nature neuroscience

Neurons in macaque area V4 acquire directional tuning after adaptation to motion stimuli

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Neurons in area V4 of the macaque are generally not selective for direction of motion, as judged from their response to directional stimuli presented after a baseline condition devoid of movement. We used motion adaptation to investigate whether stimulation history influences direction-of-motion selectivity. We found that classically nondirectional V4 neurons develop direction-of-motion selectivity after adaptation, an observation that underscores the dynamic nature of functional cortical architecture.

The ability of a neuron to process information about direction of motion is conventionally determined by how well it can discriminate between stimuli with different directions of motion when they are presented after a non-moving stimulus baseline condition[1]. This method, referred to here as the classical stimulation condition (**Fig. 1a**), has led to the notion of single-unit feature selectivity, which is central to current understanding of the mechanisms underlying sensory processing and perception[2]. Relatively little is known, however, about how the properties of neurons in higher cortical areas change as a function of adaptation[3]. A recent functional magnetic resonance imaging (fMRI) study using a motion adaptation condition found a high direction-of-motion selectivity index in macaque area V4 (ref. 4). This is notable because it seems to contradict results obtained by electrophysiology using classical stimulation conditions, which indicate that few directionally selective neurons are found in area V4 (ref. 5). The discrepancy led our group[4] to propose that initially nonselective area V4 neurons may acquire directional selectivity after adaptation. Here we test this hypothesis by recording from neurons in area V4 and asking whether adaptation to a moving stimulus affects the neuron's direction of motion selectivity.

We recorded from 62 neurons from two monkeys (*Macaca mulatta*; experiments approved by the Regierungspraesidium) and characterized the directional tuning properties of each unit using drifting coherent random dot patterns (**Fig. 1a**,**b**). In agreement with previous studies, we found that the majority (86%) of V4 neurons are not significantly tuned to direction of motion during the classical stimulation condition. We also mapped the post-adaptation tuning functions of the neurons after they had been adapted to a coherent random dot pattern moving in a particular direction for a period of approximately 1 s (**Fig. 1b**). Notably, we found that a large fraction (33%) of the non–directionally selective V4 neurons showed post-adaptation directional selectivity (**Fig. 1c–h**).

Random dot stimuli were presented after a period of exposure to uniform intensity according to the classical condition. The illustrated neuron's response did not differ significantly (**Fig. 1c**, two-tailed paired *t*-test, $P > 0.1$) when the neuron was stimulated with coherent random dot patterns moving in one of two different directions (left or down). This might lead one to conclude that this neuron cannot differentiate between stimuli moving leftward and those moving downward. However, this is no longer true after adaptation. When the random dot patterns were preceded by an adapting drifting dot stimulus that moved upward, the neuron became selective, having a higher firing rate when the stimulus moved leftward than downward (**Fig. 1d**, two-tailed paired *t*-test, $P < 0.005$). We measured the pre- and post-adaptation tuning functions of this neuron using coherent random dot patterns with eight different directions of motion distributed equally from 0° to 360° (**Fig. 1e**,**f**). Its pre-adaptation tuning function (**Fig. 1e**) did not deviate significantly from circular uniformity. In other words, the neuron was not directionally selective when tested with the classical stimulation condition (Rayleigh test, $P > 0.5$). In contrast, it showed significantly unimodal tuning after adaptation (Rayleigh test, $P < 10^{-5}$, **Fig. 1f**). The pre- and post-adaptation tuning functions of another neuron isolated from a second monkey are also shown (**Fig. 1g** and **h**, respectively).

The increased tuning for direction of motion observed after adaptation in the single-cell examples described above was also evident across the population of V4 neurons. An examination of the magnitudes of the normalized resultant vectors (which serve as directional tuning indices; see **Supplementary Methods** online) of the pre- and post-adaptation tuning functions of area V4 neurons (**Fig. 2**) showed that the average magnitude over all visually driven neurons was significantly higher after adaptation (**Fig. 2a**). This was true for each monkey independently (two-tailed paired *t*-test, $P < 10^{-3}$ for monkey D, $P < 0.05$ for monkey A).

This phenomenon is not simply the result of increased sharpening of the tuning functions of neurons that are already directionally selective. A large proportion of units that were initially not directionally selective became significantly tuned after adaptation. Out of 62 V4 neurons we recorded from, 49 (79%) were visually responsive. Of those, only seven (14%) were significantly tuned to direction of motion before adaptation (Rayleigh test, $P < 0.05$, Bonferroni corrected; the mean magnitude of the normalized resultant vectors for these neurons was 0.16 ± 0.03, mean $\pm$ s.e.m.), in agreement with other published results[5]. Of the remaining 42 initially non–directionally selective neurons, 14 (33%) became significantly tuned after adaptation (Rayleigh test, $P < 0.05$, Bonferroni corrected; the mean magnitude of the normalized resultant vectors for these neurons was 0.23 ± 0.05). If

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Published online 17 April 2005; doi:10.1038/nn1446

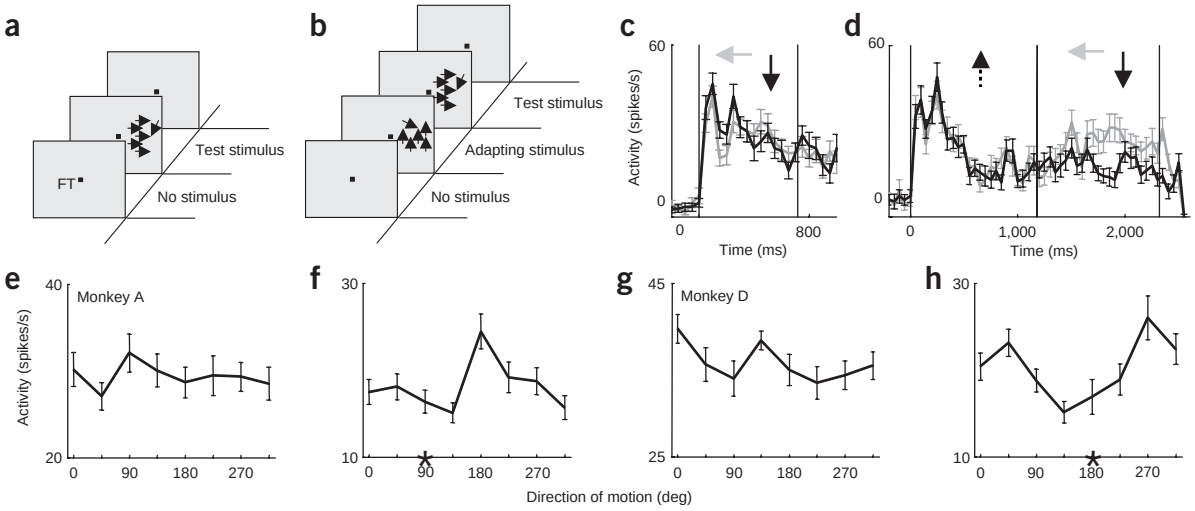

Figure 1 Classical versus adaptation stimulation condition. (**a**) Classical condition. Fixation target (FT), drifting 60% coherent random dots represented by arrows. (**b**) Adaptation condition. Adapting stimulus presented for ~1 s preceding test stimulus. (**c**) Spike-time histograms (50-ms bins) showing mean response and s.e.m. of a single neuron stimulated with drifting random dots (between the vertical lines) moving toward 180° left and 270° down (classical condition). The number of spikes elicited did not differ significantly between the two stimulus directions (two-tailed paired *t*-test, $P > 0.1$). (**d**) Spike-time histogram (50-ms bins) of the same neuron during the adaptation condition. During the adaptation phase (between first two vertical lines), the stimulus was moving upward (90°, dotted arrow). During the testing phase (between the second and third vertical lines), the stimulus was moving either left (gray) or down (black). The neuron's response was significantly different for the different directions of motion during the testing phase (two-tailed paired *t*-test, $P < 0.005$). (**e**) Pre-adaptation tuning function of the same neuron as in **c** and **d** computed using the number of spikes in a 600-ms bin starting 100 ms after stimulus onset. It was not significantly tuned (Rayleigh test for circular distribution, $P > 0.5$). (**f**) Post-adaptation tuning function of the same neuron, after adapting to upward motion (asterisk), was now significantly tuned (Rayleigh test, $P < 10^{-5}$). (**g**,**h**) As in **e** and **f** for a different neuron from another monkey. The pre-adaptation tuning function was not significantly tuned (Rayleigh test, $P > 0.3$), whereas the post-adaptation tuning function was (Rayleigh test, $P < 10^{-4}$).

we consider the responses of all 49 visually responsive neurons, 17 (35%) were significantly tuned to direction of motion after adaptation, compared to only 7 (14%) before adaptation. This difference was significant (McNemar's test using χ^2 goodness of fit, $P < 0.05$). Four representative neurons are illustrated (**Fig. 2b**). The pre-adaptation tuning functions (black) did not show significant direction-of-motion selectivity (Rayleigh test, $P > 0.05$, Bonferroni corrected). In contrast, the post-adaptation tuning functions (gray) were all significantly selective (**Fig. 2b**, Rayleigh test, $P < 0.05$, Bonferroni corrected).

We examined how the direction of motion of the adapting stimulus influenced the profile of post-adaptation tuning functions of V4 neurons that were not directionally selective before adaptation (Rayleigh test, $P > 0.05$). On average, after adaptation, V4 units became tuned to a direction of motion shifted away from the adapting direction. The mean post-adaptation tuning function relative to the direction of the adapting stimulus (0°) is not uniform along all directions of motion but has a significant dip along the direction of motion of the adapting stimulus (Wilcoxon signed-rank test, $P < 0.01$; **Fig. 3a**). This dip cannot be due to a bias present in the pre-adaptation tuning functions, because all neurons examined were non–directionally selective before adaptation (no dip, Wilcoxon signed-rank test, $P > 0.1$). A polar histogram of the number of post-adaptation tuning functions plotted against their peak direction of motion relative to the adapting direction (0°) shows that fewer post-adaptation tuning functions have their preferred direction of motion

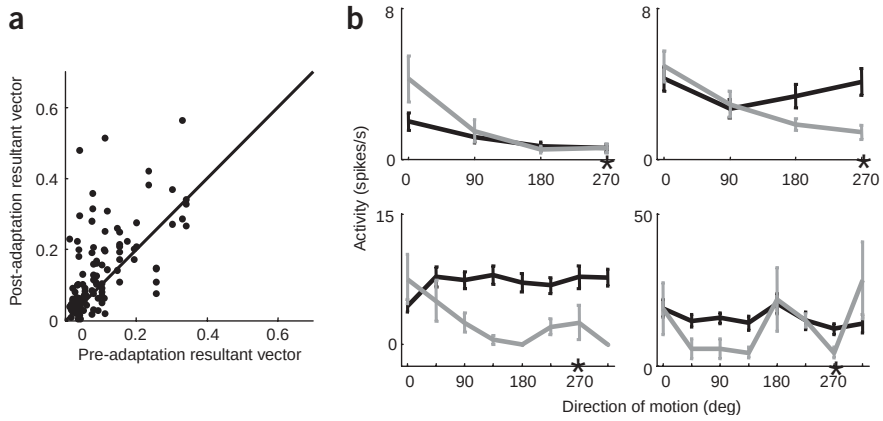

Figure 2 Population analysis. (**a**) Magnitude of resultant vectors of pre- and post-adaptation direction-of-motion tuning functions plotted against each other for all visually responsive neurons and all adaptation directions tested. Resultant vectors were computed based on number of spikes from 100 to 500 ms after stimulus transition. Only neurons whose activity was significantly higher than the no-motion baseline for both classical and adaptation conditions were included (two-tailed paired *t*-test, $P < 0.05$). Average resultant vector magnitude was significantly higher for post-adaptation than for pre-adaptation tuning functions (two-tailed paired *t*-test, $P < 10^{-5}$; individually, for monkey D, $P < 10^{-3}$ and for monkey A, $P < 0.05$). The average magnitudes of the pre- and post-adaptation resultant vectors were 0.09 ± 0.0079 (± s.e.m.) and 0.134 ± 0.01, respectively. (**b**) Non–significantly tuned pre-adaptation (black) tuning functions of four neurons (Rayleigh test for circular distribution, $P > 0.05$, Bonferroni corrected). Their post-adaptation functions (gray) were significantly tuned (Rayleigh test, $P < 0.05$, Bonferroni corrected). Black stars indicate adapting direction.

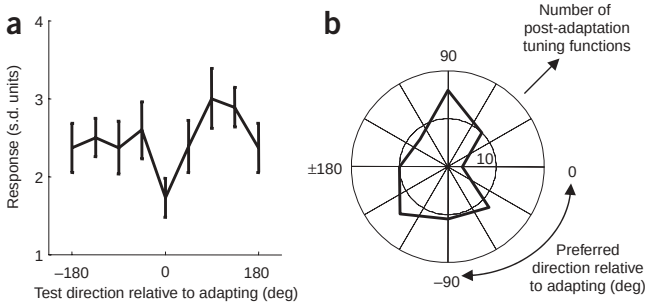

Figure 3 Relationship between direction of motion of adapting stimulus and post-adaptation tuning functions. (**a**) Average post-adaptation tuning function relative to direction of motion of adapting stimulus. The contributing neurons were selected on the condition that they were visually responsive (two-tailed paired *t*-test, $P < 0.05$, Bonferroni corrected) and their pre-adaptation tuning functions were not significantly tuned (Rayleigh test, $P > 0.05$). Before averaging, each neuron's post-adaptation tuning function was normalized by subtracting the mean activity elicited by the direction of motion that gave the minimal response and by dividing by its standard deviation (thus obtaining a *z*-score). The average post-adaptation tuning function was tuned (response along 0° adapting direction was significantly lower than average response over all other directions; Wilcoxon signed-rank test, $P < 0.01$). (**b**) Number of post-adaptation tuning functions with a particular preferred direction of motion relative to the adapting direction (0°). The number of post-adaptation tuning functions that had their preferred direction of motion along the adapting direction (0°) was significantly smaller than the average number of post-adaptation tuning functions whose preferred direction of motion was in any other direction (χ^2 test, $P < 0.05$).

aligned with the adapting direction than would be expected from a random distribution (**Fig. 3b**, χ^2, $P < 0.05$). Because the shape of the post-adaptation tuning functions depends strongly on the direction of motion of the adapting stimulus (**Fig. 3a**), our observations cannot result from a nonspecific, motion-independent adaptation mechanism.

Our findings also cannot be the result of eye movement artifacts. Monkeys typically fixated in a window of 0.5° radius, but still generated small-amplitude saccades (microsaccades) during fixation. Microsaccades can modulate the responses of neurons from area V1 to the inferior temporal cortex[6]. To ensure that the post-adaptation motion direction selectivity is not an epiphenomenon of different microsaccade patterns, we excluded from our analysis all microsaccade-containing trials for any neuron whose activity was significantly modulated by microsaccades (see **Supplementary Methods** online).

In summary, a substantial proportion (33%) of visually responsive, non–directionally selective macaque area V4 neurons became tuned to the direction of motion after adapting to a moving stimulus. One way this could happen is through input from motion-selective areas. Macaque area V4 is heavily interconnected with area MT/V5 (refs. 7,8), so some V4 neurons could be receiving input from a heterogeneous population of MT/V5 neurons with different preferred directions of motion. If a V4 neuron receives balanced input from the different directional columns in MT/V5, it will not be directionally selective when studied using classical stimulation conditions. However, it can acquire directional selectivity after adaptation, provided that its MT/V5 inputs are differentially weakened after exposure to the adapting stimulus. Experiments combining recordings with inactivation could test the contribution of MT/V5 to the direction-of-motion selectivity observed in V4 units after adaptation. A similar mechanism could work with inputs from other direction of motion–selective areas such as V1, V3 or V3A, or from V4 units classically tuned to direction of motion.

In fMRI studies, adaptation stimuli have recently been used to indirectly deduce the properties of single units[4,9,10]. Our study illustrates how fMRI can be applied to generate hypotheses that can be further tested with electrophysiology experiments, an often-cited benefit of combined fMRI-electrophysiology studies. Our findings suggest that caution should be exercised when interpreting fMRI results obtained using adaptation stimuli as evidence that neurons are classically tuned to the adapting stimuli. Simply put, the manifestation of blood oxygen level–dependent (BOLD) signal adaptation in a brain area may simply reflect adaptation in the inputs it receives from other areas.

Evidence suggests that V4 neurons are involved in the computation of visual saliency maps to guide visual attention and eye movements[11–13] by emphasizing significant aspects of the sensory input and de-emphasizing potential distractors. In addition, our findings suggest that, after adaptation, area V4 neurons are more likely to respond to changes in the direction of motion of the stimulus (that is, to have increased sensitivity to temporal kinetic contrast). This information may then be used to compute a saliency-attention map. In support of this, after V4 lesions a drop in performance occurs when motion is needed to compute saliency maps[14,15], despite the absence of substantial deficits in motion perception *per se*.

Post-adaptation changes in selectivity are probably not unique to area V4 and are likely to exist in other brain areas. Characterizing neuronal properties across the visual system under different adaptation conditions will likely yield important new information about the brain's functional organization.

Note: Supplementary information is available on the Nature Neuroscience website.

ACKNOWLEDGMENTS

This study was supported by the Max Planck Society, a National Research Service Award from the National Eye Institute (NEI) of the US National Institutes of Health to A.S.T. and a KO8 award from the NEI to S.M.S. We thank S.-P. Ku, G. Rainer, T. Siapas and N. Sigala for helpful discussions and J. Werner for computer support.

COMPETING INTERESTS STATEMENT

The authors declare that they have no competing financial interests.

Received 17 December 2004; accepted 30 March 2005
Published online at http://www.nature.com/natureneuroscience/

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