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ENHANCEMENT OF OBLIQUE EFFECT IN THE CAT'S PRIMARY VISUAL CORTEX VIA ORIENTATION PREFERENCE SHIFTING INDUCED BY EXCITATORY FEEDBACK FROM HIGHER-ORDER CORTICAL AREA 21A

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Abstract—It is often suggested that the oblique effect, the well-known phenomenon whereby both humans and animals are visually more sensitive to vertical and horizontal contours than to oblique ones, is due to the overrepresentation of cardinal orientations in the visual cortex. The functional role of feedback projections from higher-order cortical areas to lower-order areas is not fully understood. Combining the two issues in a study using optical imaging here, we report that the neural oblique effect was significantly enhanced (3.7 times higher than the normal) in the cat's primary visual cortex through orientation shifting induced by excitatory feedback from the higher-order cortical area 21a. This suggests that a reciprocal co-excitatory mechanism may underlie the perceptual oblique effect.

Key words: oblique effect, visual cortex, area 21a, area 17, feedback connection, orientation.

The phenomenon that the function of visual system of human and some mammalian animals is more sensitive to vertical and horizontal stimuli than to those obliquely oriented is well known as the "oblique effect," which was confirmed psychologically, behaviorally and physiologically (Campbell et al., 1966; Maffei and Campbell, 1970; Appelle, 1972; Annis and Frost, 1973; Howard, 1982; Shou et al., 1985; Blake and Holopigian, 1985; Heeley et al., 1997; Orban et al., 1984; Mathews and Welch, 1997; Essock, 1980; Weitheimer and Beard, 1998; Li et al., 2003) Recent studies using optical imaging and functional magnetic resonance image (fMRI) have revealed that more neurons responded preferentially to cardinal (vertical and horizontal) contours than to oblique ones in areas 17 and 18 of cats, area 17 of ferrets, primates and even in human primary visual cortex (Yu and Shou, 2000; Wang et al., 2003; Huang et al., 2006; Coppola et al., 1998; Mansfield, 1974; Furminski and Engel, 2000). The anisotropy in the functional distribution of cortical neurons is thought to provide the neural basis of the psychological or behavioral oblique effect. However, the anisotropy shown in these lower visual cortices is rather small (about 5%–7% difference). Recently, a much larger anisotropic difference (about 23% in difference) was found in higher visual area 21a in cats, using optical imaging (Huang et al., 2006).

Area 21a receives its principal inputs from area 17 and sends extensive excitatory feedback projections to area 17 in the cat (Dreher, 1986; Dreher et al., 1996). This area is often considered to be a counterpart to primate V4 or V3v in the ventral (or temporal) visual stream (Burke et al., 1998). The functional role of such feedback projections from higher-order to lower-order cortical areas is at best poorly understood. The main aim of this study was to investigate the relationship of oblique effects between areas 21a and 17. Using optical imaging combined with pharmacological methods we investigated this issue by recording an optical measure of the oblique effect in area 17 of the cat when the excitation of area 21a was reversely altered.

EXPERIMENTAL PROCEDURES

Animal preparation

Nine normal adult cats of either sex, weighing between 2.5 and 3.0 kg, were used in the current study. All experiments involving animals conformed to the policy of the Society for Neuroscience on the Use of Animals in Neuroscience Research. All procedures were performed in strict accordance with the U.S. National Institutes of Health Guide for the Care and Use of Laboratory Animals, and all experiments were designed to minimize the number of animals used and their suffering. The detailed methods used here for surgical preparation and intrinsic optical recording have been described elsewhere (Chen et al., 2003; Huang et al., 2004; Shen et al., 2006) Animals were initially anesthetized with ketamine (25 mg/kg). All pressure points and surgical incisions were infiltrated with lidocaine. During the experiment, anesthesia was maintained with i.v. pentobarbital sodium (loading dose of 4 mg/kg, followed by maintenance with 3 mg/kg/h). After i.v. and tracheal cannulation, the cat was placed in a stereotaxic apparatus (Jiangwan II type, The Second Military Medical University, Shanghai, China). Gallamine triethiodide (Flaxedil; Shanghai Dongfeng Chemicals Factory, Shanghai, China; 10 mg/kg/h) was then used for immobilization and animals were artificially respired using a pulmonary pump. The animals' physiological conditions were kept within normal ranges throughout the experiment. Thus, the end-

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Abbreviations: EEG, electroencephalogram; NMDA, *N*-methyl-D-aspartate; ROI, region of interest.

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tidal CO_2 was kept at a range from 3.5% to 4% by adjusting the rate and/or stroke volume of the pulmonary pump, body temperature was maintained near 38 °C by an automatic temperature control system and electroencephalogram (EEG) and electrocardiogram (ECG) were continuously monitored. EEG records showed a slow wave pattern and the heart rate was maintained between 200 and 260 pulses/min throughout the procedures.

The pupils of the cat were dilated with atropine (0.5%) and nictitating membranes were retracted with neosynephrine (2%). The eyes were carefully refracted and corrected with contact lenses of appropriate refractive power. To reduce the amount of spherical aberration, artificial pupils (3 mm in diameter) were placed in the front of each eye.

Area 21a was localized by its relationship to the suprasylvian and lateral sulci (Tusa and Palmer, 1980; Tusa et al., 1981). Visual cortical area 21a and area 17 were exposed at Horsley-Clarke coordinates P1-7, L7-12 and P0-10, L0-7 respectively (Huang et al., 2004). Special care was taken to ensure that the two exposed areas had similar and overlapped retinotopic fields using the method to measure cortical retinotopic topography described elsewhere (Chen and Shou, 2003). Generally the field-of-view for areas 17 and 21a was within 10° of the fovea. Then, a stainless steel chamber of 16 mm in diameter with a glass cover, whose large field is useful for identifying the precise location of area 17, was cemented onto the skull surrounding the exposed area. After careful removal of the dura, the chamber was filled with warm silicone oil and sealed with a transparent glass window. Usually optical signals were acquired from area 17 and averaged in order to get a functional map of higher quality in the same experiment. Then the drug was administrated into area 21a and optical signals were reacquired from area 17. In some case the administration of the drug could be repeated a number of times.

Area 21a was reversibly activated and inactivated by microinjections of 1.0–1.5 μl 0.2 mM glutamate (Sigma, St. Louis, MO, USA) and 1.0 μl 0.2 mM *N*-methyl-D-aspartate (NMDA, Sigma), and 1.0–1.5 μl 100–400 mM GABA (Sigma) though a microsyringe which was fixed in the stereotaxic apparatus, respectively. As a control we also injected 1.0 μl of phosphate-buffered saline (PBS, pH 7.4) at the same site. Solutions were injected slowly (over a period of 4 min) and the needle of the micro-syringe was withdrawn 10 min after the termination of injection in order to prevent leakage (Huang et al., 2004; Shen et al., 2006). The injection sites were centered in area 21a at a depth of 0.5~1.0 mm beneath the pial surface. Previous studies have indicated that 1.0 μl of 100 mM GABA tends to diffuse over a region of 1.5 mm in diameter in the mammalian cortex (Hupe et al., 1999). To reduce the extent of the mechanical damage to the injected part of area 21a, drug injections were limited to no more than three times per site. Usually the interval between two trials was more than 3 h to guarantee a sufficient recovery. After 3 days of experiments, the animal was killed for histological study. The animal was deeply anesthetized with pentobarbital sodium (25 mg i.v.) and transcardially perfused with 0.9% saline, followed by 4% paraformaldehyde in 0.1 M sodium phosphate buffer. The location of the centers of the injection sites was assessed histologically in 50 μm sections counterstained for Nissl substance with Cresyl Violet. Only data from animals with the correct injection locations within area 21a were included for further analysis.

Visual stimulation

The cats were stimulated binocularly with a whole field (30°×40°) of drifting sinusoidal wave gratings (contrast 90%, temporal frequency of 2 Hz) with a spatial frequency of 0.5 cycles/degree. These stimulus parameters elicit responses from most neurons in both areas 21a and 17 as described previously (Chen et al., 2003; Huang et al., 2004). Stimuli were randomly presented at four orientations (0°, 45°, 90°, and 135° with respect to horizontal), each moving at two opposite directions of motion (for total eight directions). The two moving directions of the gratings were always orthogonal to the orientation. The visual gratings stimuli were repeatedly presented on the screen of a high-resolution monitor (FlexScan F931, Eizo Nanao Corporation, Japan) positioned 57 cm from the cat's eyes for 2 s with 10-second blank intervals in between. The mean luminance of the blank screen was 15.1 cd/m^2.

Optical data acquisition

As in our recent studies (Chen et al., 2003; Huang et al., 2004) a slow-scan CCD camera (512×512 pixels, 24×24 μm/pixel; Dalsa, Waterloo, Ontario, Canada) was used to record the optical images of intrinsic signals from the exposed portion of area 17. A macroscope tandem-lens arrangement of two coupled 50 mm lenses (f=1:1.2) was used to achieve a very shallow depth of field (less than 100 μm) in order to minimize blood vessel artifacts and influence of surface layers in the functional maps. However, a vessel map on the cortical surface was obtained with green light (540 nm) shining on the surface of the cortex. Intrinsic signals evoked by the grating stimuli were detected under illumination with red light (640 nm) when the camera was focused on the plane of 500 μm below the pial surface, where was located within layers 2 and 3 of the cortex. Data acquisition started one second before the appearance of the 2 s stimulus and a total of five frames, each of which lasted for one second, were recorded. Since the largest intrinsic signals appear at 3~4 s after the onset of visual stimulus, we only used the fourth frame in a trial as effective data to analyze (Chen et al., 2003). To remove the activity-dependent microvascular changes, the period of stimulus presentation was followed by a 10 s interstimulus interval. The order of stimulus presentation in each trial was randomized to prevent any systematic effects of stimulus presentation order. To reduce the noise in the acquired images, signal averaging was used, with each stimulus being presented 16–64 times.

Defining the region of interest (ROI) of the functional maps in area 17

Determination of the area 17/18 border was based upon differences between these areas in spatio-temporal frequency response (Movshon et al., 1978; Bonhoeffer et al., 1995). Specifically, the location of the boundary between areas 17 and 18 was identified objectively by subtracting the two orientation maps elicited by drifting gratings of spatial frequency 0.58 and 0.14 cycles/deg respectively as described previously (Issa et al., 2000; Hung et al., 2001; Huang et al., 2004).

Before comparing the difference of two maps, a ROI in area 17 was selected and all further comparisons were restricted within it. The following criteria were taken into account. First, in order to reduce noise or artifacts, all images were corrected to minimize interference from blood vessels using the corresponding surface vascular images. Specifically, areas occupied by major blood vessels (>250 μm in diameter) and their immediate surrounding (within 100 μm) were excluded from analysis. Second, regions within 0.2 mm from the edge of the craniotomy containing bone or dura mater were not taken into account. Finally, regions not in the focal plane of the camera due to cortical curvature were not included in the analysis. Altogether, an average area of larger than 4 mm^2 of cortex per hemisphere in nine cats underwent quantitative analysis.

Data analysis

For constructing orientation maps, the functional maps elicited by two gratings of the same orientation and opposite motion directions were added. To remove the high and low spatial frequency noise, optical images were filtered with a high pass of 960 μm and a low pass of 216 μm.

Based on the circular statistics, the orientation selectivity (preferred orientation angles and orientation bias) of each pixel

was calculated by pixel-wise vector summation of the responses in the single-orientation maps elicited by four different orientations of gratings drifting in eight different directions in the following way:

$$Mo=(a^2+b^2)^{1/2},$$
$$\theta=0.5\times\tan^{-1}(b/a),$$
$$a=\Sigma_i[R_i\times\cos(2\varphi_i)],\ b=\Sigma_i[R_i\times\sin(2\varphi_i)],$$

where θ is the preferred orientation angle (range 0° to 180°) and Mo is the orientation bias of each pixel in a preferred orientation map. R_i is the signal strength (pixel luminance) and φ_i is the orientation of stimulating grating corresponding to the ith map. This data were used to construct color-coded maps of orientation preference across the cortical surface by binning data over regions of orientation space. The normal optical maps of area 17 were collected before inactivating area 21a (see Fig. 1). Only when orientation maps were stable and reliable, did we continue on to the next comparison procedure.

Pixel-by-pixel data were used for quantitative comparison between two orientation preference maps obtained under different conditions. For quantitative comparison of orientation shifts of two maps we compared the overall shift in the ROI with that in selected subregions representing the oblique angles only in the control condition.

RESULTS

Alteration of preferred orientations in area 17 by area 21a activity

Fig. 1A–C demonstrates that the orientation preference map of cat area 17 was significantly altered by application of

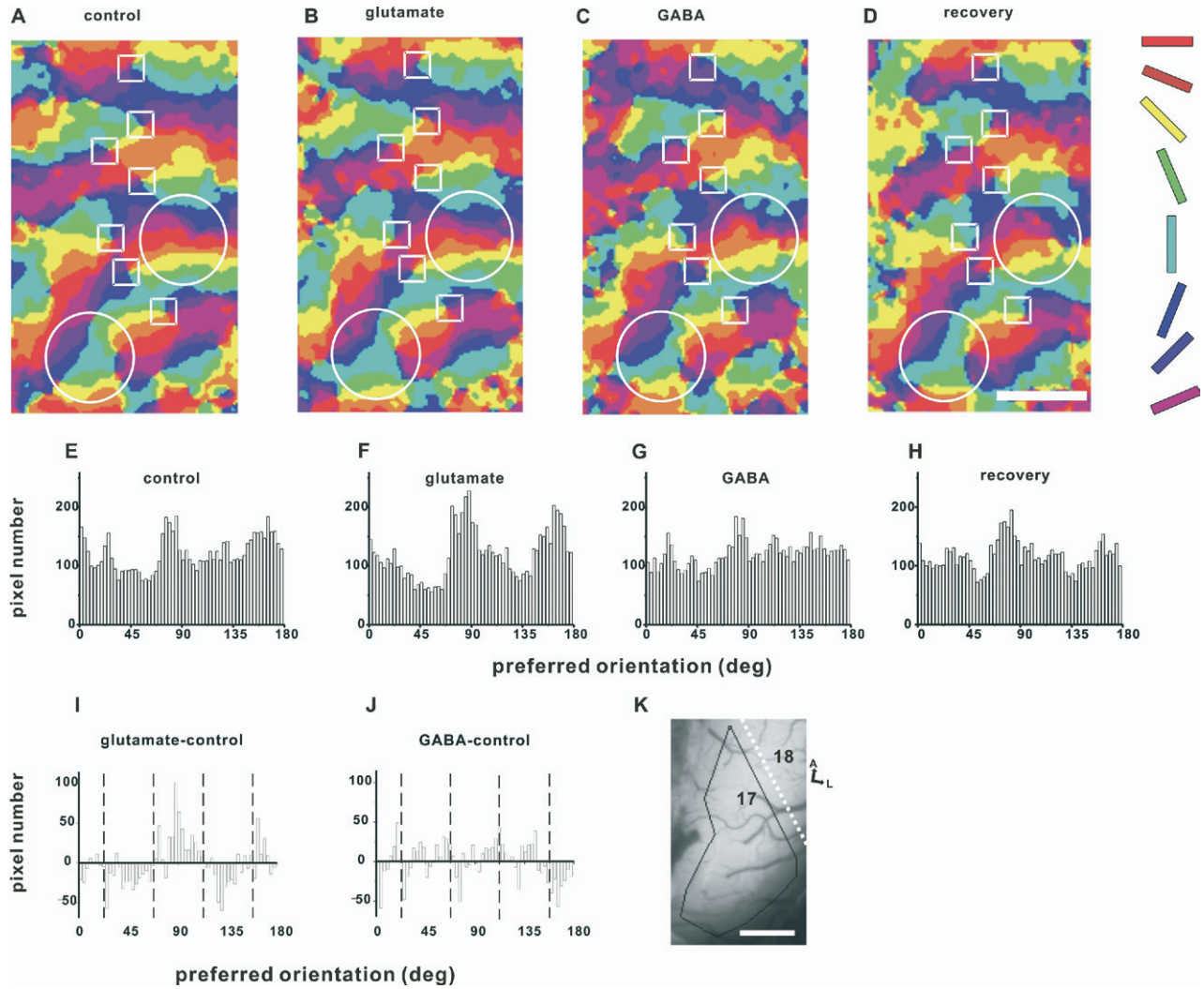

Fig. 1. Changes in neural oblique effect observed in functional orientation maps of area 17 due to injection of 1.0 μl of glutamate (0.2 mM) and 1.5 μl of GABA (400 mM) in area 21a. (A–D) Color-coded orientation maps recorded under normal (A), glutamate (B) and GABA (C) injection and recovery (D) conditions for one cat. Scale bar=1 mm. (E–H) Preferred orientation distribution histograms of pixels in the same ROI in area 17 under conditions of A, B, C and D. Note that the W-shaped distribution is significantly enhanced by glutamate and reduced by GABA. (I, J) Subtracted histograms of preferred orientation distributions in the ROI of area 17 obtained for glutamate injection minus control (I), and GABA minus control (J). Note that pixels with negative values mean those pixels with different preferred orientations in the functional map changed their original preferred orientations to new ones denoted by the positive numbers. Panel I shows that injection of glutamate caused a clear shift in many pixels from preferring oblique orientations to horizontal and vertical ones, and for injection of GABA shown in panel J, more pixels turned from preferring horizontal and vertical orientations to oblique ones. (K) The surface view of the area 17 of the cat studied and the ROI denoted by solid line. A white dotted line indicates the boundary between areas 17 and 18 which was determined by subtracting the orientation map elicited by a spatial frequency 0.58 c/day grating from the one by 0.14 c/day. Scale bar=1 mm. The true size of this blood vessel map is the same as the color maps in A–D.

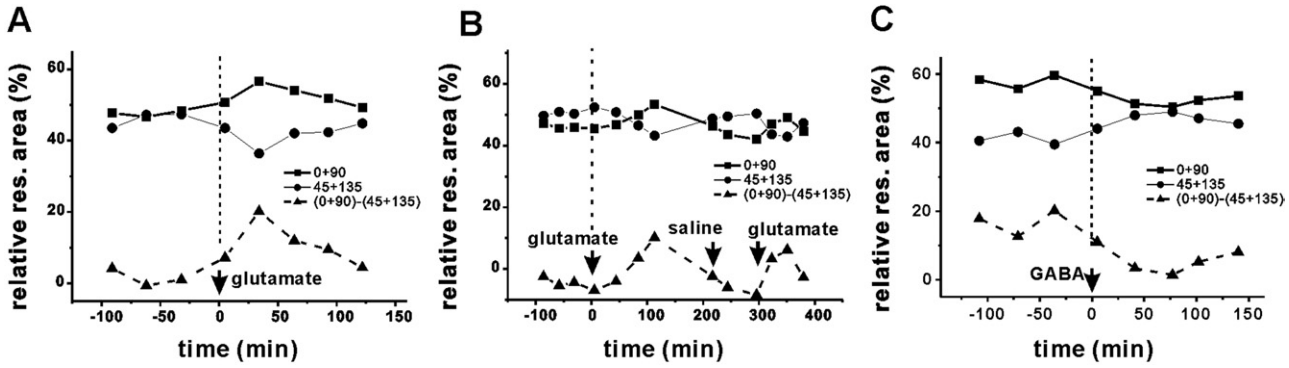

Fig. 2. Time course of the influence of applications of glutamate (A and B) and GABA (C) in area 21a on oblique effect in area 17. Dashed lines represent relative difference between cortical areas that preferred cardinal meridians and preferred oblique. Arrows indicate the onset of application of drugs or saline. Note that in addition to general enhancement of oblique effect for a cat with significant effect prior to the applying 1.5 μl 0.2 mM glutamate (A), a cat with previous counter-oblique effect in area 17 also demonstrated an oblique effect following application of 1.5 μl 0.2 mM glutamate in area 21a, and that this shift was reproducible (B). On the other hand, application of 1.5 μl 400 mM GABA in area 21a removed the strong oblique effect in area 17 completely (C).

glutamate (B) and GABA (C) to area 21a compared with the control (A) and recovery (D). In particular, significant changes in the width of orientation columns (denoted by circles) and some position shifts of "pinwheel centers" (denoted by squares) were noted. The ROI studied within area 17 (denoted by the black line in Fig. 1K) exhibited a mild oblique effect under normal condition (Fig. 1E, H). Activation of area 21a changed many neurons' preferred orientation from oblique gratings to cardinal ones, i.e. generated an enhanced oblique effect (Fig. 1F, I). While the inactivation of area 21a changed the orientation preference of some area 17 neurons from horizontal and vertical (cardinal) axes to oblique ones, i.e. a decreased the oblique effect (Fig. 1G, J). In this case, the overrepresentation of the cardinal meridians in area 17 increased significantly from 10.8% to 24.3% (or 2.25 times) due to glutamate injection and decreased significantly from 10.8% to 6.0% (or by a factor of 0.56) due to GABA injection.

Preference of the orientation shift

The neural oblique effect of area 17 varied from animal to animal and is relatively weak, with a mean overrepresentation of horizontal and vertical meridians about 5–6% more than the oblique. Interestingly, the enhancement of oblique effect of area 17 by area 21a chemical *activation* (Fig. 2A, B) and the decline of the oblique effect by 21a chemical *inactivation* (Fig. 2C) were clearly independent of the magnitude of the oblique effect measured in the normal condition. Fig. 2 presents the time causes of change in cortical area in percentage for cardinal and oblique orientations for three animals in different conditions. Notably, the enhanced oblique effect in area 17 caused by glutamate application in area 21a even appeared in a subject that exhibited little or no oblique effect (with perhaps even a small bias toward the oblique Fig. 2B); an effect comparable to the significantly enhanced oblique effect observed in the other seven cats which showed the expected bias normally (Fig. 3A). In contrast, the relative strong oblique effects normally exhibited were almost cancelled by injecting GABA in area 21a (Fig. 2C).

Overall enhancement of oblique effect in area 17

A total of 11 sets of experiments were performed on nine cats. In eight cases glutamate was injected into area 21a and in the three cases GABA was injected. Accordingly, in two cats, both injections were done (denoted by stars in

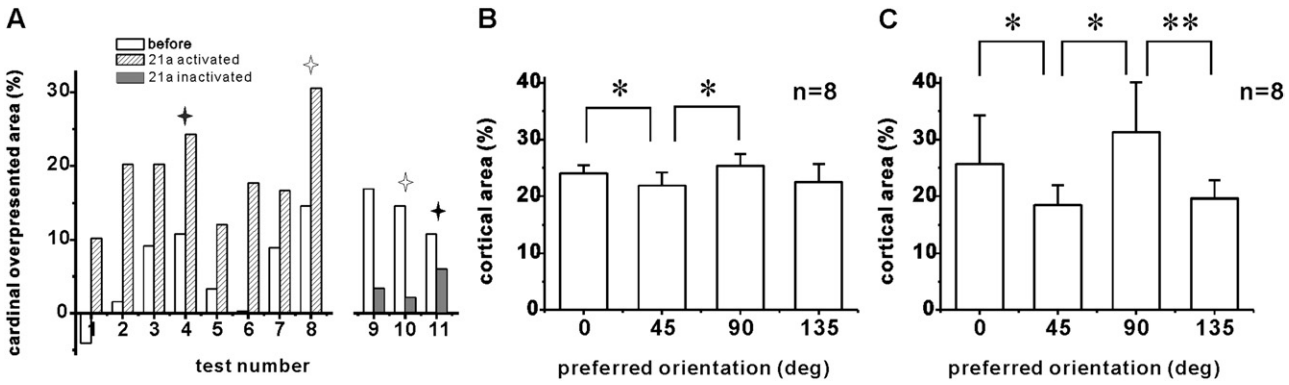

Fig. 3. Summary results of the enhanced oblique effect. (A) Summary of results from nine cats studied showing that the overrepresentation of the cardinal orientations in area 17 was increased by injecting glutamate in area 21a (1–8), and decreased by injecting GABA (9–11). For the eight cats injected with glutamate, the cortical area within the selected ROIs in area 17 preferring 0° and 90° was slightly larger than the area representing 45° and 135° under normal condition (B); but the difference became significantly larger after glutamate injection in area 21a (C). * $P<0.05$; ** $P<0.01$, paired *t*-test.

Fig. 3A). For each set of experiments, we mapped the temporal evolution of the oblique effect, as demonstrated in Fig. 2, and selected the maximum drug effect data point in the time course curve to produce Fig. 3. The change in the oblique effect was observed in all animals and was repeatable within the same animal (Fig. 3A). For the eight cats that received an injection of glutamate, a slight overrepresentation of the horizontal and vertical orientations was found in area 17 under normal condition (Fig. 3B). However, a clear enhancement of this overrepresentation could be seen under the maximum effect of injecting glutamate (Fig. 3C). The mean overrepresentation of horizontal and vertical meridians in area 17 was increased by glutamate injection on average 3.7 times, from 5.1±5.9% to 18.8±6.4%, for the eight cases ($n=8$, paired t-test, $P<0.05$), and was decreased by GABA injection in the three tests. One cat was additionally injected with 0.1 mM NMDA. A similar enhanced oblique effect was observed in this animal and no recovery from the NMDA effect was found, suggesting that NMDA receptors in area 21a might be involved in this phenomenon, but artificially prolonged, as there is no uptake mechanism for NMDA in the tissue injected. However, further study remains to be done to clarify the mechanism(s) at the receptor level. Overall, we conclude that area 21a activity changes the strength of the neural oblique effect obtained in area 17 through positive feedback.

Quantifying the range of orientation shifting

The results above indicate that the neural oblique effect of area 17 was altered by the slight shifting in preferred orientation of many area 17 neurons induced by feedback signals from area 21a. One would like to know how large a shift is required for a significant change in the effect. We compared the mean distributions of preferred orientation difference of each corresponding pixel in the ROI of optical maps obtained in control conditions and during glutamate application in the eight cats studied (Fig. 4). The majority of pixels (82%) shifted by 30° or less as depicted by open columns. This result is interesting because the activation of area 21a seems to only slightly change the preferred orientation of neurons in area 17; however, it does dramatically enhance the neural oblique effect in area 17 in all eight cats studied without exception. Furthermore, we investigated the mean distribution of the orientation differences of pixels that originally preferred oblique orientations and changed their preference to cardinal orientations during glutamate injection into area 21a, defined as the oblique-to-cardinal region and depicted as gray columns in Fig. 4. Although the majority of these pixels (65.0%) still shifted by 30° or less our statistics showed that the two histograms were distributed independently (χ^2 test, $P<0.001$), and that the mean shift in the oblique-to-cardinal region (25.9°) was significantly larger than that in the ROI (17.9°). This suggests that the slight shifting of the preferred orientations in a large number of neurons due to activation of area 21a is toward a direction that causes an enhancement of neural oblique effect in area 17, and vice versa. Feedback from higher-order cortex might have little effect on a single unit encoding a specific orientation contour, however, at a population level it can recruit more neural machinery to enhance certain kind of information, thus making an important contribution to perceptual oblique effect at higher levels via coactivation.

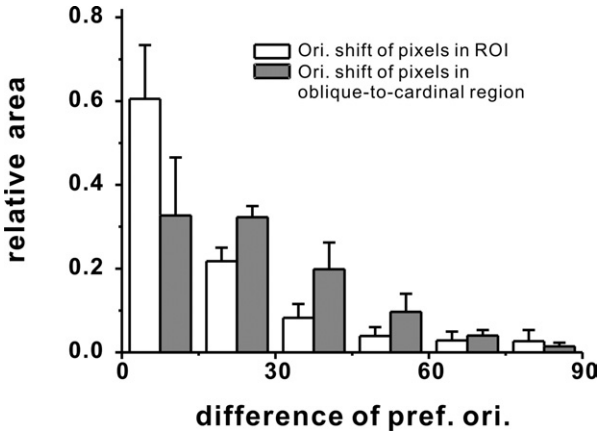

Fig. 4. Histograms of preferred orientation difference for each pixel in the ROI (open columns), and for only the oblique-to-cardinal region (gray columns) in area 17 before and during the application of glutamate in area 21a. The oblique-to-cardinal region was a part of the ROI (see Experimental Procedures), in which pixels normally preferred oblique orientations but shifted to cardinal orientations during glutamate application. The vertical axis presents relative area, in which preferred orientations of all pixels were compared in paired conditions of normal and during glutamate application. Note that while the majority of pixels in both the ROI (82%) and the oblique-to-cardinal region (64%) shifted their preferred orientations within a relatively small range of >30°, the mean shift in the oblique-to-cardinal region of 25.9° was significantly larger than that seen overall in the ROI (17.9°).

DISCUSSION

Using a combination of optical imaging and pharmacological injections the results presented here are the first evidence that positive feedback signals from area 21a dramatically alter the strength of the oblique effect within area 17 through a slight shift in the neurons' preferred orientations toward horizontal and vertical meridians. This suggests a neural mechanism underlying the enhancement of neural oblique effect in area 17 via feedback signals from the higher order visual cortical area.

The neural oblique effect is usually taken to mean that more neurons in a given cortical area preferentially respond to horizontal and vertical contours than to oblique (as demonstrated both in the electrophysiological and optical imaging studies; Mansfield, 1974; Albus, 1975; Maffei and Campbell, 1970; Shou et al., 1985; Yu and Shou, 2000; Leventhal and Hirsch, 1978; Li et al., 2003; Wang et al., 2003; Liu and Pettigrew, 2003; Huang et al., 2006). However, there are some differences in the data from different groups which have used single-neuron recording to count cell numbers of different preferred orientations in the cortex (Mansfield, 1974; Albus, 1975; Leventhal and Hirsch, 1978). However, data from different groups that use single-neuron recording methods have shown discrepancies in the strength of the neural oblique effect (Mans-

field, 1974; Albus, 1975; Leventhal and Hirsch, 1978) due perhaps to sampling problems associated with a limited number of electrode penetrations and number of neurons recorded, by different cell types and locations within the visual cortex, as well as analysis methodology (although a more recent analysis based on a sample of 4418 cells has been reported; Li et al., 2003). In contrast, the intrinsic signal optical imaging has the advantage of studying functional organization in relatively large areas of the visual cortex, exposed on the hemispheric surface. This makes it easy and reliable to study the functional influence of higher-order cortical areas on lower-order cortical areas on a larger scale (Huang et al., 2004; Shen et al., 2006). Recently, optical imaging has been used to reveal the neural oblique effect in cat's area 18 (Wang et al., 2003; Liu and Pettigrew, 2003) and in area 21a (Huang et al., 2006).

The receptive field properties of cells in areas 21a and 17 are similar in many respects (Dreher, 1986; Wimborne and Henry, 1992; Dreher et al., 1993; Tusa and Palmer, 1980; Wang et al., 2000; Wang and Dreher, 1996; Morley and Vickery, 1997). Our optical imaging and single-unit recording data (Huang et al., 2006) and other reports in previous studies showed that most cells in area 21a have their receptive fields highly concentrated within 5° of the area centralis, mainly receiving feedforward input from, and sending feedback output to, area 17 (Symonds and Rosenquist, 1984; Tusa and Palmer, 1980; Updyke, 1986; Wimborne and Henry, 1992; Dreher et al., 1993; Wang and Dreher, 1996; Wang et al., 2000). In this study, special care was taken to inject glutamate or GABA into the cortical representation of the central retina in area 21a, maximizing the likelihood of successful manipulation of the input from area 21a to the ROI in area 17.

Because the oblique effect in area 17 and 18 is rather weak (Yu and Shou, 2000; Coppola et al., 1998; Furminski and Engel, 2000; Wang et al., 2003; Huang et al., 2006), it seems unlikely that this is the sole source of the perceptual effect. However, recent study in our group has strikingly found that neural oblique effect in area 21a is about 4.6 times of that of area 17 in the cat (Huang et al., 2006). The feedback projections from area 21a not only appear to exert an excitatory influence on area 17 cells (Wang et al., 2000) but also enhance the spatial frequency tuning of area 17 significantly (Huang et al., 2004). The present results further demonstrate a descending role for area 21a in enhancing the oblique effect in area 17, which was not observed with the limited number of recorded cells by single unit recording (Wang et al., 2000) but is in agreement with the general characteristics that the corticocortical connections between higher-order and the lower-order areas are made almost exclusively by excitatory pyramidal neurons; for review see Bullier, 2004).

Therefore, it is suggested that co-excitation between cortical areas such as areas 21a and 17 might benefit the neuronal synchronizing activity of many other visual cortical areas to emphasize certain kinds of information along the visual pathway.

Given that the results here were obtained in anesthetized cats one could speculate that in the wake animals this enhancement would be even more significant. Area 21a in the cat has been suggested to be the functional homologue of area V4 (or V3) in the monkey (Burke et al., 1998). An attention-induced enhancement in the response of neurons has been found in monkey V1 and V4 (McAdams and Maunsell, 1999). If the role of V4 is similar to area 21a it is reasonable to hypothesize that during attention, increase of activity in area V4 may enhance the oblique effect in V1 through feedback signals and the reciprocal excitatory interaction between the two cortical areas may play a role in generating the perceptual or behavioral oblique effect in both monkeys and man. Zeki (1993) had pointed out that the importance of the "reentry" of signals from high order area into V1 in forming a concept although the significance of the role needs to be elucidated.

The neural oblique effect widely observed in visual cortical areas 17, 18 and 21a might be originated from the retina. It was well documented that more retinal ganglion cells are distributed along the horizontal and vertical meridians than the oblique meridians in the retina (Stone, 1978; Hughes, 1981) and more relay cells in the lateral geniculate nucleus preferred to respond the cardinal contours (Vidyasagar and Urbas, 1982; Shou and Leventhal, 1989), and the oblique effect seems to be innate (Leehey et al., 1975). The natural and indoor scenes all contain more horizontal and vertical contours than the oblique contours (Coppola et al., 1998). Thus, it is of interest to study whether there is a relationship between the visual environment and the generation of visual orientation anisotropy in the visual system.

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