Visual impairment by surrounding noise is due to interactions among stimuli in the higher-order visual cortex

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Kumano H, Uka T. Visual impairment by surrounding noise is due to interactions among stimuli in the higher-order visual cortex. J Neurophysiol 112: 620–630, 2014. First published May 14, 2014; doi:10.1152/jn.00639.2013.—Observers have difficulty identifying a target in their peripheral vision in the presence of surrounding stimuli. Although hypotheses addressing this phenomenon have been proposed, such as the integration of stimuli and surrounding suppression in the higher-order visual cortex, no direct comparisons of the psychophysical and neuronal sensitivities have been performed. Here we measured the performance of monkeys with a variant of the direction discrimination task using a center/surround bipartite random-dot stimulus while simultaneously recording from isolated neurons from the middle temporal visual area (MT). The psychophysical threshold increased with the addition of a task-irrelevant noise annulus that surrounded the task-relevant motion stimuli. The neuronal threshold of MT neurons also increased at a spatial scale similar to the psychophysical threshold. This suggests that the impaired ability in our task resulted from impairment in the MT area. Importantly, reduced neuronal performance was due to both a reduced response to preferred motion and an enhanced response to nonpreferred motion. These observations suggest that impairment caused by surrounding noise results from interactions between stimuli and noise and not from a reduction in the response of visual neurons.

HUMAN OBSERVERS CANNOT IDENTIFY the characteristics of a target in their peripheral vision in the presence of surrounding stimuli, a phenomenon that is linked to reading disorders (Martelli et al. 2009) and neurodegenerative diseases (Crutch et al. 2012). Previous psychophysical investigations have revealed a number of different phenomena in which performance declines in the presence of surrounding stimuli. These include overlap or ordinary masking, lateral masking, surround suppression, and visual crowding (Levi 2008). Neurophysiological studies have also shown effects of surrounding stimuli. The most prominent effect is surround suppression, where the surrounding stimulus suppresses the neuronal response (Allman et al. 1985). However, surrounding stimuli can also affect neuronal responses in other ways, such as collinear facilitation (Polat et al. 1998). Additionally, a crowding model proposes an interaction between the target and surrounding stimuli within the receptive field (RF) of a neuron (Levi 2008). To date, the neuronal mechanisms underlying psychophysical impairment due to surrounding stimuli are largely unknown, predominantly because a direct comparison of behavioral and neuronal sensitivities during impairment has never been performed.

In this study, we used the well-established role of the middle temporal visual area (MT) in motion-direction discrimination to better understand the neural mechanism underlying visual impairment in the presence of surrounding stimuli (Britten et al. 1992, 1996; Newsome and Paré 1988; Salzman et al. 1992). We devised a variant of the direction discrimination task in which monkeys discriminated the direction of motion of a central random-dot stimulus surrounded by a task-irrelevant noise annulus that contained no coherent motion. We recorded data from isolated neurons from area MT while two monkeys performed the task. The addition of the noise annulus led to impaired psychophysical performance. Neuronal performance was also impaired, at a spatial scale similar to that for psychophysical performance. Importantly, the degraded neuronal sensitivity was due to both a reduced response to preferred motion and an elevated response to nonpreferred motion when stimuli were surrounded by noise. These results suggest that interactions between stimuli and noise within the RFs of neurons in extrastriate areas, and not a reduction in neuronal response, underlie impaired performance in the presence of surrounding stimuli.

MATERIALS AND METHODS

The details of animal preparation and the experimental procedures were described previously (Kumano and Uka 2010; Uka and DeAngelis 2003). Below, we briefly summarize specific aspects relevant to the present study. All animal care, training, and experimental procedures were performed in accordance with National Institutes of Health guidelines and were approved by the Juntendo University Animal Care and Use Committee.

Subjects and Surgery

We used two Japanese macaque monkeys (Macaca fuscata), one female (monkey P; 6 kg) and one male (monkey K; 6 kg). Animals were prepared for experiments with standard aseptic surgeries. A post for head restraint and a recording chamber were implanted chronically in each monkey. Scleral search coils were then implanted into both eyes to monitor eye movements (Judge et al. 1980). A cylindrical recording chamber was mounted over the occipital cortex ~17 mm lateral and 14 mm dorsal to the occipital ridge at an angle of 25° above the horizontal, so that area MT could be accessed by passing through the striate cortex and extrastriate visual areas in the lunate sulcus.

Visual Stimuli

Each monkey was seated in a primate chair with its head restrained and facing a tangent screen at a viewing distance of 57 cm. A DLP projector (Mirage S+2K, Christie Digital Systems) back-projected a visual stimulus onto the tangent screen subtending a visual angle of 122° × 91°. Stimuli were presented dichoptically via a pair of
ferroelectric liquid crystal shutters (DisplayTech) that were mounted just in front of the monkey’s eyes. Stereo half-images for the left and right eyes were presented alternately at a frame rate of 100 Hz (i.e., 50 Hz refresh for each eye) synchronized with the vertical refresh of the video input. However, this study did not investigate stereoscopic processing; therefore, all stimuli were presented at the preferred disparity (see below).

Random-dot stimuli were presented with an OpenGL accelerator board with quad-buffer stereo support (Quadro FX 1400, NVIDIA). Each random-dot stereogram (RDS) was presented within a circular aperture. The dot density was 64 dots per square degree per second, with each dot subtending ~0.1°. The starting position of each dot was newly randomized in each trial. The RDS consisted of red dots (5.3 cd/m²) presented on a black background (0.10 cd/m²). Precise binocular disparities and smooth motion were achieved by plotting dots at subpixel resolution with the antialiasing technique provided by the OpenGL board.

Behavioral Task and Training

Behavioral tasks and data acquisition were controlled with a commercial software package (TEMPO, Reflective Computing), and all data analyses including online data visualization were performed with MATLAB (MathWorks). First, the monkeys were trained on a fixation task in which they were required to fixate a yellow dot (0.15° × 0.15°). The monkeys received a drop of water as a reward when the conjugate eye position remained within a 2.0° electronic window around the fixation point during stimulus presentation (500 ms). If the monkeys broke fixation during the trial, the trial was terminated and no reward was dispensed.

The monkeys were trained on the motion-direction discrimination task, in which they chose between two opposing directions of motion (Britten et al. 1992). After the monkey had fixated for 300 ms, the random-dot motion was presented for 500 ms in a peripheral visual field. The monkey was then required to indicate the direction by making a saccade to one of the two choice targets that appeared immediately after the simultaneous offset of the stimulus and the fixation point. The choice targets were located on both sides of the fixation point at an eccentricity of 5° and aligned along the axis of the direction of stimulus motion. The motion signal was titrated by manipulating the percentage of coherently moving dots, termed motion coherence. The saccade had to be made to one of the two choice targets within 1 s of their appearance, and the saccade end point had to remain within a 5.0° × 5.0° window around the target for at least 150 ms to be considered a valid choice. Correct choices were rewarded with a drop of water. Discrimination training began with 100% motion coherence, and lower coherence was introduced gradually after monkeys reached at least 75% accuracy, when the range of coherence levels was lowered to measure the psychophysical threshold.

Subsequently, the monkeys were trained on a variant of the direction discrimination task (Fig. 1) in which a coherent random-dot motion was surrounded by a noise annulus of dots with 0% coherence. Therefore, this task required the monkeys to ignore the surrounding noise and report the direction of the center stimulus. There was no gap between the center patch and the noise annulus. Initially, the task training proceeded by introduction of a very thin noise annulus. After the monkeys discriminated the direction of the central motion in the presence of the noise annulus correctly (~75% correct), the width of the noise annulus was increased gradually. Before recording commenced, the monkeys were trained extensively with center stimuli with various directions, speeds, binocular disparities, and locations in the visual field and with noise annuli of varying diameters. This allowed us to tailor the stimulus to the preference of each neuron being studied.

Fig. 1. Schematic illustration of the task. A visual stimulus consisting of central random-dot motion (inner dashed line) and a surrounding noise annulus (outer dashed line) was presented over the receptive field (RF) of a neuron (shaded area). This illustration shows the diameter of the surrounding noise at twice that of the center (2C). Filled dots represent coherently moving dots, and open dots represent randomly replotted dots. Choice targets were aligned along the axis of motion of the center patch. Monkeys were required to report the motion direction of the center patch by making a saccade to 1 of 2 targets, FP, fixation point.

Electrophysiological Recordings

We used a tungsten microelectrode (FHC) with impedance values of 0.5–2.0 MΩ at 1 kHz to record the extracellular activity of single neurons. The electrode was advanced through the cortex via a transdural guide tube with a pulse motor micromanipulator (MO-951, Narishige) mounted on the recording chamber. Raw signals from the electrode were amplified and band-pass filtered (200–10,000 Hz) with conventional electronic equipment (Bak Electronics). Single neurons were isolated with a voltage-time window discriminator (Bak Electronics). The action potential and trial event occurrence times were stored to disk at a resolution of 1 ms. Eye position was monitored with a magnetic search coil system (Sankeikizai) and then stored to disk at 250 Hz. Area MT was identified on the basis of the interpretation of the pattern of gray and white matter encountered during electrode penetration and of the physiological response properties (direction, speed, horizontal disparity tuning, RF location, and size) of both single neurons and multunit clusters. Data were collected from 60 MT neurons (32 from monkey P, 28 from monkey K). The median eccentricity of the stimulus location was 11.1° for monkey P and 14.0° for monkey K.

Experimental Protocols

After isolation of a single MT neuron, we explored RF size and location qualitatively and also assessed the tuning properties (direction, speed, and binocular disparity) of the neuron, using a small circular patch of random-dot motion. Next, we performed a set of quantitative preliminary experiments to measure the speed tuning, binocular disparity tuning, RF size and location, size tuning (area summation), and direction tuning of each MT neuron. Each of these measurements was performed in a separate block of randomly interleaved trials, with each unique stimulus being presented at least three times. During these tests a tuning curve or RF map was constructed online, and the preferred stimulus parameter was used in subsequent tests. First, speed tuning was measured by presenting dots that drifted at speeds of 0, 1, 2, 4, 8, 16, 32, and 64°/s. Binocular disparity tuning was then measured at the preferred speed by presenting dot patterns with a binocular disparity that varied from ~1.6° to +1.6° in steps of 0.4°. Next, we mapped the RF by presenting a small (~0.25 times the approximate RF diameter) patch of random dots drifting at the preferred speed and binocular disparity at each location on a 4 × 4 grid that covered the entire RF. A two-dimensional Gaussian function with an identical radius along two cardinal axes was fitted to this RF.
map. This test was designed to obtain quantitative estimates of the RF center and diameter. After determining the RF center, we assessed the size tuning by presenting dots within circular apertures at the RF center. Aperture sizes with diameters of 1°, 2°, 4°, 8°, 16°, 32°, and 64° were captured. Subsequently, direction tuning was measured by presenting eight motion directions 45° apart using all other optimal parameters. The preferred direction and its opposite (null) direction were determined by visual inspection of the tuning curve.

After these quantitative tuning tests, we recorded MT responses while the monkey performed the discrimination task. For each experiment, the direction, speed, and binocular disparity of the center patch being discriminated were adjusted to the optimal parameters of the neuron being studied. The surrounding noise annulus was always at the preferred disparity. The motion coherence of the center patch varied among five levels (5%, 10%, 20%, 40%, and 80%). Ideally, we would have tested various combinations of center and surround size. However, we were unable to do so because of time limitations. Preliminary experiments revealed that the data changed depending on eccentricity; therefore, the diameter of the center patch was set at 30% of the RF eccentricity. This size was smaller than the typical RF size of the MT neurons (Albright and Desimone 1987). The diameter of the surrounding noise was selected from among no noise and 2, 4, 8, and 16 times the center diameter. The center patch was always laid on top of the surrounding noise. The number of stimulus conditions was 50 (5 coherences × 2 directions × 5 surround diameters). Motion coherence, motion direction (preferred or null), and the diameter of the surrounding noise were randomly interleaved within a block. Whenever possible, data were collected from 20 or more repetitions of each unique stimulus condition, and data were discarded if unit isolation was not maintained for at least 10 repetitions. The average number of trial repetitions was 20 [5 standard deviations (SD)], and the mean number of total trials was 1,006 (228 SD) across the range of accepted data sets.

Data Analysis

**Psychophysical threshold.** To quantify psychophysical performance during the discrimination task, we first assessed the psychometric function by plotting the proportion of correct choices as a function of motion coherence across the range of surrounding noise diameters (Fig. 2A). The psychometric function was fit with a cumulative Weibull function with psignifit version 2.5.6, a MATLAB software package that implements the maximum-likelihood method of Wichmann and Hill (2001a). The cumulative Weibull function is given by

$$p = 1 - 0.5e^{-(c/a)^b}$$

where $c$ is the motion coherence of the center patch, $p$ is the proportion of correct responses, $\alpha$ defines the threshold at 82% correctness, and $b$ gives the slope of the curve.

**Neuronal threshold.** The neuronal response under each stimulus condition was defined as the mean firing rate across trials in the time window of visual stimulus duration (500 ms). The spontaneous firing rate was calculated from spiking activity during the presentation of a blank screen. Then, to characterize the discrimination performance of MT neurons in the task, we used ROC analysis to calculate neuronal thresholds based on the neuronantieroneuron formulation used by Britten et al. (1992). A ROC curve was constructed from the distribution of responses to the preferred and null directions at each coherence level for each surround diameter. The area under the ROC curve (AUC) was used to measure the ability of an ideal observer to discriminate between the two directions solely on the basis of the responses of the recorded neuron (Green and Swets 1966). The neurometric function was constructed by plotting the AUC against motion coherence, followed by fitting with a cumulative Weibull function using the maximum-likelihood method (Fig. 3A).
INTERACTION AMONG STIMULI UNDERLIES SURROUND IMPAIRMENT

Fig. 2B, we examined the data with a difference-of-error (DoE) function. The DoE function is given by

\[
\text{Threshold}(d) = \text{Threshold}_0 + A_1 \times \text{erf} \left( \frac{d}{a} \right) - A_2 \times \text{erf} \left( \frac{d}{b} \right),
\]

where \( d \) is the noise diameter and \( \text{Threshold}_0, A_1, A_2, \) and \( b \) are free parameters. For data without a decrease in threshold at the largest noise diameter (fitted parameter \( A_2 = 0 \)), the spatial scale was taken from the fit as the noise diameter at which the curve reached 95% of its maximal value, similar to previous analyses of size tuning measurements (DeAngelis and Uka 2003; Pack et al. 2005). For data with a decrease in threshold \( (A_2 > 0) \), the spatial scale was taken as the peak of the DoE fit. In principle, we should not fit a DoE function with parameters to data consisting of five points. Therefore, we tested cubic spline interpolation. Interpolation of these relatively coarse data, however, often produced oscillations between data points that seemed to be inappropriate, particularly near 16 times the center diameter, where the spline fit was constrained by only one point on the exterior. Therefore, we simply extracted the peak position of the DoE curve without extracting the parameter.

Receptive field measurements. We first quantified the RF size for each neuron, using the RF mapping data at \( 4 \times 4 \) resolution. A two-dimensional Gaussian function with equal radii along two axes was fitted to the RF map. We used 2 SD as a measure of the RF diameter, where SD was taken from the fitted Gaussian, as described previously (Britten and Heuer 1999).

We also assessed the RF size by fitting the size-tuning curve with the DoE function model as used above. The DoE model incorporates the subtractive interaction between the center and surrounding mechanisms and is calculated as follows:

\[
R(w) = R_0 + A_e \times \text{erf} \left( \frac{w}{a} \right) - R_s \times \text{erf} \left( \frac{w}{b} \right),
\]

where \( w \), \( A_e \), \( a \), \( b \), and \( (b > a) \) are the diameter of the stimulus, the excitatory amplitude, the size of the excitatory RF, the spontaneous firing rate (the response to zero size), and the amplitude and size of the suppressive surround mechanism, respectively. For data with a decrease in response at the largest size (fitted parameter \( A_2 = 0 \)), the RF size was taken as the peak of the DoE fit. For data without a decrease (fitted parameter \( A_2 = 0 \)), the RF size was taken from the fit as the size at which the curve reached 95% of its maximal value.

For each size-tuning curve, we computed the percentage of surround suppression as

\[
\% \text{Surround Suppression} = 100 \times \left( \frac{R_{\text{opt}} - R_{\text{largest}}}{R_{\text{opt}}} \right),
\]

where \( R_{\text{opt}} \) is the response to the optimal size (determined from the curve fit) and \( R_{\text{largest}} \) is the response to the largest size. This metric was always computed from the DoE model fit.

Choice probability. We quantified the trial-to-trial covariation between MT responses and behavioral choices by calculating the choice probability (CP) (Britten et al. 1996). For each direction, motion coherence level, and surround diameter, the responses of the MT neuron were sorted into two groups based on the choice that the monkey made at the end of each trial (preferred vs. null choice). A ROC curve was calculated from these response distributions, and the AUC gave the CP for that stimulus condition. To arrive at a single grand CP for each neuron, responses were normalized (using \( z \)-scores) separately for each stimulus condition (unique combination of direc-

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tion, motion coherence, and surround diameter). The z-scored responses were then combined across stimulus conditions into a single pair of distributions for preferred and null choices. Trials under stimulus conditions in which the monkey made choices preferentially to one target >75% of the time were excluded (Uka and DeAngelis 2004). ROC analyses were performed on this pair of distributions to yield the grand CP.

**Statistics.** We used the bootstrap technique (Efron 1979) to estimate the confidence interval of the psychophysical and neuronal thresholds. For psychophysical data, we first obtained the distributions of bootstrapped (1,000 times) thresholds under each noise condition with psignifit software (Wichman and Hill 2001b). The distributions of differences in thresholds were constructed from all possible combinations and permutations of the bootstrapped thresholds, and the 95% confidence interval was defined by the 2.5 and 97.5 percentiles of the distribution. Differences in the psychophysical thresholds between two surrounding noise conditions were considered significant if the 95% confidence intervals did not include zero.

For neuronal data, we adopted the resampling method described by Read and Cumming (2003). All calculations in this resampling were performed on the square root of the firing rates. First, for each stimulus condition (unique combination of direction, coherence, and noise diameter), residuals were calculated by subtracting the mean response measured under that condition from the response measured in individual trials. Subsequently, residuals were pooled across all stimulus conditions. At each resampling run, a value was drawn randomly (with replacement) from the pool of residuals. The selected residual was added to the original mean square-root response for a particular stimulus condition, and the sum was then squared to generate a resampled firing rate. The neurometric function generated from the hypothetical data set was fit with a cumulative Weibull function, as described above. This procedure was repeated 1,000 times, and threshold values were obtained. Similar to the approach used for psychophysical data, the differences in neuronal thresholds between two noise conditions were considered significant if the 95% confidence intervals of the difference in thresholds did not include zero.

**RESULTS**

The monkeys were required to distinguish between two possible directions of random-dot motion surrounded by a noise annulus that contained no coherent motion and to indicate their choice by making a saccade to one of two targets (Fig. 1). Because preliminary psychophysical experiments showed that the results described below changed depending on eccentricity, the diameter of the center patch was fixed at 30% of the RF eccentricity. We chose this center size as it was smaller than the typical RF size of MT neurons (Albright and Desimone 1987). Therefore, both the target (central coherent motion) and a portion of the surrounding noise annulus were presented within each RF. The diameter of the surrounding noise annulus varied from zero (no noise) to 16 times the center diameter in octave steps. Henceforth, for convenience, we refer to the diameter of the surrounding noise as no noise, 2C, 16C, etc.

**Spatial Scale of Psychophysical Performance**

Psychophysical performance depended on both the motion coherence of the center patch and the diameter of the surrounding noise annulus. The psychometric function obtained from an example experiment is shown in Fig. 2A. The proportion of correct responses was plotted against the motion coherence of the center patch across the diameters of surrounding noise. The fitted psychometric functions (Fig. 2A) revealed a detrimental effect of the surrounding noise, as can be seen by the rightward shift of the psychometric functions for conditions that included the surrounding noise annulus compared with no noise. To assess the effects of increasing noise diameter on discrimination performance, the psychophysical thresholds were plotted against the noise diameter, as shown in Fig. 2B. The threshold increased as the noise diameter increased to 13.3° and then decreased at the largest noise. Statistically, there was a difference in threshold between no noise and all diameters with noise, between 2C and 4C, between 2C and 8C, and between 4C and 8C (bootstrap, P < 0.05). This pattern is consistent with the results of a human psychophysical study that used the same task (Sasaki and Uka 2011). However, as described below, the decrease in psychophysical threshold at the largest noise was not observed consistently at the population level.

To estimate the spatial scale of performance impairment in our task, the psychophysical threshold as a function of noise diameter was fitted with a DoE function. For the example experiment shown in Fig. 2, A and B, the psychophysical threshold decreased from intermediate to the largest noise. Therefore, the peak position of the DoE fit (Fig. 2B) was taken as the size of the psychophysical interaction. In this example experiment, the psychophysical interaction size was 13.3°, which corresponded to a 4C noise condition. This corresponded to approximately the target eccentricity (11.1°).

To analyze the spatial scale of interaction at the population level, we first selected a subset of data with psychophysical thresholds <100% for all noise diameters. This is because motion coherence cannot, by definition, be greater than 100%; therefore, a threshold of >100% was unreliable. This selection left 29 data sets from monkey P and 28 from monkey K. There was a statistically significant difference in the threshold depending on the noise diameter across these data sets, even when the analysis was restricted to data from 2C to 16C (repeated-measures ANOVA, P < 0.05). Therefore, there was a systematic change in threshold depending on the noise diameter. For individual cases, thresholds changed depending on the amount of noise (2C to 16C) in 44 of 57 cases (bootstrap, P < 0.05). When the psychophysical interaction sizes were plotted against eccentricity (Fig. 2C), the regression slope through the origin was 1.28 for monkey P and 1.09 for monkey K. Note that, by task design, the data were constrained to be lower than 16C, and those below 2C were unreliable. Nevertheless, these results suggest that the psychophysical interaction size was approximately equal to the eccentricity at the population level.

**Spatial Scale of Neuronal Performance Was Equivalent to That of Psychophysical Performance**

Neuronal performance was quantified with standard ROC analyses (Britten et al. 1992). Figure 3A presents a plot of a neuron’s correct performance (area under the ROC curve) against motion coherence. In this example neuron, the increase in the noise diameter to 13.3° led to an increase in the neuronal threshold, which then decreased at the largest noise, as occurred for the psychophysical threshold (Fig. 3B). Statistically significant differences were found in the thresholds between no noise and all diameters with noise, between 2C and 4C, and between 4C and 16C (bootstrap, P < 0.05). Similar to the
approach used for psychophysical performance, we examined the spatial scale of interaction for neuronal performance, using the DoE function fit. The neuronal interaction size for this example neuron was 14.6° (Fig. 3B).

Across the data set that had neuronal thresholds <100% for all noise diameters (53 neurons: 28 from monkey P and 25 from monkey K), a statistically significant difference in threshold was found depending on the noise diameter, even when the analyses were restricted to data from 2C to 16C (repeated-measures ANOVA, \( P < 0.05 \)). For individual cases, the thresholds changed depending on the amount of noise (2C to 16C) in 23 of 53 cases (bootstrap, \( P < 0.05 \)).

To compare the sizes of the neuronal and psychophysical interactions across the population, we selected data that had neuronal and psychophysical thresholds <100% for all noise diameters. The psychophysical interaction sizes of these 52 neurons (27 from monkey P and 25 from monkey K) were plotted against the neuronal interaction sizes (Fig. 3C). The geometric mean of the ratio of the two interaction sizes (neuronal and psychophysical) was 0.96, which did not significantly differ from unity (sign test, \( P = 0.58 \)). This analysis could be problematic if the sizes of both the psychophysical and neuronal interactions were either smaller than the 2C or larger than the 16C noise diameter. However, the correspondence between neuronal and psychophysical interaction sizes held true, even when we restricted the data so that both interaction sizes were larger than the 2C and smaller than the 16C noise diameter (\( n = 33 \), sign test, \( P = 0.73 \)). Therefore, these results suggest that the sizes of the neuronal and psychophysical interactions were roughly equivalent and that the impaired performance of the monkeys could be explained by impaired performance of the MT neurons.

We further examined whether spatial interaction occurred within or beyond the RF by analyzing data obtained in a separate RF mapping experiment. A two-dimensional Gaussian function with equal radii along two axes was fitted to the RF map. We used 2 SD as a measure of RF diameter, as described previously (Britten and Heuer 1999). The RF diameter of the example neuron shown in Fig. 3A and B, was 11.9° (Fig. 3B), which was slightly smaller than the neuronal interaction size (14.6°). The neuronal threshold at 11.9° (43.6%) was similar to that at 14.6° (45.5%), suggesting that 94.4% of the rise in threshold from no noise to the peak occurred within the RF. Therefore, the detrimental interaction in neuronal performance occurred primarily within the RF of this neuron. The same held true at the population level. Overall, neuronal interaction size was slightly larger than RF diameter (Fig. 3D; Wilcoxon signed-rank test, \( P = 0.02 \)). Furthermore, 89.2% of the rise in threshold from no noise to the peak occurred, on average, within the RF.

If the spatial interaction within the RF underlies the observed impairments, we might expect larger degradation in neuronal performance for neurons that have larger RFs. To test this hypothesis, we examined the relationship between RF diameter and the impairment in neuronal performance. Because the RF size is positively related to eccentricity, we quantified RF size as the ratio of RF diameter to eccentricity. Impaired neuronal performance was quantified as the ratio of neuronal threshold at 4C noise to that at no noise. Data revealed that the RF size ratio was significantly correlated with the impaired neuronal performance (\( r_s = 0.46, P = 4.9 \times 10^{-5} \)).

Finally, we analyzed whether the inhibitory surround mechanism of MT neurons was related to the neuronal impairment caused by the surrounding annulus. We quantified the strength of the surround suppression from the size-tuning curve (DeAngelis and Uka 2003). There was no correlation between the impairment in neuronal performance (the ratio of neuronal threshold at 4C noise to that at no noise) and the strength of surround suppression (\( r_s = -0.15, P = 0.27 \)). The results suggest that the neuronal impairment by the surrounding annulus was due to interaction inside the RF and not to the RF surround.

**Degraded Neuronal Performance Was Due to Both Reduced Response to Preferred Motion and Elevated Response to Nonpreferred Motion**

Although the analyses described above revealed that the interaction sizes were equivalent in behavior and MT neuron performance and that the interaction occurred primarily within the RF, the underlying response changes in neuronal performance are yet to be elucidated. Specifically, it is unclear whether neural degradation is due to the integration of stimulus and noise information or simply to a reduction in the response to noise. To address this issue, we examined how changes in the sensitivity of neurons to motion coherence explained the observed impairment in neuronal discrimination performance. The responses of modal MT neurons scaled linearly with motion coherence (Britten et al. 1993). Therefore, for each neuron, we first fitted linear equations to the coherence-response functions for both the preferred and null directions (Fig. 4A). The intercept (responses to 0% motion coherence) was forced to be identical in the two directions. From these fits, we extracted the coherence sensitivity for both the preferred and null directions (slope of the fitted line) as well as the response to 0% motion coherence. In the example neuron shown in Fig. 4A, the response to the preferred motion direction decreased whereas that to the null motion direction increased. Thus the sensitivity to both the preferred and null directions decreased under the 2C noise condition compared with the no-noise condition.

This pattern was also observed at the population level. For all neurons, we calculated the sensitivity to both the preferred and null directions. The mean sensitivities for the preferred and null directions across the population were plotted against the noise diameter (Fig. 4C), and the mean responses to both directions at 80% motion coherence along with those to 0% motion coherence were plotted against the noise diameter (Fig. 4D). The sensitivity for the preferred direction (Fig. 4C) decreased under the 2C noise condition but increased slightly under the larger noise conditions. The sensitivity for the null direction (Fig. 4C) decreased steadily with larger noise. Although the response to the preferred direction was reduced at all noise diameters, the response to the null direction first increased and then decreased with larger noise diameters (Fig. 4D).

We also examined whether the response variance changed depending on the stimulus. We calculated the Fano factors for each stimulus condition and compared them among conditions. The Fano factor increased slightly when the noise diameter increased (repeated-measures ANOVA, \( P < 0.0001 \)). To determine which factor contributed most to impaired neuronal performance, we applied a partial correlation analy-
Because the sensitivities for the preferred and null directions are described by the responses to the preferred and null directions and 0% coherent motion, these three factors, as well as the Fano factor, were included in the partial correlation analysis. The impaired neuronal performance was quantified as the ratio of the neuronal threshold observed at 4°C noise to that observed at no noise. The changes in responses for the preferred and null directions and 0% coherent motion were quantified as the ratio of the response at 4°C noise to that at no noise.

In the partial correlation analysis, we used a subset of 54 neurons that met two criteria: 1) responses (preferred and null directions) under the no-noise condition were larger than zero (to avoid division by zero), and 2) neuronal thresholds under the no-noise and 4°C noise conditions were >100%. Significant partial correlations were obtained between the threshold ratio and the response to the preferred direction (coefficient = \(-0.53, P < 0.0001\)) and the response to the null direction (coefficient = \(0.44, P = 0.001\)). This suggests that the impaired neuronal performance was due to both a reduction in the response to the preferred direction and an elevation in the response to the null direction but not to changes in the response variance.

Because the reduction in sensitivity for the null direction was due to an increased response to the nonpreferred motion direction, the degraded neuronal performance cannot be explained simply by a reduction in response due to noise. Alternatively, both the reduction in the response to the preferred direction and the elevation in the response to the null direction could be explained by response normalization, i.e., the spatial summation properties of stimuli within an RF (Britten and Heuer 1999). Therefore, the degradation is conceivably due to interactions between stimulus and noise within the RF.

Reduced Impairment at Largest Noise

We frequently observed that the neuronal threshold under the largest noise condition was lower than that under an intermediate noise condition (Fig. 3B). This suggests that neuronal performance was recovered under the largest noise condition compared with an intermediate noise condition. Below, we analyze this observation with a more quantitative approach.
For psychometric analysis, we used the subset of neurons with psychophysical thresholds <100% for all noise diameters (n = 57, the same as that used in Fig. 2C). Across this subset, the psychophysical thresholds were significantly affected by the diameter of the surrounding noise (repeated-measures ANOVA, P < 0.0001). We then performed a pairwise multiple-comparison test using the Wilcoxon signed-rank test with Bonferroni correction (the threshold of significance, P = 0.05, was divided by the number of comparisons, 10) to compare the median thresholds among the various noise conditions. The median psychophysical threshold observed under the no-noise condition was 11.7%. The threshold increased significantly to 23.0% under the 2C noise condition but did not change significantly for larger noise diameters (P > 0.005).

We used a different subset for the neural data that had neuronal thresholds <100% for all noise diameters (28 from monkey P and 25 from monkey K). The surrounding noise had a significant effect on neuronal thresholds (repeated-measures ANOVA, P < 0.0001). The median neuronal threshold first increased from 11.1% at no noise to 30.0% at 4C noise and then decreased to 25.6% at 16C noise. Both the increase and decrease in neuronal thresholds were statistically significant (Wilcoxon signed-rank test, P < 0.0001 and P = 0.0002, respectively). Individual responses of the neurons (12 of 53) showed a decrease in threshold at the largest noise condition but did not change significantly across different stimulus conditions. Grand CPs were calculated with ROC analysis of the z-scored response distribution sorted according to the monkeys’ choices. Figure 6A shows the histogram of grand CPs for the population of MT neurons (n = 60). The median grand CP was 0.59 (0.60 for monkey P and 0.59 for monkey K), which was significantly larger than 0.5 (sign test, P < 0.0001). Seventy percent of neurons (42/60) had grand CPs that were significantly different from 0.5 (permutation test, P < 0.05), with most (39/42) being >0.5. This suggests that the responses of MT neurons were positively correlated with the choices made by monkeys in the discrimination task.

Having established a functional coupling between MT responses and behavioral choices, we next examined the relationship between the recovery of neuronal performance and grand CPs on a neuron-by-neuron basis. For each neuron, we quantified the extent of recovery in neuronal performance as the ratio in neuronal thresholds under the 4C and 16C noise conditions. A simple correlation between the recovery of neuronal performance and grand CP is inappropriate because the neuronal threshold is negatively correlated with CP (Britten et al. 1996; Nienborg et al. 2012; Purushothaman and Bradley 2005; Uka and DeAngelis 2004). Therefore, we examined the relationship between the recovery of neuronal performance at the largest noise and the magnitude of CPs. The size of a CP did not depend on either the signed motion coherence of the central target or the diameter of the surrounding noise (2-way ANOVA, P > 0.2 for both factors and their interaction). Therefore, we combined the responses across different stimulus conditions. Grand CPs were calculated with ROC analysis of the z-scored response distribution sorted according to the monkeys’ choices. Figure 6B shows the histogram of grand CPs for the population of MT neurons (n = 60). The median grand CP was 0.59 (0.60 for monkey P and 0.59 for monkey K), which was significantly larger than 0.5 (sign test, P < 0.0001). Seventy percent of neurons (42/60) had grand CPs that were significantly different from 0.5 (permutation test, P < 0.05), with most (39/42) being >0.5. This suggests that the responses of MT neurons were positively correlated with the choices made by monkeys in the discrimination task.

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Covariance Between Neuronal Responses and Behavioral Choices

The results described in the previous section suggest that the discrimination performance of MT neurons recovered at the largest noise diameter compared with an intermediate noise diameter. If the monkey relied on the activities of these neurons to perform the discrimination task, we would expect to observe a relationship between the neuronal responses and the monkeys’ behavioral choice. We calculated the correlation between the trial-to-trial fluctuation in neuronal responses and the monkeys’ choices, termed the choice probability (CP; Britten et al. 1996). Previous studies have shown that the CPs of MT neurons recorded while monkeys performed a direction discrimination task were significantly higher than chance (Britten et al. 1996; Cohen and Newsome 2009). Significant CPs may provide information regarding how individual sensory neurons contribute to perceptual decision making (Britten et al. 1996; Nienborg et al. 2012; Purushothaman and Bradley 2005; Uka and DeAngelis 2004). Therefore, we examined the relationship between the recovery of neuronal performance at the largest noise and the magnitude of CPs. The size of a CP did not depend on either the signed motion coherence of the central target or the diameter of the surrounding noise (2-way ANOVA, P > 0.2 for both factors and their interaction). Therefore, we combined the responses across different stimulus conditions. Grand CPs were calculated with ROC analysis of the z-scored response distribution sorted according to the monkeys’ choices. Figure 6A shows the histogram of grand CPs for the population of MT neurons (n = 60). The median grand CP was 0.59 (0.60 for monkey P and 0.59 for monkey K), which was significantly larger than 0.5 (sign test, P < 0.0001). Seventy percent of neurons (42/60) had grand CPs that were significantly different from 0.5 (permutation test, P < 0.05), with most (39/42) being >0.5. This suggests that the responses of MT neurons were positively correlated with the choices made by monkeys in the discrimination task.

Fig. 5. Reduced impairment at the largest noise. The thresholds at an intermediate noise diameter (4C) are plotted against the thresholds at the largest noise diameter (16C) for both psychophysical (A) and neuronal (B) thresholds. Error bars indicate SD (bootstrap resampling).
between the neuronal thresholds and the threshold ratio (Uka 2011). Finally, the monkeys seemed to selectively read out (Levi and Carney 2009; Li et al. 2000; Põder 2006; Sasaki and demonstrated less impairment with larger surrounding stimuli.

DISCUSSION

We found a significant negative correlation between neuronal thresholds under the no-noise condition and grand CPs ($r_s = -0.39$, $P = 0.004$). There was no correlation between the neuronal thresholds and the threshold ratio ($r_s = -0.04$, $P = 0.79$). We calculated a rank partial correlation between the recovery in neuronal performance and grand CP after controlling for the effect of neuronal threshold under the no-noise condition. This was equivalent to calculating the correlation between the two residuals of linear regressions (grand CP against neuronal threshold and ratio of neuronal thresholds against neuronal threshold). The resulting partial correlation was significantly positive ($r_s = 0.45$, $P = 0.0007$; Fig. 6B), suggesting that MT neurons with enhanced performance recovery at the largest noise had a stronger impact on the decisions made by the monkeys.

Our results suggest that the deterioration in discrimination performance by surrounding stimuli resulted from the integration of signals from the center and surrounds of the visual stimulus in a higher-level visual area, not from a reduced response of the visual neurons. Furthermore, neuronal performance recovered frequently at a larger noise annulus, consistent with the results of recent psychophysical studies that demonstrated less impairment with larger surrounding stimuli (Levi and Carney 2009; Li et al. 2000; Pöder 2006; Sasaki and Uka 2011). Finally, the monkeys seemed to selectively read out information from neurons that showed recovered performance with increased noise. Although the behavioral results are consistent with various types of visual impairment, the neuronal data are consistent with the integration theory of crowding (Levi 2008). We discuss the implications of our findings below.

**Behavioral Assessment of Impairment Caused by Surrounding Annulus**

There are a number of different phenomena in which performance declines in the presence of surrounding stimuli. These include overlap or ordinary masking, lateral masking, surround suppression, and visual crowding. Ordinary masking is usually effective only when the mask overlaps the signal. Therefore, the impairment observed in our task is not ordinary masking because the motion signal in the center patch and the noise in the surrounding annulus were segregated spatially. Distinguishing our task among lateral masking, surround suppression, and crowding is rather difficult. Typical psychophysical studies examining crowding have used discrete stimuli as the targets and distracters and have varied the distance between a single-element target and distracter. In contrast, the present study used a multielement target (i.e., random-dot stimulus) and varied the area of a surrounding annulus that was always adjacent to the central target (Sasaki and Uka 2011). We adopted this stimulus configuration for two reasons. First, we aimed to promote the integration of the target and distracter information within individual RFs of MT neurons. Second, by using the random-dot motion-direction discrimination task, we aimed to leverage our understanding of the role of area MT in this task (Parker and Newsome 1998) to investigate the neuronal mechanisms underlying behavioral impairment by surrounding stimuli. Several diagnostic criteria for crowding have been proposed recently (Levi 2008; Whitney and Levi 2011), the most prominent of which is that the spatial extent of crowding is proportional to target eccentricity (Bouma 1970). Our data are consistent with this criterion, although this does not demonstrate that the impairment observed in our task was indeed crowding. Another criterion is that crowding reduces identification or discrimination performance but not detection. Other criteria include target size independence, radial-tangential anisotropy, and an outward-inward asymmetry. Whether these criteria apply to our task is currently unknown, and the question merits future psychophysical study.

Several recent human psychophysical studies have found that visual impairment paradoxically decreased when a large amount of surrounding stimuli was presented (Levi and Carney 2009; Li et al. 2000; Pöder 2006; Sasaki and Uka 2011). The mechanisms hypothesized to explain this recovery in performance include figure-ground segregation (Li et al. 2000), bottom-up salience (Pöder 2006), and contraction of the integration field when large surrounding stimuli were presented (Sasaki and Uka 2011). In contrast to human performance, the behavioral performance of monkeys did not recover consistently at the largest surrounding annulus. Nevertheless, we did record several individual sessions in which performance recovered (e.g., Fig. 2B), suggesting that performance can recover at the largest surrounding annulus. However, this phenomenon was poorly reproducible. Although we trained the monkeys extensively, it is possible that, on some days, the monkeys did not focus on the center target but instead discriminated the...
Neuronal Mechanisms of Impairment Caused by Surrounding Annulus

This study quantified neuronal and behavioral discriminability in a manner that made them directly comparable (Parker and Newcombe 1998). The psychophysical and neuronal interaction sizes were similar (Fig. 3C), suggesting that the impairment occurred in a higher-level visual area such as the MT. This implies that the monkeys could not filter out surrounding stimuli at scales much smaller than the RF of MT neurons, presumably because they do not have access to neurons that have small RFs and the sensitivities required to solve the task. The detrimental interaction occurred within the RF of individual MT neurons. Therefore, the impaired performance was due mostly to integration within the RF and not solely to suppressive influences from the area surrounding the RF. Indeed, neuronal impairment was greater for neurons with a larger RF. When the RF sizes were estimated with the area-summation curve, the neuronal interaction sizes were larger than the size of the RF. This suggests that some of our results could be explained by effects beyond the RF. Interestingly, neuronal impairment was not correlated with the optimal neuronal size determined from the peak of the size-tuning curve. Similarly, neuronal impairment was not correlated with the degree of surround suppression. Because the size-tuning curve considers both the excitatory and inhibitory components of the RF, we speculate that neuronal impairment is more closely related to the excitatory than to the inhibitory RF.

Neuronal impairment was correlated with a reduced response to the preferred direction and an increased response to the null direction. Therefore, impairment by the surrounding noise annulus was due to reduced sensitivity that arose from interactions between the center and surround stimuli in both the preferred and null directions. Importantly, the sensitivity decrement for the null direction was due to an elevated, not a suppressed, response. This suggests the importance of not only measuring responses to the optimal stimulus but also characterizing all components that contribute to discrimination.

Response linearity to motion coherence was preserved with the addition of the surrounding annulus; only the slopes changed. The change in slopes could be explained by excitatory responses to 0% coherent motion and a normalization of the response (Britten and Heuer 1999). Because the response to 0% coherent motion is weaker than that to preferred motion but stronger than that to null motion, the addition of the surrounding annulus could decrease the response to preferred motion and increase the response to null motion without disrupting linearity. Therefore, impairment by surrounding stimuli could be explained by interactions between stimuli and noise in visual neurons, such as response normalization.

Selective Readout of Task-Relevant Sensory Signals

Several recent studies using CP have revealed selective and flexible strategies employed by monkeys during the performance of particular tasks (Nienborg and Cumming 2007; Purushothaman and Bradley 2005; Sasaki and Uka 2009; Uka and DeAngelis 2004). Ignoring the surrounding noise is an efficient strategy in the task used in the present study. If monkeys had full command of the neurons from which information should be read out, the best strategy for solving the task would be to selectively read out the information from neurons that did not exhibit a reduced sensitivity with surrounding noise. If this were the case, we might expect a correlation between CP and the degree to which neurons exhibited reduced sensitivity with surrounding noise. We did not find such a relationship.

Instead, we found that CPs were higher in neurons with increased recovered performance at the largest noise diameter (Fig. 6B). The MT neurons with recovered performance were relevant to the task because they were good at “ignoring” the surround at a larger surround size. One might wonder why the recovery in neuronal performance and CPs were correlated despite the lack of recovery in average psychophysical performance. One interpretation is that the monkey may have used signals from neurons with recovered sensitivity on some days. However, when the monkey failed to use these signals, behavior did not recover. To examine this possibility, we split the data into two sets: one with recovered behavior at 16 C compared with 4 C noise and one without. For the data showing behavioral recovery at the 16 C noise (n = 29), CP and the recovery in neuronal performance were significantly correlated (r = 0.41, P = 0.027). For the data showing no recovery (n = 25), there was no correlation (r = 0.14, P = 0.50). These results suggest that, on some days, monkeys selectively read out task-relevant MT neurons, resulting in recovered performance at the largest noise annulus, but they failed to do so on other days.

This raises the question of how monkeys selectively read out information from neurons that led to recovered performance at the largest noise size but did not read out information from those without degraded sensitivity. We speculate that this could be related to the mechanisms underlying the two types of neurons. Degraded sensitivity could be explained by response normalization. Conversely, recovery in performance at the largest noise diameter may be due to both surround suppression and response normalization (Kumano and Uka 2012). Therefore, it is possible that monkeys could selectively read out neurons with differing degrees of surround suppression but not with response normalization. The results of studies on the functional architecture of MT neurons support this view. Specifically, neurons with surround suppression are clustered within the MT (Born 2000), but no such clustering has been observed for response normalization. Future studies addressing this issue may shed new light on how selective readout is achieved in the brain.

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DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: H.K. and T.U. conception and design of research; H.K. performed experiments; H.K. analyzed data; H.K. and T.U. interpreted results of experiments; H.K. prepared figures; H.K. drafted manuscript; H.K. and T.U. edited and revised manuscript; H.K. and T.U. approved final version of manuscript.

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