

# Fine Discrimination Training Alters the Causal Contribution of Macaque Area MT to Depth Perception

Syed A. Chowdhury<sup>1</sup> and Gregory C. DeAngelis<sup>1,2,\*</sup>

<sup>1</sup>Department of Anatomy and Neurobiology, Washington University School of Medicine, St. Louis, MO 63110, USA

<sup>2</sup>Department of Brain and Cognitive Sciences, Center for Visual Science, University of Rochester, Rochester, NY 14627, USA

\*Correspondence: [gdeangelis@cvs.rochester.edu](mailto:gdeangelis@cvs.rochester.edu)

DOI 10.1016/j.neuron.2008.08.023

## SUMMARY

When a new perceptual task is learned, plasticity occurs in the brain to mediate improvements in performance with training. How do these changes affect the neural substrates of previously learned tasks? We addressed this question by examining the effect of fine discrimination training on the causal contribution of area MT to coarse depth discrimination. When monkeys are trained to discriminate between two coarse absolute disparities (near versus far) embedded in noise, reversible inactivation of area MT devastates performance. In contrast, after animals are trained to discriminate fine differences in relative disparity, MT inactivation no longer impairs coarse depth discrimination. This effect does not result from changes in the disparity tuning of MT neurons, suggesting plasticity in the flow of disparity signals to decision circuitry. These findings show that the contribution of particular brain area to task performance can change dramatically as a result of learning new tasks.

## INTRODUCTION

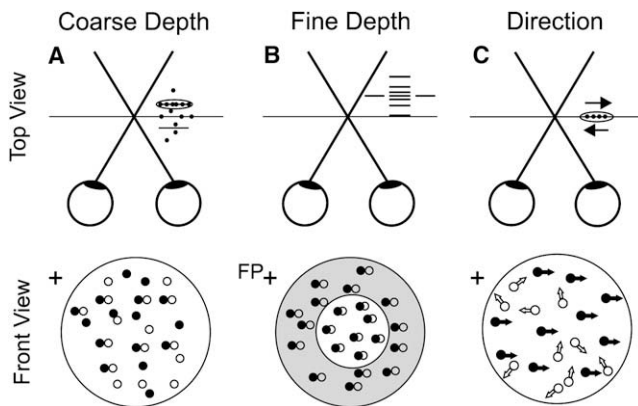
Even in adulthood, humans and animals commonly learn to perform new tasks, gaining proficiency through practice. When a subject learns a new perceptual task by repeated exposure to sensory stimuli, a persistent modification of the brain takes place to improve performance (Fahle, 2005; Ghose, 2004; Gilbert et al., 2001). The neural correlates of perceptual learning may involve changes in the tuning properties of neurons that provide relevant sensory information and/or changes in how these sensory responses are routed to and decoded by brain areas involved in decision-making (Doshier and Lu, 1998, 1999; Gold, 2005).

Previous physiological studies have focused mainly on the effects of perceptual learning on sensory representations (Buonomano and Merzenich, 1998; Gilbert et al., 2001; Weinberger, 1995). In the auditory and somatosensory systems, learning can substantially alter the tuning properties and topographic organization in primary cortical areas (Jenkins et al., 1990; Recanzone et al., 1992, 1993; Wang et al., 1995; Weinberger, 1993). In

contrast, perceptual learning elicits little change in the basic tuning properties of neurons in primary visual cortex (Crist et al., 2001; Ghose et al., 2002; Schoups et al., 2001). Somewhat larger changes in tuning properties have been observed at higher levels of visual processing such as area V4 (Raiguel et al., 2006; Yang and Maunsell, 2004). In contrast, the effects of learning on the selective transmission of sensory signals to decision circuitry have been relatively unexplored. However, a recent study has shown that learning of motion discrimination is manifested in parietal cortex circuitry thought to be involved in decision-making, with little plasticity in sensory representations of visual motion (Law and Gold, 2008).

Physiological studies of perceptual learning generally examine how training alters the neural representation of sensory information that is relevant to the newly learned task. Here, we address an important related question: How does learning a new task affect the neural substrates of previously learned tasks? Given that the same neural representations of sensory cues and/or decision variables may be used to perform multiple tasks, learning-induced changes in these representations may alter how particular brain regions contribute to tasks learned previously. We addressed this question by training monkeys to perform a fine depth discrimination task and examining how this learning affects the causal contribution of area MT to coarse depth discrimination. We have previously shown that area MT contributes to coarse judgments of absolute disparity (near versus far) in the presence of noise (Figure 1A) (DeAngelis et al., 1998; Uka and DeAngelis, 2003, 2004, 2006). In contrast, electrical stimulation of MT does not alter fine judgments of relative depth (Figure 1B) (Uka and DeAngelis, 2006). These results suggest that learning to perform the fine depth task recruits visual areas that represent relative disparities, which are thought to be necessary for high stereoacuity (Prince et al., 2000; Westheimer, 1979).

These findings prompted us to ask how learning the fine depth task alters the causal contribution of area MT to coarse depth discrimination. We report that reversible chemical inactivation of area MT prior to fine depth training severely impairs performance of the coarse depth task. Surprisingly, after animals learned the fine depth task, inactivation of MT no longer affected coarse depth discrimination, indicating considerable plasticity in the contribution of area MT to stereopsis. Single-unit recordings revealed no differences in the disparity selectivity of MT neurons before and after fine depth training, indicating that the change in MT's contribution to coarse depth discrimination does not result



**Figure 1. Schematic Illustration of the Three Discrimination Tasks**  
Upper panels show a top-down view of the stimulus geometry; lower panels show a front view.

(A) The coarse depth task. In each trial, “signal” dots appeared at one of two disparities ( $\pm 0.5^\circ$ ), either near or far relative to the plane of fixation (short horizontal line segments), and the monkey reported whether the net depth was near or far. Here, the stimulus consists of 50% signal dots and 50% noise dots. Filled and open dots represent the left and right half-images, respectively.

(B) The fine depth task. The stimulus is a bipartite random-dot stereogram in a center/surround configuration. The disparity of the surround was fixed at either  $+0.2^\circ$  or  $-0.2^\circ$ , and the disparity of the center patch varied in fine steps around this value. Monkeys reported whether the center patch was in front of or behind the surround patch.

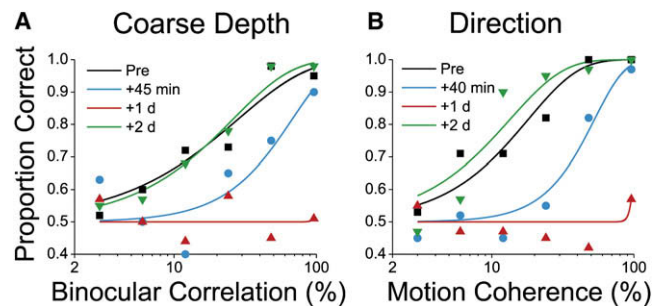
(C) The direction discrimination task. “Signal” dots (filled) moved either rightward or leftward, and the monkey reported the direction of global motion. Here, the stimulus consists of 50% signal dots and 50% noise dots (50% coherence).

from a loss of sensory information. Our findings show that the linkage between task performance and neuronal activity in a particular brain area can be modified by the process of learning a new task. These findings may be explained by changes in the transmission of sensory signals to decision circuitry, without changes in the sensory representation of binocular disparity itself.

## RESULTS

We studied the effect of reversible chemical inactivation of area MT on monkeys’ performance of three visual discrimination tasks: coarse depth discrimination, fine depth discrimination, and direction discrimination. Our goal was to examine the contribution of area MT to coarse depth discrimination before and after monkeys were trained on the fine depth task. Thus, experiments were performed on two monkeys (Bk and J) prior to any training on the fine depth task and on two monkeys (Bk and R) following fine depth training (monkey Bk contributed to each group). Both experimental groups performed the direction discrimination task as a control for negative effects of reversible inactivation.

Figure 1 illustrates the three discrimination tasks schematically. In the coarse depth task (Uka and DeAngelis, 2003), the monkey discriminated between two different absolute disparities (near versus far) in the presence of noise (Figure 1A). Task difficulty was manipulated by varying the percentage of binocularly correlated dots in the stimulus. In the fine depth task (Uka and



**Figure 2. Data from a Representative Experiment Performed on Monkey Bk Prior to Learning the Fine Depth Task**

Each panel shows the proportion of correct responses as a function of stimulus strength. Black data points show psychophysical performance prior to inactivation (“Pre”). Cyan data show performance within an hour following inactivation (“+40 min” or “+45 min”), and red data show performance on the following morning (“+1 d”). Green data show performance 2 days after injection (“+2 d”). Smooth curves are the best fits of a Weibull function.

(A) Effects of inactivation on the coarse depth task.  
(B) Effects of inactivation on the direction discrimination task.

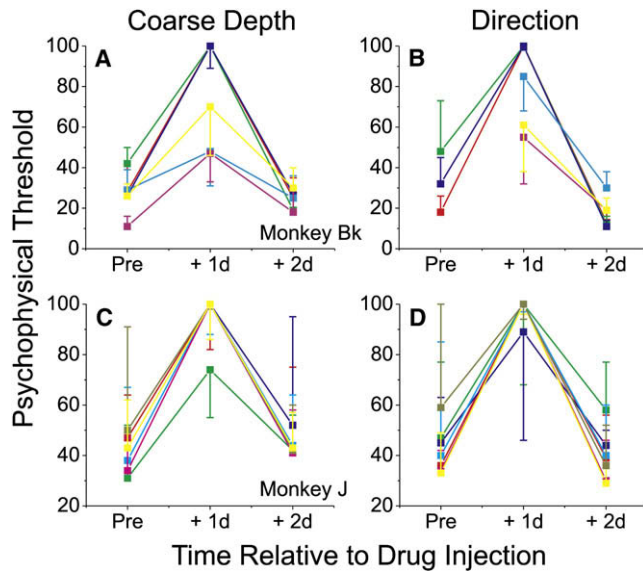
DeAngelis, 2006), the monkey judged the relative depth between two concentric patches of dots, i.e., whether the center patch was near or far relative to the surround (Figure 1B). No disparity noise was added to the display; rather, difficulty was manipulated by presenting very small relative disparities between the center and surround. In the direction discrimination task (Britten et al., 1992), monkeys reported whether the global motion of a noisy random-dot stimulus was leftward or rightward, and task difficulty was varied by manipulating the percentage of dots that moved coherently (Figure 1C).

We first describe the effects of reversible inactivation on performance of the coarse depth and direction tasks prior to any training on the fine depth task, and we then describe the effects of inactivation on all three tasks.

### Inactivation Effects Prior to Fine Depth Training

Figure 2 shows data from a representative experiment performed on monkey Bk prior to training on the fine depth task. A “microinjectrode” (see Experimental Procedures) was lowered into the middle layers of area MT, and the receptive field of multiunit activity was mapped to determine the location and size of a visual stimulus that filled most of the classical receptive field. Psychophysical data were then collected for the coarse depth and direction tasks prior to drug injection (Figure 2, “Pre”, black squares). The monkey performed both tasks well prior to injection, with psychophysical thresholds of 28% for coarse depth discrimination and 18% for direction discrimination (see Experimental Procedures).

Next, 1–2  $\mu$ l of muscimol, a GABA agonist, was slowly injected (0.05  $\mu$ l/min) into area MT through the microinjectrode. Within  $\sim$ 25 min, neuronal activity declined sharply as the drug diffused outward from the end of the cannula (see, e.g., Figure S1 available online). After injection, the monkey again performed blocks of the coarse depth and direction tasks. For both tasks, performance was clearly diminished within 40–45 min following drug injection, with psychophysical thresholds of 68% for coarse depth and 53% for direction discrimination (Figure 2, cyan).



**Figure 3. Summary of Inactivation Effects on Coarse Depth and Direction Discrimination prior to Fine Depth Training**

Each panel shows psychophysical thresholds at three time points: prior to muscimol injection (“Pre”), the day following injection (“+1d”), and 2 days after inactivation (“+2d”). Each colored curve represents data from a single experiment, and data of the same color in (A) and (B) come from the same experiment (also true for [C] and [D]). Error bars show the 95% confidence interval for each threshold measurement. Note that thresholds were not allowed to exceed 100% in the curve-fitting procedure.

(A and B) Data from monkey Bk.

(C and D) Data from monkey J.

On the morning after drug delivery (~20 hr postinjection), performance of both tasks was devastated, with percent correct near 50% even for the highest binocular correlation or motion coherence (Figure 2, “+1d”, red). Thus, muscimol had a long-lasting suppressive effect on MT activity at the concentration we used (as confirmed by recordings; see *Experimental Procedures*). On the second day following injection, psychophysical performance returned to normal (Figure 2, “+2d”, green). In this experiment, there was no significant difference between psychophysical thresholds measured preinjection versus +2d ( $p > 0.05$  for both tasks, bootstrap analysis). By comparison, thresholds for both tasks were significantly higher at +1hr and +1d relative to +2d ( $p < 0.05$ , bootstrap). The long-lasting effect of muscimol allowed us to collect extensive behavioral data following each injection while still demonstrating full recovery.

Figure 3 summarizes data obtained from two monkeys (Bk and J) during performance of the coarse depth and direction tasks. In each panel, psychophysical thresholds are plotted at three time points: preinjection, 1 day postinjection, and 2 days postinjection. Error bars reflect the 95% confidence interval for each threshold. For monkey Bk, thresholds were significantly elevated (+1d versus +2d) in 5 of 6 individual experiments for the coarse depth task (Figure 3A) and 6 of 6 experiments for the direction task (Figure 3B;  $p < 0.05$ , bootstrap). Note that weaker effects of muscimol were seen in the same subset of experiments for both tasks (yellow, magenta, and cyan points), suggesting that some of the variation in drug efficacy across experiments was

methodological. For monkey J, thresholds were significantly elevated in 6 of 7 individual experiments for coarse depth (Figure 3C) and 5 of 7 experiments for direction discrimination (Figure 3D). Combining across experiments, we found a highly significant difference between psychophysical thresholds measured at +1d and +2d for both the coarse depth task (monkey Bk:  $p = 0.004$ ; monkey J:  $p < 0.001$ ; paired t test) and the direction discrimination task (monkey Bk:  $p = 0.001$ ; monkey J:  $p < 0.001$ ).

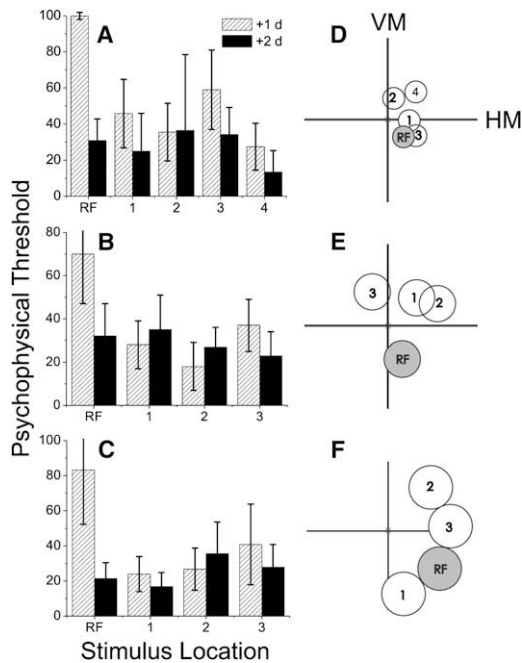
To address the possibility that muscimol had a nonspecific effect on behavior, we examined the spatial localization of behavioral effects. In six experiments on direction discrimination and seven experiments on coarse depth discrimination, we measured the effect of muscimol on performance when the visual stimulus was placed at a location in the opposite visual hemifield (diametrically opposite the fixation point). We found no significant difference between psychophysical thresholds measured at +1d and +2d in these controls (Figure S2; coarse depth:  $p = 0.46$ ; direction:  $p = 0.53$ ; paired t test).

To further localize behavioral deficits, we presented the visual stimulus at multiple locations relative to the MT receptive field in some experiments. Figure 4A shows an example result for the direction discrimination task. When the visual stimulus was centered on the multiunit receptive field (RF, gray shading), there was a large (>200%) and highly significant elevation of threshold at +1d (hatched bar) relative to +2d (black bar). When the visual stimulus was shifted by about 2/3 of the receptive field diameter (locations 1 and 3), direction thresholds were still elevated by ~50% at +1d, although these elevations were not individually significant. When the visual stimulus did not overlap the multiunit receptive field at all (locations 2 and 4), there was no elevation of direction thresholds at +1d. Analogous results are shown in Figures 4B and 4C for two additional experiments. Perceptual deficits associated with muscimol were abolished when the visual stimulus did not overlap the multiunit receptive field, indicating that muscimol affected the region of visual space represented by neurons near the tip of the injectrode.

### Inactivation Effects after Fine Depth Training

Robust effects of muscimol on coarse depth and direction discrimination are not surprising given that electrical microstimulation was previously found to bias judgments in these tasks (DeAngelis et al., 1998; Salzman et al., 1992). The key question is how the contribution of MT to these tasks is affected by training monkeys to perform the fine depth discrimination. If MT does not contain the disparity signals necessary for fine depth discrimination (Uka and DeAngelis, 2006), then fine depth training should recruit other visual areas into play. How does recruiting these other areas alter the contribution of MT to coarse depth discrimination?

To address this question, we trained monkey Bk extensively on the fine depth task, which led to a gradual 3-fold reduction in psychophysical thresholds over a period of weeks (Figure S3). This gradual improvement in sensitivity is consistent with perceptual learning and is similar to effects of learning on direction discrimination in monkeys (Law and Gold, 2008). This improvement is unlikely to reflect operational learning, as the monkey previously learned the coarse depth task, which has the same operational rule. Indeed, the monkey performed the fine depth task correctly when large disparities were presented from the beginning of the



**Figure 4. Effects of Stimulus Location on Behavioral Deficits Resulting from MT Inactivation**

Each row shows data from one experiment. Hatched bars show psychophysical thresholds on the day following muscimol injection (“+1d”); black bars show thresholds following recovery (“+2d”). Each pair of hatched and black bars corresponds to a stimulus location as diagrammed at right (HM, horizontal meridian; VM, vertical meridian). Error bars in (A)–(C) show the 95% confidence interval for each threshold measurement.

(A and D) Data from a direction discrimination experiment. Following inactivation (hatched bars), psychophysical threshold was significantly elevated at the location of the receptive field (RF, gray circle), modestly elevated at locations 1 and 3, and unaffected at locations 2 and 4.

(B and E) Data from a coarse depth discrimination experiment, showing threshold elevation only at the location of the receptive field.

(C and F) Data from an additional direction discrimination experiment, showing a similar pattern of results.

training period; however, thresholds declined gradually as the animal learned to extract fine relative disparity information.

After this training period, we examined effects of muscimol on all three tasks: fine depth, coarse depth, and direction discrimination. Figure 5 shows a representative result. Reversible inactivation produced no significant effect on performance of either the fine (Figure 5A) or coarse (Figure 5B) depth tasks ( $p > 0.05$ , bootstrap). However, muscimol produced a large deficit in

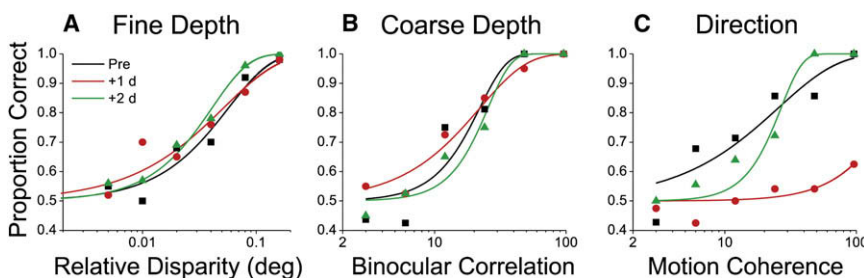
performance of the direction discrimination task (Figure 5C;  $p < 0.001$ ), similar to that seen before fine depth training.

Figures 6A–6C summarize the results from monkey Bk following training on the fine depth task. Consistent with our previous microstimulation results (Uka and DeAngelis, 2006), reversible inactivation of MT did not impair fine depth discrimination. Specifically, the relative disparity threshold was not significantly elevated in any of the eight experiments (Figure 6A;  $p > 0.05$ , bootstrap), and the average threshold was not significantly different between +1d and +2d ( $p = 0.20$ , paired t test). This lack of effect on fine depth discrimination was not due to failure of inactivation, because the same muscimol injections dramatically impaired direction discrimination (Figure 6C;  $p < 0.001$ , paired t test), with significant effects in all eight individual experiments ( $p < 0.05$ ). In a few experiments, we halved the size of the center patch to place the disparity boundary within the classical receptive field, and we again found no significant effects of inactivation on fine depth discrimination ( $p > 0.05$ , bootstrap).

Strikingly, after fine depth training, inactivation of MT in monkey Bk failed to produce any significant effect on coarse depth discrimination. Across the same eight sessions, none of the coarse depth thresholds changed significantly from +1d to +2d (Figure 6B;  $p > 0.05$ , bootstrap), and the average thresholds did not differ significantly between these two time points ( $p = 0.24$ , paired t test). These data lie in clear contrast to those obtained from the same monkey before training on the fine depth task (compare Figure 6B to Figure 3A) despite the use of identical experimental protocols and despite similar effects of muscimol on direction discrimination (compare Figure 6C to Figure 3B). We found no significant changes in eye movements that were correlated with this striking change in behavior (Experimental Procedures; Figures S4–S6).

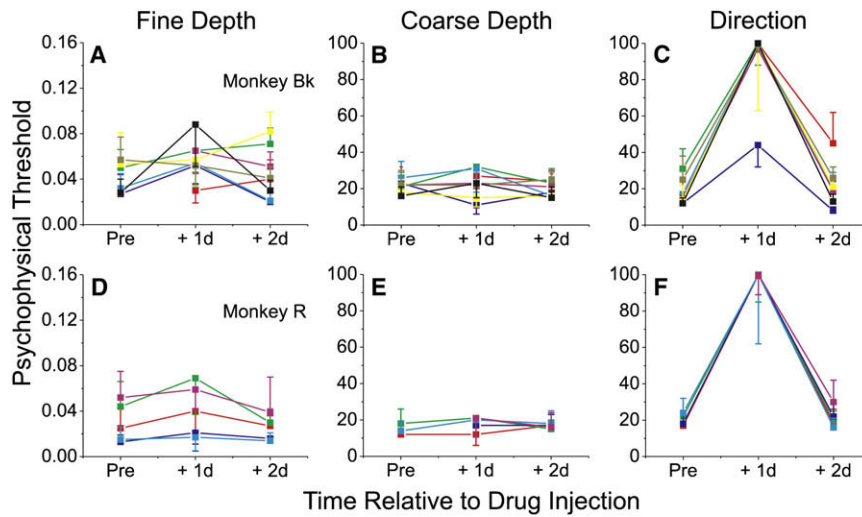
Figures 6D–6F show analogous data from another animal (monkey R) that was tested on all three tasks. Again, there was a highly significant effect of inactivation on direction discrimination (Figure 6F;  $p < 0.001$ ), but no significant effect on either fine depth (Figure 6D;  $p = 0.07$ ) or coarse depth (Figure 6E;  $p = 0.46$ ) discrimination (paired t tests). Thus, training monkeys to perform fine depth discrimination alters the contribution of area MT to the coarse depth task.

It should be noted that we have previously reported significant effects of microstimulation on coarse depth discrimination in animals that had been trained to perform the fine depth task (Uka and DeAngelis, 2006). However, effects of microstimulation in that study were significantly smaller than those obtained in an earlier study without any fine depth training (DeAngelis et al., 1998) despite the fact that larger currents were often used (Figure S7). Thus,



**Figure 5. Data from a Representative Experiment Performed after Monkey Bk Learned the Fine Depth Task**

The effect of inactivation was tested on all three discrimination tasks: fine depth (A), coarse depth (B), and direction (C). Data are shown in the format of Figure 2.



**Figure 6. Summary of Results from All Experiments Performed on Monkey Bk and Monkey R after Fine Depth Training**

Results are shown for the fine depth (A and D), coarse depth (B and E), and direction (C and F) tasks. The format of each panel is identical to that of Figure 3. Data for monkey Bk are shown in the top row; data for monkey R are shown in the bottom row. Error bars show the 95% confidence interval for each threshold measurement.

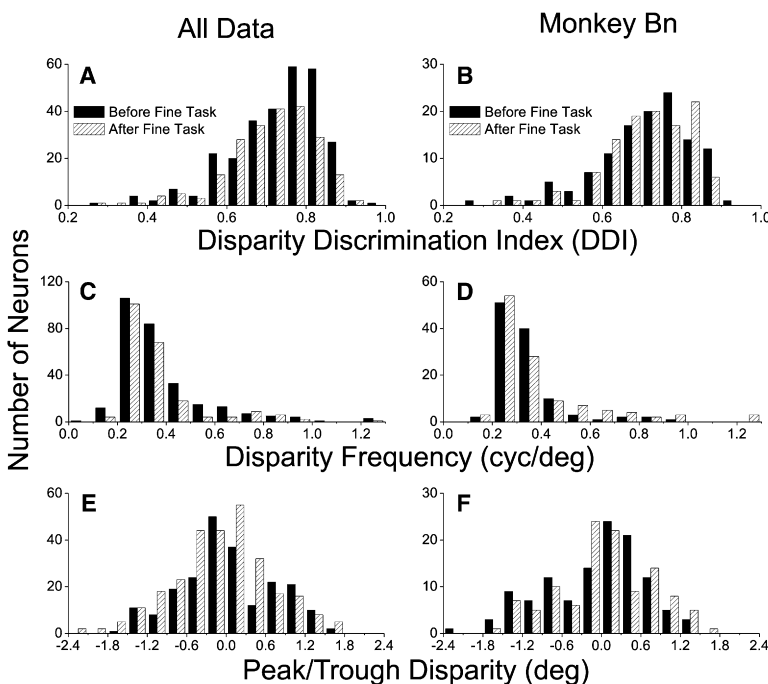
fine depth training acts to reduce, but not eliminate, effects of microstimulation on coarse depth discrimination. The quantitative difference between microstimulation and inactivation results likely reflects differences in the nature and sensitivities of the two methods. MT may still contribute to coarse depth discrimination following fine depth training (as suggested by microstimulation), but other areas may compensate for the loss of MT during inactivation. Microstimulation of MT could also indirectly activate other pathways that contribute to coarse depth perception.

**Effect of Fine Depth Training on Disparity Selectivity in MT**

One possible explanation for the inactivation results is that fine depth training alters the disparity tuning of MT neurons and makes them less informative for coarse depth discrimination. For

example, if fine depth training were to weaken disparity selectivity, broaden tuning curves, or shift disparity preferences toward the plane of fixation (zero disparity), these changes could render MT responses less useful for coarse depth discrimination. To address this possibility, we analyzed disparity tuning curves from MT neurons recorded before and after fine depth training. Specifically, data were analyzed from 284 MT neurons in two monkeys (Bn and J) that had not been trained on the fine depth task. Data were also analyzed from 217 neurons from two monkeys (Bn and R) after fine depth training (monkey Bn contributed to both groups). For each neuron, horizontal disparity tuning was measured in response to random-dot stereograms (DeAngelis and Uka, 2003), and tuning curves were fit with Gabor functions (see Experimental Procedures) to quantify various tuning parameters.

Figure 7A compares distributions of the disparity discrimination index (DDI; see Experimental Procedures) (DeAngelis and Uka, 2003; Prince et al., 2002) measured before (black bars) and after (hatched bars) fine depth training. Data were analyzed



**Figure 7. Summary of Disparity Tuning Properties of Single MT Neurons before and after Fine Depth Training**

(A), (C), and (E) show pooled data from two animals (monkeys Bn and J, black bars) before fine depth training and data from two animals (monkeys Bn and R, hatched bars) after fine depth training. (B), (D), and (F) show data from monkey Bn, who contributed to both training groups. (A and B) Distributions of the disparity discrimination index (DDI), a measure of tuning strength. (C and D) Distributions of disparity frequency, a measure of tuning width. (E and F) Distributions of the disparity at which each neuron shows its peak response (or trough response for tuned-inhibitory neurons).

using a two-way ANOVA with training history and monkey identity as factors. The DDI did not differ significantly between the two training groups ( $p = 0.55$ , ANOVA), although there was a modestly significant difference between animals ( $p = 0.005$ ). Training history also did not significantly affect DDI when we examined only the data from monkey Bn using a nonparametric test (Figure 7B;  $p > 0.1$ , Kolmogorov-Smirnov [K-S] test). We have previously shown that DDI is strongly correlated with neuronal sensitivity in the coarse depth task (Uka and DeAngelis, 2003), so this finding indicates that fine depth training does not reduce the sensitivity of MT neurons for discriminating coarse depth.

Figure 7C shows the distribution of disparity frequency, a measure of tuning width (Cumming and DeAngelis, 2001; DeAngelis and Uka, 2003; Prince et al., 2002). Again, there was no difference due to training for either the entire data set ( $p = 0.15$ , ANOVA on log-transformed data) or the data from monkey Bn (Figure 7D;  $p > 0.1$ , K-S test). Finally, Gabor fits were also used to determine the disparity at which each tuning curve showed its dominant peak or trough. The distribution of this peak/trough disparity was also not significantly different before and after fine depth training (all data: Figure 7E;  $p = 0.21$ , ANOVA; monkey Bn: Figure 7F;  $p > 0.1$ , K-S test).

Overall, the available data provide no evidence that fine depth training altered the representation of horizontal disparities in MT. Thus, plasticity resulting from fine depth training does not occur at the level of disparity representation in area MT.

## DISCUSSION

Prior to fine depth training, area MT carries disparity signals that are crucial for coarse depth discrimination. Remarkably, after learning the fine depth task, MT inactivation has no significant effect on coarse depth discrimination. Yet the disparity tuning of single MT neurons is normal after fine depth training, and strong effects of muscimol on direction discrimination confirm that MT was reliably inactivated. How do we interpret these findings? Psychophysical studies (Prince et al., 2000; Westheimer, 1979) have shown that relative disparity signals are important for fine depth discrimination, and we have previously shown that area MT does not carry these signals for the stimulus configuration used here (Uka and DeAngelis, 2006). Thus, learning to perform the fine depth task likely involves recruiting areas that represent relative disparities, with the ventral stream being a good candidate (Umeda et al., 2007). We suggest that these areas, once recruited, are able to mediate performance of the coarse depth task when MT is temporarily inactivated. This is plausible because relative-disparity-selective neurons can provide information regarding absolute disparities (when a zero-disparity reference is available), whereas the converse is not true.

Our single-unit recordings provide no evidence that fine depth training altered the neural representation of disparity in MT. Rather, our results suggest a change in how strongly the disparity signals from area MT are weighted by decision circuitry, relative to disparity signals from other brain areas. The relevant decision circuitry for depth judgments is unclear, but it is known that neurons in parietal areas CIP, LIP, and VIP exhibit disparity selectivity (Colby et al., 1993; Genovesio and Ferraina, 2004;

Gnadt and Mays, 1995; Taira et al., 2000). Area MT is known to project to parietal regions (Born and Bradley, 2005), and area LIP is thought to serve as part of the decision circuitry for interpreting motion signals from MT (Gold and Shadlen, 2007; Roitman and Shadlen, 2002). Thus, parietal cortex may represent decision variables for depth judgments, and our findings suggest that these decision circuits may weight disparity signals from the ventral stream more heavily following fine depth training. A common decision stage for both the coarse and fine depth tasks might explain why learning the fine depth task alters the contribution of area MT to the coarse depth task but does not alter MT's role in direction discrimination.

## Implications

Our findings have several general implications. First, our results suggest that perceptual learning may have widespread collateral effects on previously learned behaviors. Most studies of perceptual learning have focused on a single task and have not considered how learning a new task affects the neural substrates of tasks learned previously. Our findings show that learning a new task (fine depth) can alter the composition of the pool of sensory signals that contribute to performance of previously learned tasks (e.g., coarse depth). If learning has recruited additional areas into mediating performance of the coarse depth task, then we may expect to see a change in psychophysical threshold for this task. Indeed, for monkey Bk, we found that the average coarse depth threshold (20.4%) after fine depth training was lower than before training (25.5%), and this difference, while modest, is statistically significant (Mann-Whitney U test,  $p = 0.011$ ; t test,  $p = 0.023$ ; data pooled across Pre and +2d time points). This finding is consistent with the possibility that recruitment of additional (e.g., ventral stream) areas improves performance of the coarse depth task, although the effect is rather small and must be interpreted cautiously. Another possibility is that recruitment of ventral stream areas following fine depth training could be manifested behaviorally as interactions between disparity processing and other visual cues such as form information, and this may be tested in the future. In any case, one should not assume that the neuronal plasticity that accompanies learning is restricted to areas that mediate performance of the newly learned task.

Second, our findings highlight the need to control for task sequence effects in physiological studies of the neural basis of perception. Had we only examined the effects of MT inactivation after animals were trained to perform both the fine and coarse depth tasks, we might have concluded that MT plays no role in stereopsis at all. Thus, when the neural contributions to multiple tasks are examined, it may be critical to control for the order in which different tasks are learned. These training-related interactions may be more common for tasks that are closely related (perhaps by sharing common decision circuitry) than for unrelated tasks.

Third, our results are consistent with the idea that learning could act largely by changing the weights by which different sources of sensory signals are transmitted to decision circuitry, rather than by changing the tuning properties of the sensory neurons themselves (though the latter might also occur). When perceptual learning acts by modifying the routing and/or weighting

of sensory signals to decision circuitry, plasticity takes place mainly at the level of neural decoding rather than encoding (Doshier and Lu, 1998, 1999; Gold, 2005). This interpretation of our results is consistent with the findings of a recent study that found that perceptual learning of direction discrimination modifies the correlation between neural activity and behavior in area LIP but does not change the sensitivity of neurons in area MT (Law and Gold, 2008). In contrast, perceptual learning has been shown to modify tuning properties of primary sensory cortical neurons in other systems (Jenkins et al., 1990; Recanzone et al., 1992, 1993; Wang et al., 1995; Weinberger, 1993). Thus, an important challenge for future work will be to understand the conditions that lead to plasticity at the level of decoding rather than sensory encoding.

### Technical Considerations

One concern may be that drug injections prior to fine depth training damage area MT and lead to a gradual reduction in MT's contribution to the coarse depth task. The data suggest that this is very unlikely. Prior to fine depth training, muscimol consistently impaired performance of the coarse task (Figures 3A and 3C), and the resulting threshold elevation (+1d versus +2d) did not change significantly across sessions (linear regression,  $p = 0.38$ ,  $n = 13$ ). After fine depth training, effects of muscimol on the coarse depth task were lacking from the first experiment. Whereas the effect of muscimol on coarse depth discrimination changed abruptly after fine depth training, the effects on direction discrimination did not. This pattern of results is not consistent with a gradual degradation of MT function due to injections.

We have not directly measured the region of neural inactivation, but our behavioral data allow us to estimate drug spread. We have shown (Figure 4) that moving the visual stimulus just off of the classical receptive field eliminates the effect of inactivation. Since one typically has to travel  $\sim 2$  mm across the surface of area MT to find abutting receptive fields (DeAngelis and Newsome, 1999), we can infer that the drug affects a region of MT having a diameter of  $\sim 2$  mm. This estimate is consistent with those of previous studies that have attempted to measure the extent of muscimol-induced inactivation more directly (Allen et al., 2008; Arikan et al., 2002; Edeline et al., 2002; Martin and Ghez, 1999). The correspondence between behavioral effects and receptive field location suggests that the drug was well targeted to area MT.

Behavioral effects of muscimol lasted at least 24 hr in our study. Previous studies have also reported long-lasting effects of muscimol, from 10 to 24 hr (Hikosaka and Wurtz, 1985; Martin and Ghez, 1993, 1999). It seems clear that the duration of muscimol effects increases with drug dosage, although the precise nature of the dose-response relationship is not known (Edeline et al., 2002; Martin and Ghez, 1999). We used a concentration of muscimol (10 mg/ml) higher than in most previous studies, and this likely accounts for long duration effects given that muscimol has a much higher affinity for and tighter binding with the GABA<sub>A</sub> receptor than GABA itself (Krogsgaard-Larsen and Johnston, 1978; Nicholson et al., 1979). For our purposes, the long-duration effect of muscimol was valuable as it allowed us to collect behavioral data during inactivation over two consecutive sessions while still observing complete recovery on

the second day postinjection. This approach reduces damage to the cortex caused by passage of the injectrode while still allowing considerable data collection.

### Open Issues

Our findings raise a number of interesting questions for consideration in future studies. First, why do monkeys initially rely so heavily on area MT for coarse depth discrimination when other areas are capable of contributing as well? A common feature of the coarse depth and direction tasks is that they involve discriminating weak signals in noise. Perhaps MT neurons carry motion and disparity signals that are most robust to external noise. Second, why does extensive training on the fine depth discrimination task induce plasticity when fine relative disparity signals are presumably needed for precise 3D vision under natural conditions? Perhaps stereoacuity, as measured here, is not indicative of the normal range of demands on the stereo vision system. Alternatively, the specific nature of the visual stimuli may require signals that are not ordinarily needed in a natural environment. It would be interesting to test whether tasks involving other forms of relative disparity signals (e.g., 3D curvature judgments) invoke a similar redistribution of disparity processing. Third, which regions of visual cortex are important for mediating performance of the fine depth task? Recent work (Janssen et al., 2000, 2001; Umeda et al., 2007) suggests that relative disparity signals are more prominent in ventral stream areas such as V4 and IT. Thus, we may expect that reversible inactivation of V4 should impair fine depth discrimination. Following fine depth training, it is possible that disparity selectivity in area V4, or other areas containing relative disparity signals, may be modified by training. Alternatively, fine depth training might not alter the tuning of V4 neurons but may increase the weight of their contribution to the relevant decision circuitry.

It is worth noting that a previous study found no clear effects of permanent lesions of MT or V4 on depth discrimination thresholds (Schiller, 1993). Lesions of both MT and V4 produced only minor deficits. This might be taken as evidence that neither the dorsal nor ventral streams mediate disparity discrimination. However, that conclusion is uncertain because the task used by Schiller did not test discrimination around psychophysical threshold, and this may allow performance to be mediated (weeks or months after the lesions) by a variety of areas, such as V3 and V3A, that are also known to carry robust disparity signals (Adams and Zeki, 2001; Felleman and Van Essen, 1987; Poggio et al., 1988). This highlights the importance of using threshold tasks with differing demands, as well as reversible inactivation, for dissecting the contributions of different areas to stereo vision. It is also possible that neurons in parietal areas, such as areas CIP, LIP, and VIP (Colby et al., 1993; Genovesio and Ferraina, 2004; Gnadt and Mays, 1995; Taira et al., 2000), might provide relative disparity signals that are useful for performing the fine depth task, but this has not been examined directly.

A limitation of the present study is that stimuli for the coarse and fine depth tasks differ in multiple respects: absolute versus relative disparity, range of disparities, presence or absence of noise, and spatial geometry. Although it seems likely that absolute versus relative disparity processing is the key difference, we

cannot rule out contributions from other stimulus dimensions. In future studies, it will be most desirable to employ a fixed set of stimuli that contain both absolute and relative disparity variations and to cue the animal to make different judgments that rely on absolute or relative disparities. This should help isolate the effect of task from low-level stimulus effects. Note, however, that our main conclusion—that learning the fine depth task alters the role of area MT in the coarse depth task—does not depend critically on which stimulus features were most important to the animal in performing the two tasks.

## EXPERIMENTAL PROCEDURES

### Subjects and Surgery

Four adult male rhesus monkeys (*Macaca mulatta*) participated in these studies. Three animals (monkeys Bk, J, and R) were involved in reversible inactivation experiments, and three animals (monkeys Bn, J, and R) participated in single-unit recording experiments. Animals were prepared for experiments using standard surgical procedures described elsewhere (DeAngelis and Newsome, 1999; DeAngelis and Uka, 2003). A head restraint post was attached to the skull using bone screws and acrylic. Scleral coils were implanted in both eyes for monitoring eye position, including both version and vergence. A cylindrical recording chamber was mounted over occipital cortex roughly 17 mm lateral to the midline and 14 mm dorsal to the occipital ridge. The long axis of the chamber resided in a parasagittal plane and was inclined 25° relative to the horizontal plane. All animal care and experimental procedures were approved by the Institutional Animal Care and Use Committee at Washington University and were in accordance with NIH guidelines.

### Visual Stimuli

Monkeys viewed a flat-screen 22-inch color monitor (Sony GDM-F500) from a distance of 57 cm. The display subtended a visual angle of 40° × 30° and had a resolution of 1152 × 864 pixels. Visual stimuli were random-dot stereograms (RDSs) generated by an OpenGL accelerator board (Oxygen GVX1, 3DLabs). Dot density was 64 dots/deg<sup>2</sup>/s, with each dot subtending ~0.1°. The starting position of each dot within the circular aperture was randomized for each trial. Precise disparities and smooth motion were achieved by plotting dots with subpixel resolution using hardware antialiasing. Additional details regarding visual stimuli can be found elsewhere (Uka and DeAngelis, 2003, 2004).

Stereoscopic images were displayed by presenting the left and right half-images alternately at a refresh rate of 100 Hz. The monkey viewed the display through a pair of ferroelectric shutters (Displaytech) that were synchronized to the video refresh. To minimize ghosting effects (stereo crosstalk was less than 3%), the RDS consisted of red dots presented on a black background.

For the coarse and fine disparity tasks, all dots within the RDS moved coherently (100% motion coherence) at a fixed velocity (rightward motion, 6 deg/s). When they reached the boundary of the stimulus, dots resumed motion from the opposite side of the circular aperture. In the direction discrimination task, motion coherence was varied to manipulate task difficulty while speed was fixed (6 deg/s).

### Training and Tasks

Monkeys were trained to perform a visual fixation task and three different visual discrimination tasks (detailed below). In each case, the monkey was required to foveate a small yellow target (0.15° × 0.15°) and to maintain fixation within a 1.6° × 1.6° electronic window. In the fixation task, monkeys received a liquid reward for simply maintaining fixation during stimulus presentation (1.5 s). If the monkey's conjugate eye position left the fixation window prematurely, the trial was aborted immediately and data were discarded. In the discrimination tasks, the monkey was required to maintain fixation during stimulus presentation and then to execute a saccade to one of two targets to signal his choice. Correct responses were rewarded with a drop (0.1–0.15 ml) of water or juice.

Three monkeys were trained to perform multiple discrimination tasks (in separate blocks of trials). Monkeys J and Bk were initially trained to perform

a coarse depth discrimination task (DeAngelis et al., 1998; Uka and DeAngelis, 2003) and a direction discrimination task (Britten et al., 1992). After a set of reversible inactivation experiments were completed, monkey Bk was trained to perform the fine depth discrimination task and subsequently underwent another round of inactivation experiments in which all three discrimination tasks were performed. Monkey R had been previously trained to perform both the coarse and fine depth tasks for another study (Uka and DeAngelis, 2006) and thus participated in a single set of inactivation experiments involving all three discrimination tasks. Altogether, we tested coarse depth and direction discrimination in two monkeys (J and Bk) before fine depth training, and we tested all three tasks after fine depth training in two monkeys (Bk and R). The tasks were designed as follows (see also Uka and DeAngelis, 2006).

### Coarse Depth Task

For the coarse depth task (Figure 1A), the stimulus was a single circular patch of drifting dots (rightward motion, 6 deg/s) against a background of stationary dots at zero disparity. The strength of the disparity signal was titrated by manipulating the percentage of binocularly correlated dots. Correlated (i.e., signal) dots were assigned one of two fixed disparities during each trial—either near (−0.5°) or far (+0.5°)—and the remaining (noise) dots were assigned random disparities from −2° to +2°. Dots retained their identities (signal or noise) throughout a trial; hence, the exact distribution of noise disparities was fixed within a given trial but varied across trials. Unlike in previous studies (Uka and DeAngelis, 2003, 2006), we did not tailor the disparity and velocity of signal dots to the tuning of neurons at the injection site. This was done because muscimol injection affects a region of cortex much larger than a single disparity or direction column.

Monkeys reported whether the signal dots appeared to be near (crossed) or far (uncrossed) relative to the fixation point. Thus, the coarse depth task involved judgments of absolute disparity (Uka and DeAngelis, 2006). At the end of each trial, the monkey signaled his depth percept by making a saccade to one of two targets (located 5° below and above the fixation point, respectively) that appeared 200 ms after offset of the RDS. Binocular correlation took on values of 0%, 3%, 6%, 12%, 24%, 48%, and 96%. Although the largest binocular correlation was generally not needed to measure psychometric functions (Uka and DeAngelis, 2003, 2006), it was included in these studies to help constrain measurements of psychophysical thresholds when inactivation effects were large.

### Fine Depth Task

In the fine depth task (Figure 1B), a bipartite (center/surround) RDS was presented. Dots within the center patch moved at a fixed velocity (rightward, 6 deg/s), whereas the surround patch remained stationary. The center patch was sized to be ~20% smaller than the classical receptive field, and the outer diameter of the surround patch was twice that of the center patch. Binocular correlation was fixed at 100%, and task difficulty was manipulated by changing the disparity of the center patch in fine steps relative to the surround. Monkeys were trained to report whether the center patch was in front of or behind the surrounding annulus. Both patches of dots could have near or far disparities relative to the fixation point; thus, the task was to judge the relative disparity of the two stimuli. For inactivation experiments, the relative disparities between center and surround patches were ±0.005°, ±0.01°, ±0.02°, ±0.04°, ±0.08°, and ±0.16°. Unlike in our previous single-unit study (Uka and DeAngelis, 2006), the disparity of the surround patch was not tailored to the steep slope of the tuning curve of neurons near the electrode tip (for the reasons described above). Rather, the pedestal disparity was either −0.2° or +0.2°, chosen randomly from experiment to experiment. This pedestal disparity was larger than all relative disparities of the center patch, such that the absolute disparities of the center patch would be all near or all far in each experiment. Thus, to perform this task well, the monkey needed to rely on relative disparity signals (Prince et al., 2000; Uka and DeAngelis, 2006).

Monkeys R and Bk were fully trained on the coarse depth task before performing the fine task. They initially performed the fine task with the surround disparity set to zero, and the range of relative disparities was gradually reduced over several sessions until psychophysical thresholds dropped below 0.1°. When the surround disparity was moved away from the plane of fixation, both monkeys' psychometric functions initially shifted by approximately the amount of the surround disparity. Thus, both monkeys initially reported the disparity of the center patch relative to the fixation point, not relative to surround.

In other words, the monkeys initially judged the absolute disparity of the center patch. Over several weeks of training, the monkeys learned to report the relative disparity between center and surround stimuli, and their psychophysical thresholds improved severalfold (Uka and DeAngelis, 2006). Thus, during learning of the fine disparity task, there was ample time for neuronal plasticity to occur.

#### Direction Discrimination Task

As a control for negative effects of reversible inactivation, all monkeys were trained to perform a standard direction discrimination task (Britten et al., 1992). The axis of motion was horizontal (either rightward or leftward moving dots), and motion coherence was varied from 3% to 96% in octave steps. Again, no attempt was made to tailor the velocity of motion to the preference of neurons; rather, we simply chose a speed of motion (6 deg/s) that would activate most MT neurons (DeAngelis and Uka, 2003). Motion stimuli were presented at zero disparity. The monkey made a saccade to one of two targets, located 5° to the right and left of the fixation point, to signal his motion percept.

The three discrimination tasks were run in separate blocks of trials. Within each task, all stimulus conditions were randomly interleaved, and 10–20 repetitions of each unique stimulus condition were tested.

#### Data Acquisition

In single-unit recording experiments, a tungsten microelectrode (0.3–1 M $\Omega$ , FHC Inc.) was inserted into area MT through a transdural guide tube. In reversible inactivation experiments, a custom-made “microinjectrode” (modified from Chen et al., 2001) was inserted into MT through a 23G guide tube. The microinjectrode consists of a fine tungsten microelectrode (3  $\mu$ m tip diameter and 75  $\mu$ m shaft diameter, FHC Inc.) that is located inside a 32G cannula and extends ~300–400  $\mu$ m past one end of the cannula. The other end of the cannula mates to a piece of 25G tubing connected to a minipump (Harvard Apparatus Model 11) via a connector and tubing. The injectrode is sealed such that liquid entering the cannula can only exit through the opening near the tip of the microelectrode.

Raw neural signals were conventionally amplified and bandpass filtered (500–5000 Hz). A window discriminator (Bak Electronics) was used to isolate the action potential of single neurons or to threshold raw neural signals into multiunit activity. Times of occurrence of action potentials and trial events were stored to disk with 1 ms resolution. Tasks and data acquisition were controlled by TEMPO software (Reflective Computing), and data analyses were performed using MATLAB (The MathWorks).

#### Reversible Inactivation Protocol

Before inserting the microinjectrode into the brain, the minipump was used to retract a known volume of drug from inside the injectrode assembly. This prevented the drug from being drawn out from the injectrode while it was lowered into cortex. Once the injectrode entered area MT, it was advanced to a depth roughly 700–800  $\mu$ m below the surface of MT (such that drug would diffuse into both the upper and lower layers of cortex). We then mapped the response of multiunit activity recorded through the electrode, determined the boundaries of the classical receptive field, and estimated the velocity and disparity preferences of the site. In most experiments, the multiunit receptive field was mapped quantitatively using a grid of small patches of drifting random-dot stimuli (Nguyenkim and DeAngelis, 2003). This measurement was used to specify the position and size of stimuli relative to the multiunit receptive field. We aimed to make the size of the stimulus (center patch in the fine disparity task) ~20% smaller than the classical receptive field to increase the chances that muscimol inactivated the portions of area MT that represented the visual stimulus.

After completing baseline psychophysical measurements, the GABA agonist muscimol (10 mg/ml) was injected very slowly (0.05  $\mu$ l/min) using the minipump. The known volume required to fill the injectrode was injected, followed by an additional 1–2  $\mu$ l of the drug. Neural activity was monitored through the electrode during drug injection, and typically within ~20 min following the start of injection, electrical activity at the electrode tip was greatly reduced (see, e.g., Figure S1). In a few experiments, we observed no clear reduction in neural activity following drug injection, presumably due to blockage of the injectrode and/or failure of a seal along the drug delivery pathway. Data from these experiments were excluded. Otherwise, we report data from all experiments in which the drug caused a clear reduction in neuronal activity, regardless of whether there was any effect on behavior.

Once a drug effect on neuronal activity was confirmed, the animal again performed two or more of the discrimination tasks, in separate blocks. The order of the tasks was counterbalanced across experiments. On the following two days after an injection, the animal again performed the same discrimination tasks using identical stimulus parameters. We typically observed that drug effects were robust on the morning following injection (“+1d”) and then recovered completely on the second day after injection (“+2d”) (see Figure S8 for additional time course information). In all experiments, we measured behavior during and after reversible inactivation. In most experiments, we also measured behavior just prior to inactivation (“Pre”).

Several control experiments were performed to validate the effects of muscimol. In a few experiments, we performed sham injections of saline (0.9% NaCl) and saw no reduction in neuronal activity following injection. This argues against a direct effect of pressure on neuronal activity, which we guarded against by injecting drug very slowly. In other control experiments, we inserted a standard microelectrode into the same guide tube (at the same depth) and attempted to record neuronal activity on the morning following a muscimol injection (+1d). We found strongly suppressed activity in MT at +1d (with normal activity in area MST), which returned to typical levels of vigor on the second day after injection (+2d). Thus, the time course of drug effects on behavior was roughly mirrored by the time course of drug effect on neuronal activity.

To examine the spatial localization of drug effects, we tested behavior in the visual hemifield opposite to the receptive field and found no significant effect of inactivation (see Figure S2). To further localize drug effects, we occasionally measured behavior with stimuli placed at multiple locations in and around the receptive field of neurons at the injection site. The perceptual deficits accompanying muscimol injection were well localized to the region of the visual field represented by neurons at the injection site (see Results and Figure 4).

#### Single-Unit Recording Protocol

Selectivity of MT neurons for horizontal disparity was examined in two monkeys prior to any training on fine depth discrimination and in two monkeys after fine depth training. Data for these comparisons were drawn from a previously published data set (DeAngelis and Uka, 2003), and details of the experimental procedures are presented there.

Briefly, the receptive field of each MT neuron was mapped either qualitatively or quantitatively using small patches of drifting random dots. Each isolated neuron was subjected to a battery of quantitative tests that included measurements of direction tuning, speed tuning, size tuning (area summation), and horizontal disparity tuning. Only the disparity tuning data were analyzed further here. Each neuron was typically tested with nine stimulus disparities: 0°,  $\pm 0.4^\circ$ ,  $\pm 0.8^\circ$ ,  $\pm 1.2^\circ$ , and  $\pm 1.6^\circ$ .

#### Data Analysis

##### Behavioral Data

To quantify behavioral sensitivity, the proportion of correct responses was plotted as a function of the relevant stimulus variable for each task, and these psychometric functions were fitted with Weibull functions using a maximum likelihood method (Uka and DeAngelis, 2003) (e.g., Figure 2 and Figure 5). Psychophysical threshold was defined as the point where the fitted function crossed 82% correct. For the coarse depth and direction tasks, Weibull fits were not allowed to have thresholds that exceeded 100%. Allowing the threshold to exceed 100% often resulted in questionable fits and impaired our ability to estimate confidence intervals. 95% confidence intervals were estimated by bootstrapping (1000 resamplings) and are shown in all summary data figures (e.g., Figure 3).

##### Single-Unit Tuning Data

The disparity tuning curve of each single unit was fit with a Gabor function (DeAngelis and Uka, 2003):

$$R(d) = R_0 + A \times e^{-0.5 \frac{(d-d_0)^2}{\sigma^2}} \times \cos(2\pi f(d-d_0) + \Phi)$$

where  $d$  is the stimulus disparity,  $R_0$  is the baseline response level,  $A$  is the amplitude,  $d_0$  is the center of the Gaussian envelope,  $\sigma$  is the standard deviation of the Gaussian,  $f$  is the frequency of the sinusoid, and  $\Phi$  is the phase of the sinusoid (relative to the center of the Gaussian). Parameters from the fitted

functions were used to compare disparity selectivity between animals that had been trained on the fine disparity task and those that had not.

#### Eye Movement Analyses

To examine whether reversible inactivation affected eye movements, we analyzed data that were collected from scleral coils in each eye. The positions of both eyes were sampled at 1 kHz and stored to disk at 250 Hz. For each trial, we computed the mean position of each eye during the 1.5 s stimulus presentation. Vergence was computed as the difference between left eye and right eye positions, such that zero indicates correct convergence on the display screen and positive values correspond to near convergence. Version was computed as the average of left and right eye positions. We analyze horizontal version here, but results were similar for the vertical component of version.

Representative vergence and version data from four sessions are shown in Figure S4. We computed the standard deviation (SD) of vergence and version to quantify the precision and stability of eye movements (see Figure S5 legend). This analysis revealed no significant effect of muscimol on the SD or either vergence or version (Figure S5). Comparing eye movements before and after fine depth training, we also found no significant difference in vergence and version SD for monkey Bk (Figure S5). Finally, we asked whether the change in psychophysical thresholds due to muscimol (+1d versus +2d) was correlated with changes in vergence or version SD. We found no significant correlation between inactivation effects and changes in the SD of vergence or version (Figure S6). This suggests that the effects of muscimol on behavior were not an indirect effect of deficits in eye movements. This is sensible given that the effects of muscimol were localized to regions of visual space that did not include the fixation point.

In some experiments (e.g., Figures S4E and S4F), we observed small changes in mean version or vergence angles from one session to the next (e.g., +1d versus +2d). Many factors could contribute to small offsets in eye position between sessions, and we do not consider such effects to be reliable. Although we attempted to maintain the same eye calibration from one session to the next, small changes or drifts in calibration often resulted from changes in the position of the animal and various pieces of hardware with respect to the field coil. Although we observed no significant tendency for muscimol or training to alter mean values of version and vergence, we had little power to detect small differences due to variations in eye calibration.

#### SUPPLEMENTAL DATA

Supplemental Data include eight figures and can be found online at [http://www.neuron.org/supplemental/S0896-6273\(08\)00749-6](http://www.neuron.org/supplemental/S0896-6273(08)00749-6).

#### ACKNOWLEDGMENTS

We are grateful to Amy McArdle, Heidi Loschen, and Donna Lalor for excellent care and training of animals. We thank Akiyuki Anzai for helpful comments on the manuscript. This work was supported by National Eye Institute grant EY013644 to G.C.D.

Accepted: August 8, 2008

Published: October 22, 2008

#### REFERENCES

- Adams, D.L., and Zeki, S. (2001). Functional organization of macaque V3 for stereoscopic depth. *J. Neurophysiol.* *86*, 2195–2203.
- Allen, T.A., Narayanan, N.S., Kholodar-Smith, D.B., Zhao, Y., Laubach, M., and Brown, T.H. (2008). Imaging the spread of reversible brain inactivations using fluorescent muscimol. *J. Neurosci. Methods* *171*, 30–38.
- Arikan, R., Blake, N.M., Erinjeri, J.P., Woolsey, T.A., Giraud, L., and Highstein, S.M. (2002). A method to measure the effective spread of focally injected muscimol into the central nervous system with electrophysiology and light microscopy. *J. Neurosci. Methods* *118*, 51–57.
- Born, R.T., and Bradley, D.C. (2005). Structure and function of visual area MT. *Annu. Rev. Neurosci.* *28*, 157–189.
- Britten, K.H., Shadlen, M.N., Newsome, W.T., and Movshon, J.A. (1992). The analysis of visual motion: a comparison of neuronal and psychophysical performance. *J. Neurosci.* *12*, 4745–4765.
- Buonomano, D.V., and Merzenich, M.M. (1998). Cortical plasticity: from synapses to maps. *Annu. Rev. Neurosci.* *21*, 149–186.
- Chen, L.L., Goffart, L., and Sparks, D.L. (2001). A simple method for constructing microinjection sites for reversible inactivation in behaving monkeys. *J. Neurosci. Methods* *107*, 81–85.
- Colby, C.L., Duhamel, J.R., and Goldberg, M.E. (1993). Ventral intraparietal area of the macaque: anatomic location and visual response properties. *J. Neurophysiol.* *69*, 902–914.
- Crist, R.E., Li, W., and Gilbert, C.D. (2001). Learning to see: experience and attention in primary visual cortex. *Nat. Neurosci.* *4*, 519–525.
- Cumming, B.G., and DeAngelis, G.C. (2001). The physiology of stereopsis. *Annu. Rev. Neurosci.* *24*, 203–238.
- DeAngelis, G.C., and Newsome, W.T. (1999). Organization of disparity-selective neurons in macaque area MT. *J. Neurosci.* *19*, 1398–1415.
- DeAngelis, G.C., and Uka, T. (2003). Coding of horizontal disparity and velocity by MT neurons in the alert macaque. *J. Neurophysiol.* *89*, 1094–1111.
- DeAngelis, G.C., Cumming, B.G., and Newsome, W.T. (1998). Cortical area MT and the perception of stereoscopic depth. *Nature* *394*, 677–680.
- Dosher, B.A., and Lu, Z.L. (1998). Perceptual learning reflects external noise filtering and internal noise reduction through channel reweighting. *Proc. Natl. Acad. Sci. USA* *95*, 13988–13993.
- Dosher, B.A., and Lu, Z.L. (1999). Mechanisms of perceptual learning. *Vision Res.* *39*, 3197–3221.
- Edeline, J.M., Hars, B., Hennevin, E., and Cotillon, N. (2002). Muscimol diffusion after intracerebral microinjections: a reevaluation based on electrophysiological and autoradiographic quantifications. *Neurobiol. Learn. Mem.* *78*, 100–124.
- Fahle, M. (2005). Perceptual learning: specificity versus generalization. *Curr. Opin. Neurobiol.* *15*, 154–160.
- Felleman, D.J., and Van Essen, D.C. (1987). Receptive field properties of neurons in area V3 of macaque monkey extrastriate cortex. *J. Neurophysiol.* *57*, 889–920.
- Genovesio, A., and Ferraina, S. (2004). Integration of retinal disparity and fixation-distance related signals toward an egocentric coding of distance in the posterior parietal cortex of primates. *J. Neurophysiol.* *91*, 2670–2684.
- Ghose, G.M. (2004). Learning in mammalian sensory cortex. *Curr. Opin. Neurobiol.* *14*, 513–518.
- Ghose, G.M., Yang, T., and Maunsell, J.H. (2002). Physiological correlates of perceptual learning in monkey V1 and V2. *J. Neurophysiol.* *87*, 1867–1888.
- Gilbert, C.D., Sigman, M., and Crist, R.E. (2001). The neural basis of perceptual learning. *Neuron* *31*, 681–697.
- Gnadt, J.W., and Mays, L.E. (1995). Neurons in monkey parietal area LIP are tuned for eye-movement parameters in three-dimensional space. *J. Neurophysiol.* *73*, 280–297.
- Gold, J.I. (2005). Multiple roles of experience in decoding the neural representation of sensory stimuli. In *Percept, Decision, Action: Bridging the Gaps* (Novartis Foundation Symposium No. 270).
- Gold, J.I., and Shadlen, M.N. (2007). The neural basis of decision making. *Annu. Rev. Neurosci.* *30*, 535–574.
- Hikosaka, O., and Wurtz, R.H. (1985). Modification of saccadic eye movements by GABA-related substances. I. Effect of muscimol and bicuculline in monkey superior colliculus. *J. Neurophysiol.* *53*, 266–291.
- Janssen, P., Vogels, R., and Orban, G.A. (2000). Three-dimensional shape coding in inferior temporal cortex. *Neuron* *27*, 385–397.
- Janssen, P., Vogels, R., Liu, Y., and Orban, G.A. (2001). Macaque inferior temporal neurons are selective for three-dimensional boundaries and surfaces. *J. Neurosci.* *21*, 9419–9429.
- Jenkins, W.M., Merzenich, M.M., Ochs, M.T., Allard, T., and Guic-Robles, E. (1990). Functional reorganization of primary somatosensory cortex in adult

- owl monkeys after behaviorally controlled tactile stimulation. *J. Neurophysiol.* 63, 82–104.
- Krogsgaard-Larsen, P., and Johnston, G.A. (1978). Structure-activity studies on the inhibition of GABA binding to rat brain membranes by muscimol and related compounds. *J. Neurochem.* 30, 1377–1382.
- Law, C.T., and Gold, J.I. (2008). Neural correlates of perceptual learning in a sensory-motor, but not a sensory, cortical area. *Nat. Neurosci.* 11, 505–513.
- Martin, J.H., and Ghez, C. (1993). Differential impairments in reaching and grasping produced by local inactivation within the forelimb representation of the motor cortex in the cat. *Exp. Brain Res.* 94, 429–443.
- Martin, J.H., and Ghez, C. (1999). Pharmacological inactivation in the analysis of the central control of movement. *J. Neurosci. Methods* 86, 145–159.
- Nguyenkim, J.D., and DeAngelis, G.C. (2003). Disparity-based coding of three-dimensional surface orientation by macaque middle temporal neurons. *J. Neurosci.* 23, 7117–7128.
- Nicholson, S.H., Suckling, C.J., and Iversen, L.L. (1979). GABA analogues: conformational analysis of effects on [3H]GABA binding to postsynaptic receptors in human cerebellum. *J. Neurochem.* 32, 249–252.
- Poggio, G.F., Gonzalez, F., and Krause, F. (1988). Stereoscopic mechanisms in monkey visual cortex: binocular correlation and disparity selectivity. *J. Neurosci.* 8, 4531–4550.
- Prince, S.J., Pointon, A.D., Cumming, B.G., and Parker, A.J. (2000). The precision of single neuron responses in cortical area V1 during stereoscopic depth judgments. *J. Neurosci.* 20, 3387–3400.
- Prince, S.J., Pointon, A.D., Cumming, B.G., and Parker, A.J. (2002). Quantitative analysis of the responses of V1 neurons to horizontal disparity in dynamic random-dot stereograms. *J. Neurophysiol.* 87, 191–208.
- Raiguel, S., Vogels, R., Mysore, S.G., and Orban, G.A. (2006). Learning to see the difference specifically alters the most informative V4 neurons. *J. Neurosci.* 26, 6589–6602.
- Recanzone, G.H., Merzenich, M.M., Jenkins, W.M., Grajski, K.A., and Dinse, H.R. (1992). Topographic reorganization of the hand representation in cortical area 3b owl monkeys trained in a frequency-discrimination task. *J. Neurophysiol.* 67, 1031–1056.
- Recanzone, G.H., Schreiner, C.E., and Merzenich, M.M. (1993). Plasticity in the frequency representation of primary auditory cortex following discrimination training in adult owl monkeys. *J. Neurosci.* 13, 87–103.
- Roitman, J.D., and Shadlen, M.N. (2002). Response of neurons in the lateral intraparietal area during a combined visual discrimination reaction time task. *J. Neurosci.* 22, 9475–9489.
- Salzman, C.D., Murasugi, C.M., Britten, K.H., and Newsome, W.T. (1992). Microstimulation in visual area MT: effects on direction discrimination performance. *J. Neurosci.* 12, 2331–2355.
- Schiller, P.H. (1993). The effects of V4 and middle temporal (MT) area lesions on visual performance in the rhesus monkey. *Vis. Neurosci.* 10, 717–746.
- Schoups, A., Vogels, R., Qian, N., and Orban, G. (2001). Practising orientation identification improves orientation coding in V1 neurons. *Nature* 412, 549–553.
- Taira, M., Tsutsui, K.I., Jiang, M., Yara, K., and Sakata, H. (2000). Parietal neurons represent surface orientation from the gradient of binocular disparity. *J. Neurophysiol.* 83, 3140–3146.
- Uka, T., and DeAngelis, G.C. (2003). Contribution of middle temporal area to coarse depth discrimination: comparison of neuronal and psychophysical sensitivity. *J. Neurosci.* 23, 3515–3530.
- Uka, T., and DeAngelis, G.C. (2004). Contribution of area MT to stereoscopic depth perception: choice-related response modulations reflect task strategy. *Neuron* 42, 297–310.
- Uka, T., and DeAngelis, G.C. (2006). Linking neural representation to function in stereoscopic depth perception: roles of the middle temporal area in coarse versus fine disparity discrimination. *J. Neurosci.* 26, 6791–6802.
- Umeda, K., Tanabe, S., and Fujita, I. (2007). Representation of stereoscopic depth based on relative disparity in macaque area v4. *J. Neurophysiol.* 98, 241–252.
- Wang, X., Merzenich, M.M., Sameshima, K., and Jenkins, W.M. (1995). Remodelling of hand representation in adult cortex determined by timing of tactile stimulation. *Nature* 378, 71–75.
- Weinberger, N.M. (1993). Learning-induced changes of auditory receptive fields. *Curr. Opin. Neurobiol.* 3, 570–577.
- Weinberger, N.M. (1995). Dynamic regulation of receptive fields and maps in the adult sensory cortex. *Annu. Rev. Neurosci.* 18, 129–158.
- Westheimer, G. (1979). Cooperative neural processes involved in stereoscopic acuity. *Exp. Brain Res.* 36, 585–597.
- Yang, T., and Maunsell, J.H. (2004). The effect of perceptual learning on neuronal responses in monkey visual area V4. *J. Neurosci.* 24, 1617–1626.