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ORIENTATION BIAS OF THE EXTRACLASSICAL RECEPTIVE FIELD OF THE RELAY CELLS IN THE CAT'S DORSAL LATERAL GENICULATE NUCLEUS

C. SUN,[a] X. CHEN,[a] L. HUANG[a] AND T. SHOU[a,b]*

[a]*Vision Research Laboratory and Liren Laboratory, Center for Brain Science Research, School of Life Sciences, Fudan University, Shanghai 200433, China*

[b]*Laboratory of Visual Information Processing, Institute of Biophysics, Chinese Academy of Sciences, Beijing 100101, China*

Abstract—The spatial properties of the extraclassical receptive fields (ECRF) of neurons responding to a stimulus restricted to it and its interaction with the classical receptive field (CRF) in visual information processing were investigated in 74 relay cells in the dorsal lateral geniculate nucleus (LGNd) of anesthetized cats. The results demonstrate that the ECRF of most relay cells in the LGNd responded preferentially to a grating stimulus of low spatial frequency through a mechanism of spatial summation. These biased cells showed a significant orientation bias which was relatively smaller than that of the CRF. The preferred orientations of the ECRF were not correlated with those of the CRF in most relay cells. The orientation biased ECRFs and CRFs interacted with each other in a non-linear way, resulting in a great diversity of response properties. Overall, the CRF played a more significant role than the ECRF in determining a cell's orientation bias and preferred orientation. The ECRF mostly showed a modulatory role mainly in suppressing and/or in partially facilitating the neural response to stimulation in the CRF although in some cases, the ECRF did determine a cell's responsiveness and orientation sensitivity.

These results suggest that the ECRF might contribute to the ability of the LGNd neurons to detect some complex features such as texture segmentation and provide a subcortical contribution to the integrative field of visual cortical cells through receiving inputs from retinal ganglion cells with similar orientation biased extended surrounds [Neuroscience 98 (2000) 207].

Key words: spatial frequency, classical receptive field, vision, orientation turning, interaction.

Most receptive fields of retinal ganglion cells and relay cells in the dorsal lateral geniculate nucleus (LGNd) in higher mammals are described as having a concentric organization, consisting of an excitatory center and an antagonistic surround (Kuffler, 1953; Enroth-Cugell and Robson, 1966; Hochstein and Shapley, 1976). The local area in the retina within which visual stimuli evoke a cell's discharges is defined as the classical receptive field (CRF) of the cell (Kuffler, 1953; Hubel and Wiesel, 1959, 1961). For decades, it has been known that visual stimuli restricted to the area outside of the CRF could not evoke the neuron's discharges directly but do modulate the responses to the stimuli on the CRF. The area outside of the CRF is so defined as the extraclassical receptive field (ECRF) or integrative field (Ikeda and Wright, 1972; DeAngelis et al., 1992, 1994; Li and Li, 1994; Hupe et al., 1998, 2001; Walker et al., 1999; Freeman et al., 2001; Solomon et al., 2002).

The physiological function of the ECRF has been primarily studied in cells of the visual cortex. In cats and primates, stimuli presented to the ECRF of cortical neurons most frequently suppress and less often facilitate the responses of the CRF (Li and Li, 1994). On the other hand, the functional influence of the ECRF on the CRF in the cat's LGN is primarily one of inhibition (Hubel and Wiesel, 1959; Cleland et al., 1983; Li and He, 1987; Felisberti and Derrington, 1999; Jones et al., 2000). A disinhibitory surround beyond the CRF of the retinal ganglion cells in cats has also been reported following stimulation by flashing bars of different length or spots of different size (McIlwain, 1966; Ikeda and Wright, 1972; Li et al., 1992). However, until recently, there have been few reports about direct response to a visual stimulus delivered to the ECRF alone.

A recent report from this laboratory reported, interestingly, that in more than half of retinal ganglion cells of the cat, the extended surround which consists of the ECRF with a partial surround of the CRF, responds alone to grating stimuli restricted on it and exhibits a significant orientation bias (OB) when stimulated by gratings of appropriate combinations of spatial frequencies and orientations. Moreover, the extended surround interacted with the CRF center in a non-linear manner (Shou et al., 2000). That study of the ECRF initiated a new concept, namely, that the neuron processes much more information, in a larger field, than previously thought, despite research for over half a century. Solomon et al. (2002) further studied the suppressive properties of the ECRFs of parvocellular, magnocellular, and koniocellular cells in the primate lateral geniculate nucleus.

The goal of this study is to determine the role of the ECRF of relay cells in the LGNd in visual information processing of orientated contours that may provide the basis of form perception. Specially designed annular and circular shapes containing gratings of various spatial fre-

*Correspondence to: T. Shou, Vision Research Laboratory and Liren Laboratory, Center for Brain Science Research, School of Life Sciences, Fudan University, Shanghai 200433, China. Tel: +86-21-65642355, Fax: +86-21-65643528.
E-mail address: tdshou@fudan.edu.cn (T. Shou).

Abbreviations: CRF, classical receptive field; DOG, difference of Gaussians; ECRF, extraclassical receptive field; LGNd, dorsal lateral geniculate nucleus; OB, orientation bias.

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quencies and orientations were employed experimentally to stimulate different parts of a receptive field.

EXPERIMENTAL PROCEDURES

Surgical procedures and physiological recording

The detailed methods for recording single-unit activity from the relay cells in LGNd of anesthetized and paralyzed cats have been described elsewhere (Kratz et al., 1978; Sanderson, 1971; Shou et al., 1986; Shou and Zhou, 1989; Zhou et al., 1994, 1995). All investigations involving animals conformed to the guidelines of the Chinese Association for Physiological Sciences on the Ethical Use of Animals and the National Institutes of Health for Care and Use of Laboratory Animals (revised 1996). All efforts were made to minimize the number of animals used and their suffering. Cats, from the Silver Root Animal Company, Shanghai, China, were initially anesthetized with ketamine (20 mg/kg). During the rest of the experiment, light anesthesia was maintained with i.v. pentobarbital sodium given at an initial dose of 4 mg/kg followed by an infusion of 3 mg/kg·h. Gallamine triethiodide (Flaxedil; Shanghai Dongfeng Chemicals Factory, Shanghai, China; 8–10 mg/kg·h) was used for immobilization. An indication of the level of the anesthesia was gained from the heart rate and EEG. The animal's rectal temperature, end-tidal CO_2, heart rate, ECG and EEG were continuously monitored and kept within normal limits. All pressure points and incisions were infiltrated with local long-acting anesthetic (1% lidocaine HCl). Pupils were maximally dilated with atropine sulfate (1%), and appropriate contact lenses were used to protect the cornea. Neo-Synephrine (5%) was administered to retract the nictitating membranes. Since we had found that most eyes of the pentobarbital sodium anesthetized, gallamine triethiodide-paralyzed cats had astigmatism ranging from 0.25–2.25 diopters with a mean of 0.75 diopters (Shou et al., 1986), special care was taken to avoid astigmatism by using a combination of spherical and cylindrical lenses when needed. Artificial pupils of 3 mm in diameter were used for cat eyes.

The action potentials of cat LGN relay cells were extracellularly recorded with a glass microelectrode filled with 3 M NaCl. The impedance of microelectrodes ranged from 5 to 15 MΩ. Signals were amplified and passed to an audio monitor and a data collection system (CED micro 1401; Cambridge Electronic Design, Cambridge, UK), whose output was stored in a computer and analyzed by Spike2 software (version 4; Cambridge Electronic Design).

Visual stimuli

The receptive fields of isolated units were first mapped by using a hand-held target on a tangent screen 57 cm from the cat's eye. The disks were carefully plotted on the screen and this was done repeatedly throughout the experiment to ensure that the eye movement was prevented completely. Visual stimulation was generated on a computer display (FlexScan F931; EIZO, Japan) by a Visual Stimuli Generator 5 (Cambridge Research Systems Ltd, UK).

All the stimulus patterns were presented on a display with uniform background of mean luminance 17 cd/m^2. After mapping the approximate center of CRF by a hand-held target, we first recorded a series of discharges of the neuron to a flashing light point of 27 cd/m^2 in luminance moving across the CRF along the horizontal and vertical directions to determine the precise position of the center of CRF, where the maximal discharge was evoked. The light spot with diameter 0.5° flashed 10 times at 2 Hz for each fixed position and then shifted in a randomized interleaved sequence for a total of 10 positions in step of 0.5°. Then, a stimulating area-response amplitude curve was measured by increasing the diameter of a flashing round area that was centered precisely on the center of the cell's CRF. According to the area-response curve we determined the borders of the CRF and the ECRF for each cell precisely and ensured that all the visual stimuli and physiological measures of the CRF and ECRF were reliable for the study.

The main stimuli were two drifting sinusoidal gratings that independently appeared within an inner round patch (diameter 1.5°–4° in visual angle) and an outer concentric annulus (inner diameter 1.5°–4°, outer diameter 7°–22°). Within the round patch and annulus, the two drifting gratings were randomly presented in various orientation and spatial frequency combinations. The orientation of each grating was orthogonal to the direction of drift. The motions of the two drifting gratings were always kept phase-locked at a constant temporal frequency of 2–4 Hz. Their mean luminance and contrast were 17 cd/m^2 and 0.7, respectively. The diameters of the circular and annular stimuli used for each cell were carefully selected from the area-response curve described above.

Data analysis

The amplitude of the fundamental Fourier component of averaged post-stimulus time histogram of a cell's response to grating stimuli was defined as response (spikes/second). The spontaneous response has been subtracted. The relay cells were categorized as ON- and OFF-center, X and Y type cells according to criteria commonly used (Enroth-Cugell and Robson, 1966; Hochstein and Shapley, 1976). Circular statistics were employed to quantify the preferred orientation and OB as previously reported (Batschelet, 1981; Shou and Leventhal, 1989; Worgotter et al., 1990; Zar, 1994; Zhou et al., 1995). The responses of each cell to the different orientations of stimuli presented were measured as a series of vectors. The vectors were added and divided by the sum of the absolute values of the vectors. The polar angle of the resultant vector is the cell's preferred orientation. The length of the resultant summed vector provides a quantitative measure of OB of each cell. A bias >0.1 indicates that the cell showed statistically significant OB at the level of 0.005 (Leventhal and Schall, 1983; Shou and Leventhal, 1989; Worgotter et al., 1990; Thompson et al., 1994; Zhou et al., 1995; Shou et al., 1995). Student's *t*-test and χ^2 test were applied to the data for group comparison and histogram analysis. Except mentioned, all tests were based on *t*-test.

RESULTS

Seventy-four LGN relay cells including 52 Y cells and 22 X cells (49 ON-center cells and 25 OFF-center cells) were studied in 11 adult cats. The neurons that we recorded were at about 3–10° eccentricity, mainly about 5°. The spatial frequency tuning and orientation tuning curves of each cell were measured when visual stimuli of appropriate combinations of grating orientations and spatial frequencies were employed on the CRF, ECRF, and the CRF and ECRF combined (hereafter termed "the whole area"), respectively.

Area tuning and spatial frequency tuning properties

For each cell studied, an area turning curve was routinely measured. The area tuning curve of a typical LGN neuron is shown in Fig. 1A. When the stimulating area increased in diameter, the cell's response first elevated to a peak marked by an arrow, then fell to a minimum marked by the second arrow and finally increased gradually to a plateau. The first arrow indicates the diameter of the CRF center and the second arrow defines the border of the cell's concentric CRF and the ECRF. The large area outside of

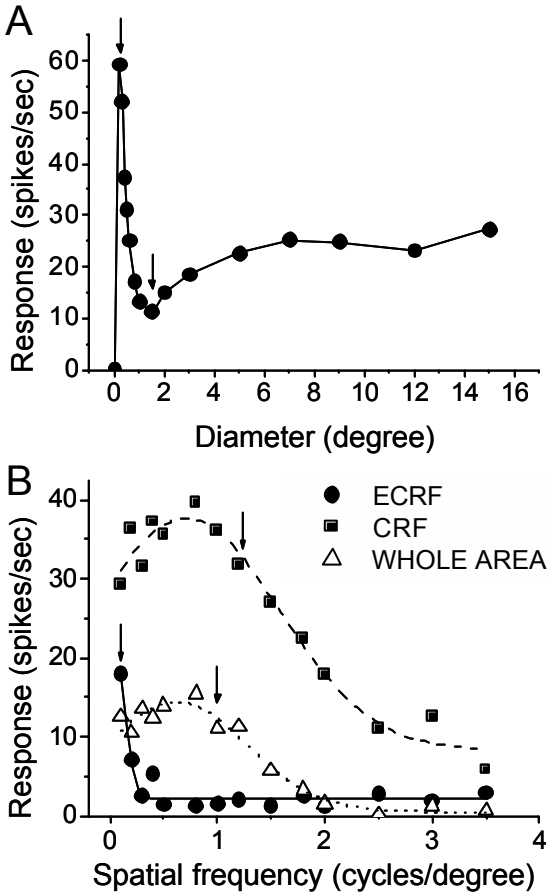

Fig. 1. (A) An area-response curve of a typical LGN relay cell. The stimulus is a stationary flashing spot of increasing diameter, whose center is fixed at the CRF's center, and with a flash frequency of 2 Hz. The first arrow shows the center diameter of the CRF, indicating an excitatory spatial summation. The second arrow shows the surround diameter of the CRF, indicating inhibitory surround summation. With further enlargement the stimulus diameter, the response amplitude partially recovers. (B) Spatial frequency tuning curves of the components of the CRF, the ECRF and the whole area of a relay cell. The three arrows indicate the optimal spatial frequencies of gratings employed to elicit the cell's best OB of the CRF, the ECRF and the whole area (1.2, 0.1 and 1.0 cycles/degree, respectively). The grating stimuli were identical in mean luminance (17 cd/m^2), contrast (0.70), and temporal frequency (2 Hz). Note that a nonlinear interaction between the CRF and the ECRF suppressed the responses of the whole area at high frequency, to which the ECRF alone had no response.

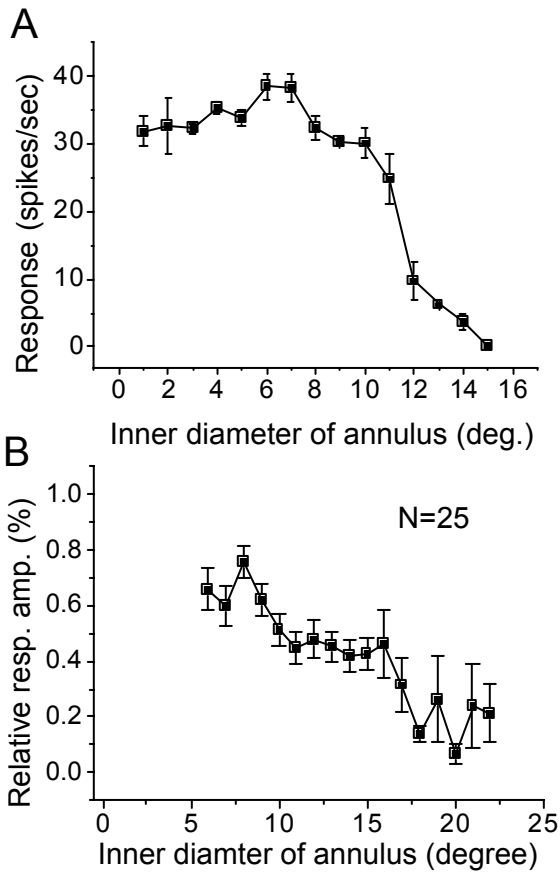

Fig. 2. Spatial summation in the ECRF of LGN neurons. (A) Response curve of the ECRF to gratings within an annulus whose outer diameter was fixed at 16° and inner diameter was increasing gradually. The gratings had a spatial frequency of 0.1 cycles/degree and temporal frequency of 2 Hz. Note that when the inner diameter of the annulus increased from 8° to 15° the response of the cell decreased roughly in a linear manner. (B) Averaged response curve from 25 neurons, showing a similar spatial summation.

the second arrow is defined as the ECRF, which could expand from 7° to 22° in visual angle due to different cells in the study. One of the main findings in this study is that the ECRF of the most LGNd cells (74.3%, 55 in 74) responded directly to grating stimuli of low spatial frequency in absence of stimulation on the CRF. The spatial frequency tuning curves of the CRF, the ECRF, and the whole area for a representative cell are shown in Fig. 1B. The curve of the CRF (solid squares) always shows the greatest response amplitude and cutoff spatial frequency, and that of the ECRF (solid circles) shows the lowest. The spatial frequency response curve for stimulation of the whole area (triangles) lies intermediate between the other two. The curve of the whole area indicates that the simultaneous stimulation of the ECRF induced a strong inhibitory effect on the CRF response, especially at higher spatial frequencies. In contrast to the classical linear model of the difference of Gaussians (DOG model; Rodieck and Stone, 1965; Enroth-Cugell and Robson, 1966; Hochstein and Shapley, 1976), the response of the whole area declined at spatial frequencies to which stimulation of the ECRF alone gave no response. This indicates a strong nonlinear interaction between the CRF and the ECRF.

Spatial summation of the ECRF

To test the spatial summation of the ECRF, the response curve of the ECRF of a neuron was measured when it was stimulated by gratings within an annulus whose outer diameter was constant at 16° and inner diameter was increasing gradually from 1° to 16°. The response amplitude of the ECRF remained unchanged until the inner diameter reached 7°, at which point it declined gradually as the width of the grating annulus became thinner (Fig. 2A), indicating

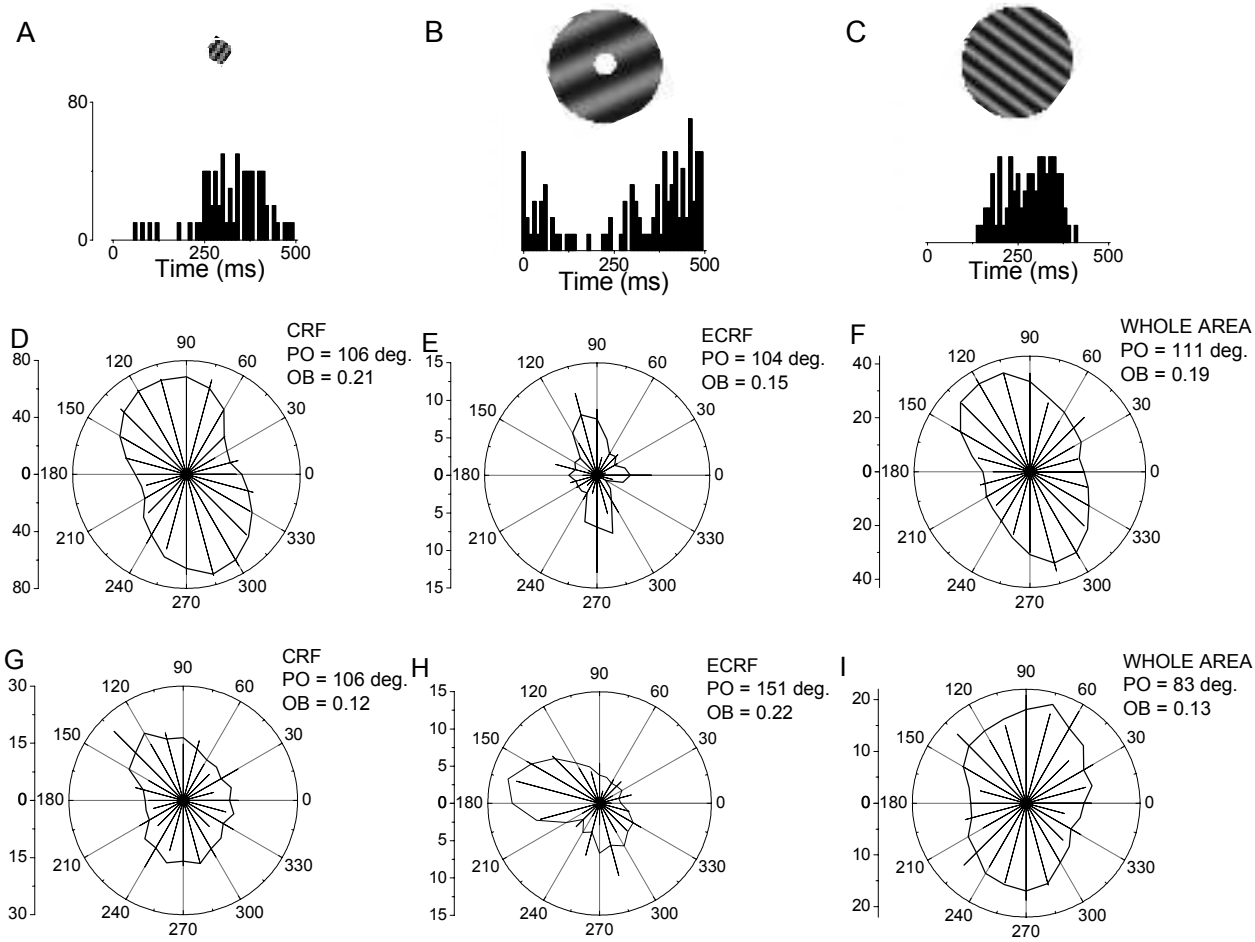

Fig. 3. (A–C) The stimulus configurations (CRF, ECRF and whole area, respectively) and corresponding post-stimulus time histograms of a cell's responses to them; (D–F) the orientation turning curves of a relay cell. Note that the three polar curves are similar in preferred orientation. (G–I) Another relay cell's orientation turning curves. Note that the preferred orientation of the ECRF is orthogonal to the preferred orientation of the CRF (or the whole area). The vertical scales in D–I are in spikes/s.

a spatial summation. The averaged spatial summation curve for 25 LGNd cells is shown in Fig. 2B, suggesting the general responses of the ECRF depend on the contribution from a population of widespread subunits over a large area in the retina.

Preferred orientation

It has been known that most retinal ganglion cells (Levick and Thibos, 1980, 1982; Shou et al., 1995) and LGNd neurons (Vidyasagar and Urbas, 1982; Shou et al., 1986; Shou and Leventhal, 1989) in the cat are orientation-biased in responses to moving grating stimuli. Interestingly, we found that the LGNd cells studied showed significant orientation sensitivity of the ECRF, in addition to that shown in the CRF and the whole area. Orientation turning curves in polar plots of the CRF, the ECRF and the whole area of two cells measured with optimal spatial frequencies are shown in Fig. 3D–I. The preferred orientations of the CRF and the ECRF were similar in some cells, such as the one shown in Fig. 3D and 3E but not always parallel (an example shown in Fig. 3G and 3H).

Most of the cells (80.4%, 37 in 46 cells) showed a significant difference in preferred orientations between the CRF and ECRF (larger than 30°, or either of the ECRF and CRF with an OB less than 0.1; Fig. 4A), indicating that the orientation sensitivities of the CRF and ECRF may originate independently. The preferred orientation of the whole area was well aligned with that of the CRF in 64% (27 in 42 cells) of the cells studied, where preferred orientation difference was less than 30° (Fig. 4C), but the preferred orientation difference of the ECRF and the whole area were randomly distributed (Fig. 4B), showing that the influence of the orientation sensitivity of the CRF is stronger than that of the ECRF on the whole area. In fact, according to the DOG model (Rodieck and Stone, 1965; Li et al., 1991), the CRF has a bigger weight than the ECRF.

Orientation bias

To our surprise, we found that in most cells studied (72.7%, 40 in 55 cells, 33 Y cells, and 7 X cells), the ECRFs showed significant OB (bias >0.1; $P<0.005$) according to the circular statistical criteria when they were

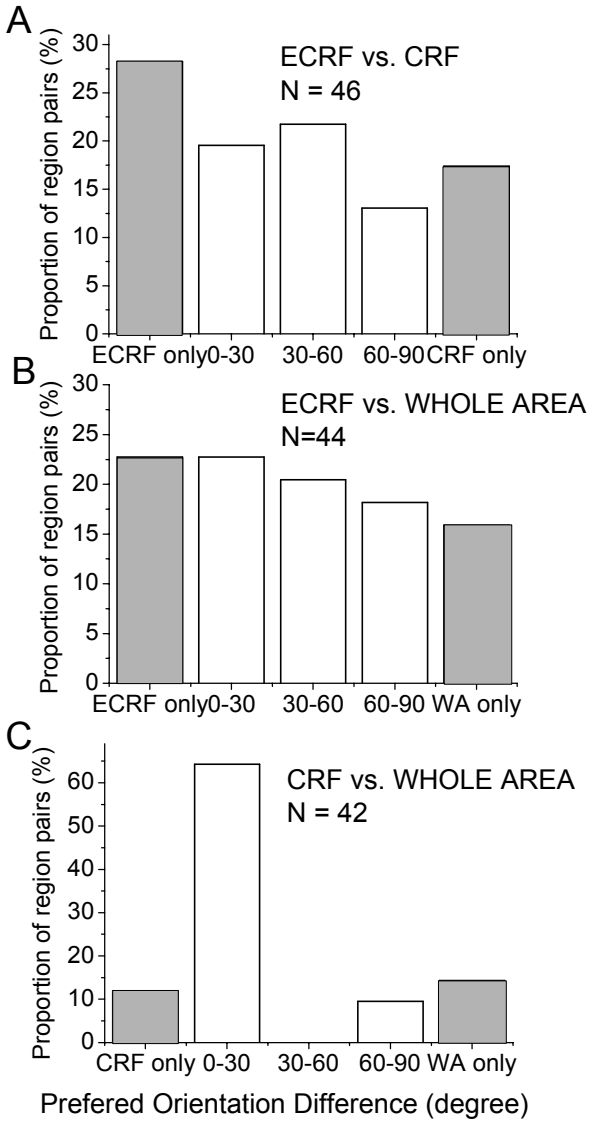

Fig. 4. Comparison of preferred orientation difference of relay cells who were stimulated by two of three different stimuli. Comparison between the ECRF and the CRF (A), the ECRF and the whole area (B), the CRF and the whole area (C). Note that the preferred orientation of the ECRF of 34% of cells is significantly different from that of the CRF (a difference $>30°$), but the whole area's preferred orientation is generally aligned to the CRF's preferred orientation.

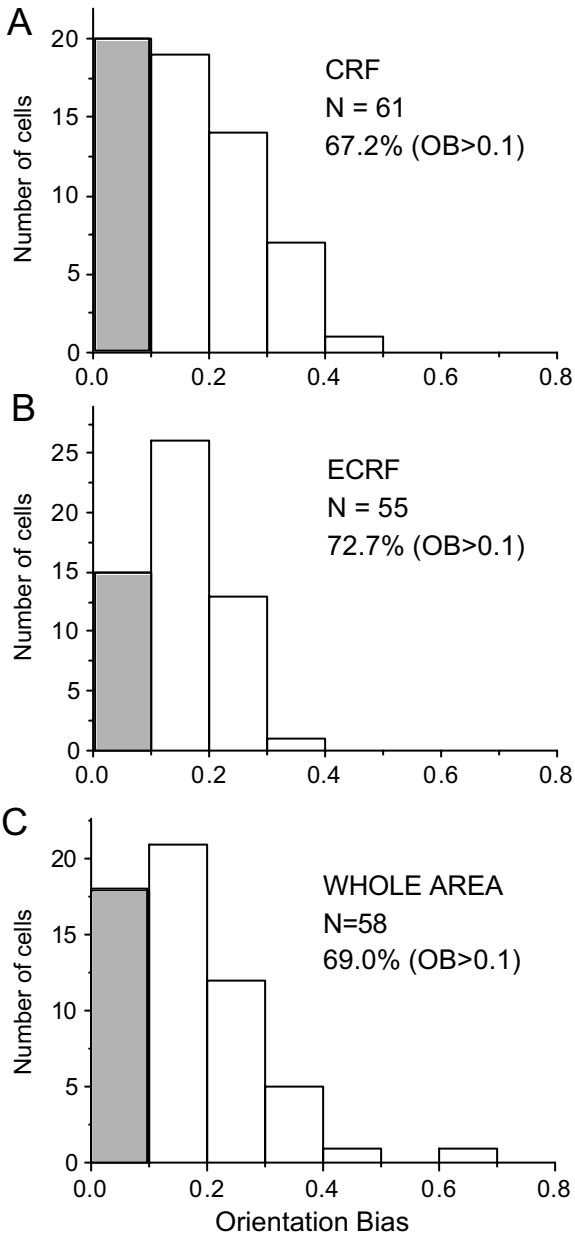

Fig. 5. Distribution of OB of relay cells for the CRF only (A), the ECRF only (B) and the whole area, covering both the CRF and ECRF (C) were separately stimulated with gratings of optimal spatial frequency for each part. The shaded columns represent the number of receptive fields showing no orientation sensitivity (OB$<$0.1). Note that there is no significant difference in mean OB among their mean OB (χ^2 test, all $P>0.05$).

stimulated with gratings of relatively low spatial frequencies (Fig. 5B). In contrast, 67.2% of the cells (41 in 61 cells, 31 Y cells and 10 X cells) studied did so when their CRFs were stimulated alone with gratings mostly in relatively high spatial frequencies (Fig. 5A). In fact, there was a significant difference in mean OB between the biased CRF and the biased ECRF, whose mean biases were 0.21 ± 0.08 (hereafter, referred to as mean$\pm$S.D.) and 0.18 ± 0.06, respectively (χ^2 test, $P=0.023<0.05$), though for all 74 cells studied including unbiased cells, there was no significant difference in mean OB among the CRF (0.17 ± 0.10), the ECRF (0.15 ± 0.07) and the whole area (0.17 ± 0.12; χ^2 test, $P>0.05$ for all), as shown in Fig. 5.

The majority of cells studied (69.0%, 40 in 58 cells, 27 Y cells and 13 X cells) exhibited statistically significant OB (0.17 ± 0.12) when the whole areas were stimulated with optimal gratings of medium spatial frequency. Interestingly, in 11.8% (6 in 51 cells) of cells studied, the grating stimuli on the CRF alone failed to elicit a significant OB, while the stimulation on the ECRF or on the whole area did elicit a significant OB. Obviously, the ECRF are dominantly responsible for the OB of these cells. This does not seem

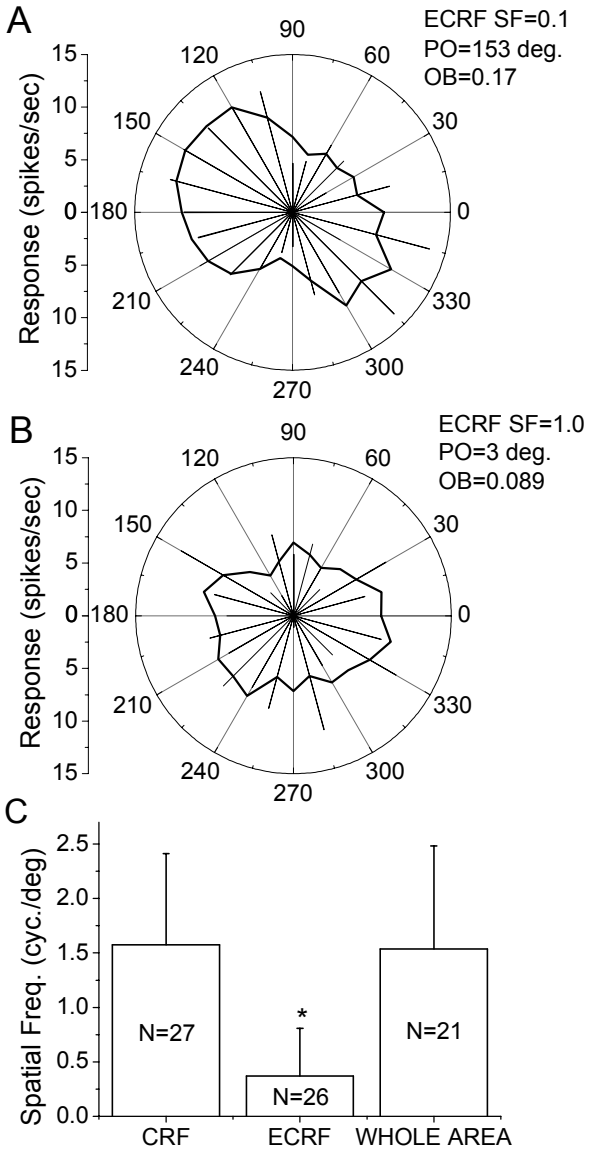

Fig. 6. Spatial dependent orientation sensitivity of the ECRF. (A) The ECRF showed significant orientation sensitivity in response to a grating of low spatial frequency (0.1 cycle/degree). (B) The orientation sensitivity diminished when the spatial frequency increased to 1 cycle/degree. (C) Comparison of the mean optimal spatial frequencies used to evoke the responses showing the maximal OB of the CRF, the ECRF and the whole area. The CRF and whole area have almost the same optimal spatial frequency, but the optimal spatial frequency is much lower for the ECRF than those of the CRF and the whole area.

to agree with the previous note that the OB of ganglion cells is only a reflection of an elliptical receptive field center (Leventhal and Schall, 1983).

Spatial dependent orientation sensitivity of ECRF

One of the significant characteristics of the ECRF we found was that their OB depend on the spatial frequency of stimulating gratings used (Fig. 6A and B). As shown in Fig. 1B, the three arrows indicate the optimal spatial frequencies of grating stimuli, to which the CRF, the ECRF and the whole area exhibited the largest OB, respectively. The mean optimal spatial frequencies for the three corresponding areas are shown in Fig. 6C. To evoke an OB for the ECRF alone, the optimal spatial frequency of the ECRF used was mostly in a range of 0.1–0.3 cycles/degree, which was about 4.3 times lower than the optimal spatial frequencies of the CRF and whole area respectively (*t*-test, $P<0.05$ for both).

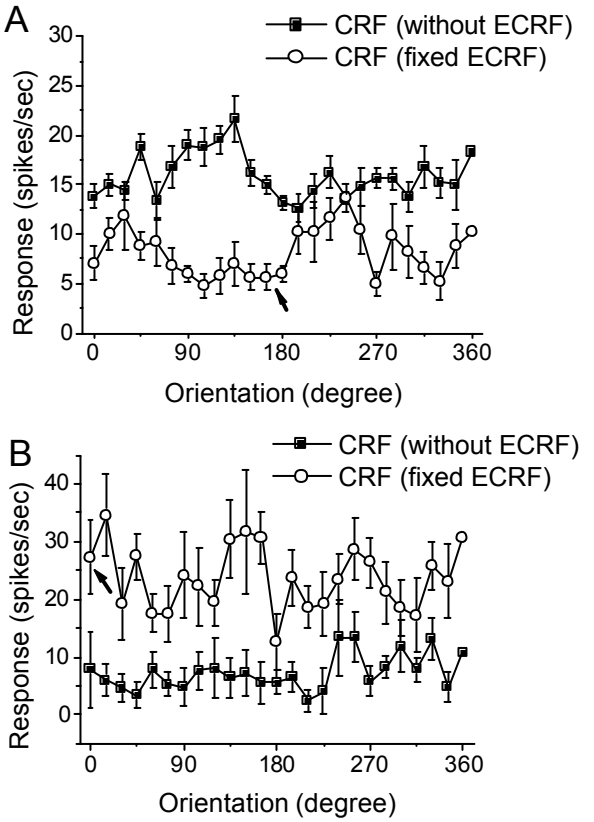

Fig. 7. Effect of an annular fixed-orientation grating stimulation presented to the ECRF on the orientation tuning curves of the CRF. (A) An inhibitory effect of the ECRF on the CRF. The arrow indicates the orientation in which the annular grating stimulated in the ECRF. (B) A facilitating effect of the ECRF on the CRF is observed. The arrow indicates the orientation of the annular grating in the ECRF. The vertical short bar indicates the standard deviation.

Interaction of the CRF and ECRF

The interaction between the CRF and the ECRF was studied in 26 cells. The stimuli were two concentric drifting gratings, each of which covered the CRF and the ECRF, respectively. Their orientations and spatial frequencies were varied independently. One was varied in grating orientation from 0° to 360° with 15° intervals and of optimal spatial frequency while the others parameters were fixed at their optimal values, and vice versa.

The influence of the ECRF on the cell's firing rate was either inhibitory (Fig. 7A) or facilitatory in most orientations (Fig. 7B). Statistically, 50.0% (13/26) of cells studied had inhibitory ECRFs and 19.2% (5/26) of cells studied had facilitating ECRFs. The remaining 30.8% (8/26) cells

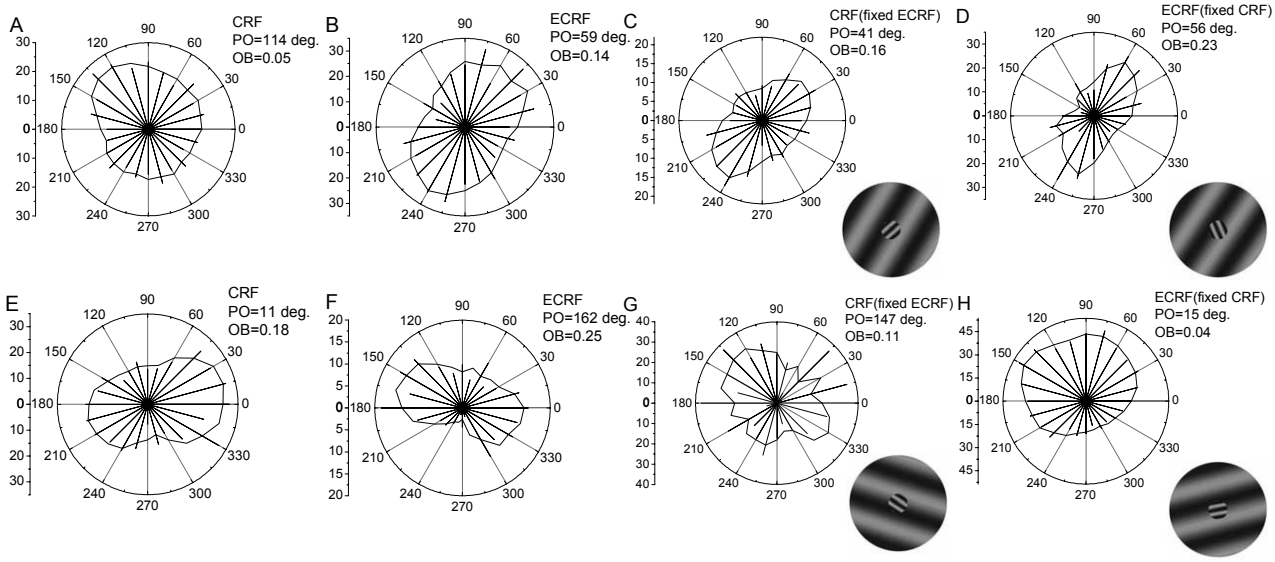

Fig. 8. Orientation turning curves of the CRF (A, E) and the ECRF (B, F), and those based on their interactions (C, D, G, H). (C) The fixed-orientation stimulus in the ERCF enhanced the OB of the CRF when the concentric gratings stimulated the CRF and the ECRF spontaneously. (D) On the other hand, the fixed-orientation stimulus in the CRF also enhanced the OB of the ECRF at the same time. (G) The fixed-orientation stimulus in the ERCF reduced the OB of the CRF when the concentric gratings stimulated the CRF and the ECRF simultaneously. (H) On the other hand, a fixed-orientation stimulus presented to the CRF also reduced the OB of the ECRF at the same time.

showed facilitation in some orientations and inhibition in other orientations.

The interaction between the CRF and the ECRF not only influenced their responsiveness but also their OB and preference. The cell shown in Fig. 8A–D demonstrates a mutual OB enhancement for CRF plus ECRF while the ECRF clearly dominates the cell's preferred orientation. The orientation tuning of the CRF changed from the orientation-unbiased (OB=0.05) to significantly biased (OB=0.16) with the additional stimulation in the ECRF, and the OB of the ECRF increased from 0.14 to 0.23 due to the stimulus in the CRF. In contrast, the cell shown in Fig. 8E–H demonstrates a reciprocal weakening of OB. The OB of the ECRF declined from 0.25 to 0.04 losing its bias due to an additional stimulus in the CRF and the OB of the CRF decayed from 0.18 to 0.11 with a preferred orientation shift of 44° due to an additional stimulus in the ECRF.

The overall effects of interaction of the CRF and the ECRF on the cells' orientation sensitivities are summarized in Fig. 9A and 9C. It appears that for most neurons studied their OBs of the CRF have no significant change except a few cells, since most data points located along a line of slope one (Fig. 9A). There was no difference in the mean value of the OB of the CRF with (0.15 ± 0.10) and without (0.15 ± 0.13) an additional stimulus in the ECRF ($P=0.997$, $N=25$). There were two exceptions (8%, 2 in 25 cells) with biased CRF lose their bias due to additional stimulation on the ECRF. Meanwhile, there were three cells (12%, 3 in 25 cells) with unbiased CRF becoming biased when the ECRF was simultaneously stimulated. It is also notable that the OB of CRF of one cell increased dramatically from 0.13 to 0.45 and that of another cell decreased from 0.20 to 0.01, indicating the strong influence of the ECRF on the CRF.

In contrast, it appears that most data points located below a line of slope one (Fig. 9C), indicating that for most neurons studied their OBs of the ECRF significantly decreased due to an additional stimulus on the CRF. Accordingly, the mean value of the OB of the ECRF dropped from 0.12 ± 0.06 to 0.071 ± 0.06 ($P=0.003$, $N=24$). In fact, the orientation sensitivity of the ECRF disappeared (OB$<$0.10) completely in 45.8% (11 in 24) of cells studied, and was maintained only in 16.7% (4 in 24) cells under the influence of an additional stimulus in the CRF. It is also notable that one cell emerged its OB from unbiased (OB from 0.08 to 0.14) and another two cells increase their OB from 0.14 to 0.15 to 0.23.

The effects of interaction of the CRF and the ECRF on the cells' preferred orientation are shown in Fig. 9B and 9D. The grating stimuli on the ECRF did not change the preferred orientation of the CRF in all cells tested, except one shown in Fig. 9B. However, when the CRF and the ECRF were both stimulated, the preferred orientation of the ECRF changed over 30° in the two of four cells that still maintained the orientation sensitivity of the ECRF (Fig. 9D). Taken together, it seems likely that for most cells studied, the interactions between the CRF and ECRF are non-linear and the influence of the CRF is much stronger than those of the ECRF on the cells' orientation sensitivities.

DISCUSSION

This study provides the first demonstration that the ECRFs of the most neurons in the LGNd respond to grating stimuli independently and exhibit significant orientation sensitivity

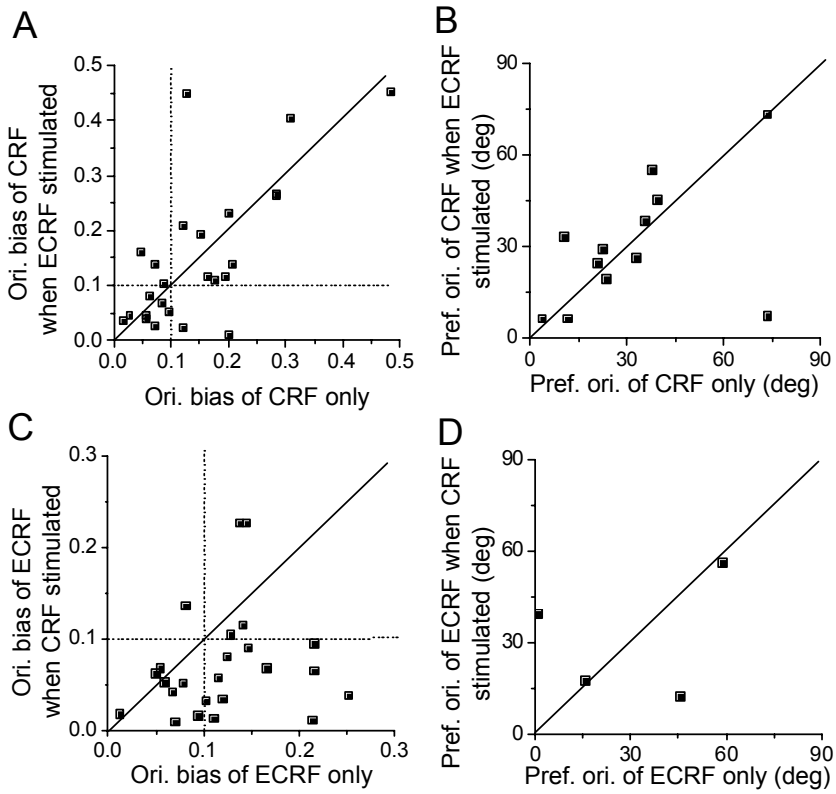

Fig. 9. Interactive effect between the CRF and the ECRF on orientation sensitivity of relay cells in LGNd. (A) Effect of ECRF grating stimulation on the OB of the CRF. The horizontal axis represents OB when the CRF was restrictively stimulated by gratings of different orientations in the optimal spatial frequency. The vertical axis represents OB of the CRF when the ECRF was stimulated simultaneously by a grating of its optimal orientation and spatial frequency. (B) Comparison of prefer orientations of the CRF with and without an additional stimulus in the ECRF. Preferred orientations of the CRF of most cells did not change due to the influence of the ECRF stimulation. Note that in one exceptional case, the preferred orientation was shifted up to 65°. (C) Effect of CRF grating stimulation on the OB of the ECRF. OB of the ECRF is mostly suppressed by a stimulus within the CRF. (D) Comparison of prefer orientations of the ECRF with and without an additional stimulus in the CRF. Preferred orientation of the ECRF changed due to the additional CRF grating stimulus. Note that the preferred orientations changed more than 30° in two of four cells studied. Lines of slope one are drawn in Fig. 9A–D.

to drifting gratings of low spatial frequency in anesthetized cats. The response components of the CRF and the ECRF interact with each other non-linearly, changing the cell's OB and preferred orientation. Furthermore, the contribution of the ECRF to the spatial frequency tuning of the whole receptive field is also demonstrated to be non-linear. This property of the CRF and its ECRF, of different preferred grating orientations and spatial frequencies, might enable some cells to selectively respond to more sophisticated visual patterns, such as required for image segmentation. Given the similar observation in the cat retina (Shou et al., 2000), a new concept emerges identifying an important role for the large-scale ECRF outside the CRF of subcortical neurons in visual information processing in the mammalian visual system.

The key point of the experiment is precisely to determinate the position of the CRF center and the sizes of the CRF and the ECRF. During experiments, we carefully measured (i) a two-dimensional response distribution using a moving small flash spot; and (ii) an area-response curve using a stationary flashing spot of increasing diameter for each cell. These procedures ensured the precision and the reliability of our experiment.

Properties of the ECRF

There have been many reports showing that the ECRF does modulate the response of the CRF (McIlwain, 1966; Ikeda and Wright, 1972; Cleland et al., 1983; Li and He, 1987; Li and Li, 1994; Felisberti and Derrington, 1999; Jones et al., 2000; Solomon et al., 2002), but previous report has not shown that the ECRF responds independently to stimuli alone until recently. Shou et al. (2000) reported a surprising result that the direct response to stimuli on the large "extended surround," which was about 1° beyond the CRF center, was observed in retinal ganglion cells in anesthetized cats. We used similar stimuli, except a small difference in the inner diameter of the annulus of drifting gratings, to elicit the independent responses of the ECRF of relay cells in the LGNd. The response properties we found for the ECRF in the retinal ganglion cells and the LGNd cells are similar in many respects. First, in more than half of both retinal and thalamic cells, the ECRFs are able to respond directly to drifting gratings in spatial frequencies lower than those used for the CRF. Second, in about three quarters of cells studies the ECRF stimulated alone respond selectively to

the orientation of grating stimuli significantly (OB>0.1; 75.8% of cells in retina, 72.7% of cells in LGNd). Third, the orientation sensitivity of the ECRF appears only when the low spatial frequency stimulating gratings were employed, while that of the CRF (or the center of it) was mainly found when high spatial frequencies were used. Fourth, for each cell the preferred orientation of the ECRF is independent of that of the CRF. As a result, the CRF and the ECRF show different OB at different spatial frequencies. Finally there is a non-linear interaction between the ECRF and the CRF which we suggest could assist in texture segmentation. Furthermore, we found that the CRF mostly had more significant influence than that of the ECRF on the entire whole receptive field in the LGNd neurons.

Overall, based on these similarities and the fact that each relay cell only receives input from one or two ganglion cells in the retina (Malpeli and Baker, 1975), it is reasonable to conclude that the response properties of the ECRF of the LGNd neurons may originate from their retinal counterparts, ganglion cells.

Influence of the ECRF on the CRF

Many investigators have argued that the modulations of the ECRF to the CRF are solely inhibitory in the LGN neurons of primates and cats (McClurkin and Marrocco, 1984; Marrocco and McClurkin, 1985; Sillito et al., 1993; Felisberti and Derrington, 1999; Solomon et al., 2002). However, we found that the while modulations of the ECRF on the CRF response are mainly inhibitory, some interactions are excitatory in the LGN neurons (Fig. 7B). While this result is not fully in agreement with the above reports, it is consistent with those reports in cortical cells revealing that the modulation of the ECRF on the CRF is either inhibitory or excitatory and mainly inhibitory in primates and cats (Li and Li, 1994; Walker et al., 1999, 2000). It should be noticed that for many LGN cells, the influence of the ECRF on the CRF is somehow complicated. In some orientations, the influence of grating stimuli on the CRF is inhibitory but at other orientations the influence is excitatory. Because the LGN neurons receive feed-forward projections from the retina, this may reflect the complexity of the neural network of the inner and outer layers in the retina, through which the large area of the ECRF of retinal ganglion cells is formed (Shou et al., 2000).

Mechanism of the ECRF

For decades, investigators reported that the ECRF area did not respond to a stimulus restricted to it, but did modulate the response to the stimuli on the CRF in the retina (Ikeda and Wright, 1972; Li et al., 1991; Li et al., 1992), the lateral geniculate nucleus (Solomon et al., 2002) and visual cortex (Li and Li, 1994; Rossi et al., 1996; Lamme et al., 1998; Rossi and Paradiso, 1999; Li et al., 2000) of anesthetized animals. Accordingly, it was widely accepted that the ECRF is completely silent. Very recently, however, the ECRF of many cortical cells in V1 of the awake monkeys were demonstrated to respond directly to texture stimuli located entirely outside the classical RF, up to 5° from the RF border in some cases (Rossi et al., 2001; Li et al., 2000). Some authors thought that anesthesia suppressed figure–ground activity of visual cortical cells through suppressing the ECRF function (Lamme et al., 1998; Li et al., 2000). It was explained likely that the cell responses to the ECRF stimulation alone were only observed in alert monkeys, but not in anesthetized animals. However, this is not the case because we did find significant responses of the ECRF in most LGN cells in anesthetized cats by using drifting gratings of optimal spatial frequency covering large areas of the ECRF (up to 10°–15° in diameter).

The relay cells of LGNd receive visual signals from retinal ganglion cells. The ganglion cells receive inputs from linear and non-linear subunits, such as horizontal cells, bipolar and amacrine cells in the outer and inner plexiform layers in the retina. In fact, horizontal cells, due to their large field of electrical synaptic connections, receive inputs from a very large area of the retina; therefore, if an optimal grating stimulus of low spatial frequency drifts over the ECRF alone, it may synchronously elicit a detectable response of a retinal ganglion cell through the large spatial summation of horizontal cells which makes a suprathreshold spike possible (Shou et al., 2000). The spatial summation of the ECRF shown in Fig. 2 clearly supports the above idea because the LGN neurons receive direct projections from one or two retinal ganglion cells and have similar receptive field properties to them. Furthermore, two types of orientation-sensitive amacrine cell have been found in the rabbit's retina (Bloomfield, 1994). If amacrine cells like these also occur in cat retina they may contribute essentially to the OB of the ECRF of retinal ganglion cells. Therefore, the finding here in the LGN may reflect a retinal origin of the ECRF responsiveness to grating stimuli in the sub-cortical pathway.

Recently, a similar phenomenon, that the neurons respond to luminance changes on the region beyond the neurons' CRFs, was observed mainly in the visual cortex and to less extent in the lateral geniculate nucleus of the anesthetized cat (Rossi and Paradiso, 1999). Micro-injections of GABA and its antagonist in the visual cortex could influence the modulatory effect of the ECRF to CRF of LGN neurons (Sillito et al., 1993). Taken together with our finding, there is the possibility that the feedback projection from the visual cortex may also contribute to the direct response of the ECRF observed here.

Functional implication

Orientation sensitivity is essential to the perception of form and used to be considered as a unique property of visual cortical neurons (Hubel and Wiesel, 1962, 1965). However, relatively small but significant OB were found in most retinal ganglion cells and relay cells in the LGN (Levick and Thibos, 1980, 1982; Vidyasagar and Urbas, 1982; Leventhal and Schall, 1983; Shou et al., 1986; Soodak et al., 1987; Shou and Leventhal, 1989; Thompson et al., 1994; Zhou et al., 1995). The report further provides evidence supporting a new contribution of orientation sensitivity from the ECRF at the subcortical level to forming the orientation

selectivity of integration fields or the ECRF of neurons in the visual cortex.

The receptive field of LGN neurons consists of a CRF and an ECRF which respond preferentially to different orientations and spatial frequencies, as previously reported in cat's retinal ganglion cells. It was suggested that the interaction between the ECRF and CRF might help the retina detect feature segmentation (Shou et al., 2000). In the visual cortex, the ECRF may enable the cortical cells to detect complex patterns, such as texture segmentation (Sillito et al., 1995; Walker et al., 1999, 2000). Present results support the idea that the nonlinear interaction between the ECRF and the CRF in the LGN neurons may reflect the retinal input and contribute to detecting complex patterns at cortical level. There are several lines of evidence supporting the proposal that the ECRF could enhance contrast sensitivity and recognition of local texture segmentation (Fahle et al., 2000; Prins and Mussap, 2000; Yu and Levi, 2000; Casco et al., 2001). In fact, visual cells respond to natural scenes more strongly than simple laboratory stimuli on the CRF (Berry et al., 1988; Barinaga, 1998). Our findings provide new evidence supporting the subcortical contribution for processing complex pattern information to the integrative field of visual cortical cells.

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