells were determined to be from MT by their physiological characteristics (directionality and RF position and size) and by the position of the electrode in the cortex. Only responses of neurons with a ratio of responses to preferred and antipreferred direction ≥3 were accepted for analyses. For a given neuron, we defined as the preferred direction the peak of a Gaussian fit to the responses to 12 different directions (sampled every 30°) in a condition when a single RDP was placed inside the RF while the animals detected a luminance change of the fixation point. The experiments in this study complied with the National Institute of Health Guide for the Care and Use of Laboratory Animals and were approved by the Regierungspräsidium Niedersachsen.

Stimuli. We used RDPs of small bright dots (density: 8 dots per degree^2, luminance 117 cd/m^2) plotted within a stationary circular virtual aperture on a background of either 1 or 25 cd/m^2, in earlier and later recording sessions, respectively. The size of the aperture was chosen to match the boundaries of the classical RF of the neuron under study as determined by a hand-mapping procedure. Movement of the dots was created by an appropriate displacement of each dot at the monitor refresh rate of 76 Hz. In every trial, three RDPs of equal size were presented, one positioned inside the recorded cell's classical RF, the other two positioned at equal eccentricity outside of the cell's RF.

Behavioral Task. The monkeys were trained to attend to a moving RDP (the target) in the presence of two other moving RDPs (the distractors) while maintaining fixation on a stationary fixation point. A trial started as soon as the monkey's eye position was within a fixation window of 1° radius centered on a fixation square (size: 0.2 × 0.2°); 150 ms after the monkey touched a lever, a white square (0.35 × 0.35°), serving as the cue, appeared at an eccentricity of 1.5° on a virtual line connecting the upcoming target to the fixation point. The cue lasted for 250 ms. After a blank period of 500 ms three RDPs appeared at different, but iso-eccentric, positions on the screen. Three stimuli were used to prevent the monkey from splitting attention and reduce the predictability of target assignments. These three RDPs coherently moved in either the preferred or antipreferred direction of the neuron under study for the remainder of the trial. All combinations of preferred or antipreferred directions in each stimulus were possible.

The experiment consisted of three conditions. In the simple cueing condition (33% of trials), the animals obtained a liquid reward for releasing the lever in response to a brief (130 ms) and subtle direction change in the target within a response time window of 60–700 ms after the change. The direction change occurred randomly between 13 and 3,700 ms after onset of coherent motion in the RDPs. The distractors could also change direction during the trial, but with a temporal separation of at least 500 ms. Trials in which both distractors, but not the target, changed their direction were rewarded after 4,250 ms, if the monkey did not release the lever. Trials in which the monkey broke fixation or responded outside of the reaction time window were considered errors and were aborted without reward. In the shift cueing condition (33% of trials), the cue appeared again (duration: 250 ms), randomly between 150 and 2,200 ms after onset of coherent motion, making one of the other two RDPs the target. The appearance of the second cue signaled the monkey to shift attention to the newly cued RDP and respond to direction changes in the new target. These direction changes could happen between 13 and 1,050 ms after the onset of the second cue. Again, in case of two distractor changes the monkey was rewarded to hold the lever until trial end. In the third condition, termed stay cueing (33% of trials), the timing of events was identical to the shift cueing trials with the exception that the second cue reappeared at the same position as the first cue, instructing the monkey to keep its attention focused on the target. The different conditions were randomly interleaved within the experiment.

Data Analysis. Data were analyzed offline by using Matlab (The MathWorks) and R. Average hit and false alarm rates were computed for each recording session in 10-ms bins (0–1,000 ms) after shift and stay cue onset, respectively, before being averaged across recording sessions. Average performance was fitted by using a local polynomial regression (loess) analysis, and bootstrap-estimated errors of the fit were obtained by resampling residuals.

For the analysis of neuronal data, only correctly completed trials were included. Response rates were determined by convolving the spike train in each trial with a Gaussian kernel ($\sigma = 30$). Only spikes that occurred before the first direction change (target or distractor event) after appearance of the second cue were considered. Responses were averaged across trials and normalized to the average response in the Stay A In condition (600–100 ms before cue onset), after subtraction of spontaneous firing rate. Population responses were computed by averaging across the normalized responses.

The effects of spatial attention were assessed in a time window of 600–100 ms before onset of the second cue. For each recorded neuron, the AI was computed: $AI = (fr_{AIn} - fr_{AOut})/(fr_{AIn} + fr_{AOut})$, where fr_{AIn} and fr_{AOut} are the mean responses if attention was directed to the stimulus inside and outside the RF, respectively. The AI is a conservative measure of the average attentional effect, which reduces the effect of outliers. Only trials in which the RDP inside and the attended RDP outside the RF moved in the preferred direction of the neuron were included in the analysis. The statistical significance of the AI was evaluated by using a one-sample *t* test.

To assess the time course of neuronal modulation we determined the slope of the average activity by fitting a linear regression line to each 50-ms interval, shifted by 1 ms (from cue onset to 350 ms after cue onset). We then determined the time points for which the slope was maximal and minimal, respectively. In case of the Shift A In → Out condition, in which two decreases of activity were evident, we first determined the point in time of maximal slope and then the minimal slopes before and after this temporal marker. We used a bootstrapping procedure to obtain confidence intervals for the latencies of modulation. A total of 1,000 bootstrap replications were simulated by randomly selecting individual neurons from the original recorded population with replacement. For each replication, the time points of maximal and minimal slopes were determined, using the procedure described above. The distribution of obtained latencies was used to construct 95% confidence intervals based on the BCa method (31). This slope-based method for latency estimates avoids the use of multiple statistical comparisons associated with a bin-based procedure in which the latency is often defined as the first of a number of bins that meet a significance criterion (32, 33). Furthermore, in comparison to procedures in which a theoretical function is fitted to the time course (8, 34), this procedure does not make assumptions about the shape of the time course of activity. Maximal and minimal slopes were compared against 0 by using *t* tests.

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