

Origin of orientation tuning in the visual cortex

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The results of recent experiments have thrown new light on the neuronal connections underlying orientation-selective responses in the primary visual cortex of adult animals. The pattern of afferent input from the lateral geniculate nucleus to the cortex appears to be specific for orientation, while intracortical inhibitory connections appear to be non-specific in this respect. Experimental and theoretical studies have suggested that the development of cortical cell orientation tuning is an activity-dependent process.

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Introduction

Perhaps the most striking feature of the responses of primary visual cortex neurons in higher mammals is their selectivity for stimulus orientation. This selectivity must be produced at the level of the cortex, as the major visual input to the cortex comes from the lateral geniculate nucleus (LGN), where cells show little or no orientation selectivity [1]. When Hubel and Wiesel [2] originally described cortical cell orientation tuning, they proposed a model whereby neurons in the visual cortex could construct orientation selectivity from non-selective inputs by receiving synapses from several geniculocortical afferents whose receptive fields were aligned in visual space. An alternative model suggests that cortical orientation selectivity does not depend on afferent input, but rather on intracortical inhibitory circuitry. This cross-orientation inhibition model suggests that cortical orientation selectivity might be established, or at least refined, by each cortical cell receiving inhibitory inputs from other cortical cells with orthogonal orientation preferences [3,4]. Several studies designed to test these two models have been published in the past year.

The development of cortical orientation specificity has been widely studied, with somewhat conflicting results reported in the literature. Orientation-specific responses appear to be present at birth in the monkey [5], but in the kitten the reported percentage of orientation-specific neurons recorded in primary visual cortex near the end of the first postnatal week varies widely, from zero [6,7], through 25–30% [8–11], to 100% [12]. These discrepancies may be the result of the difficulty involved in recording from very immature animals where neurons have low spontaneous activity, respond sluggishly and habituate rapidly [12]. The difficulty of maintaining young kitten cortex in a state that is sufficiently responsive to determine the selectivity of responses, together with the

possibility that kitten cortical neurons may already be tuned for orientation at birth, make the cat an unattractive model system for studying development of orientation. In the past year, several new approaches have been used to study orientation development, and in particular to determine whether the development of orientation-specific responses is dependent on the presence of neuronal activity, as the development of normal ocular dominance characteristics has been shown to be [13].

The pattern of geniculocortical afferent input to a single orientation column

In the past, several attempts have been made to test Hubel and Wiesel's model that cortical simple cell orientation is a result of input from LGN cells with receptive fields aligned in space. These experiments studied the arrangement of afferent inputs to single cortical cells, either through cross-correlation analysis of LGN and cortical responses [14], which had the disadvantage of not being able to record from all of the LGN inputs to a given cortical cell, or through intracellular recordings of post synaptic potentials in simple cells [15], which had the disadvantage of not revealing which of the excitatory potentials were of geniculate origin.

A recent report, which provides evidence for Hubel and Wiesel's model, examined the receptive field locations of geniculate afferents that provide input to a single orientation column in ferret primary visual cortex [16••]. In this study, cortical cell responses were recorded and their orientation preferences determined throughout the depth of the cortex, along a radial microelectrode penetration that remained within an orientation column. Cortical cell responses were then eliminated by superfu-

Abbreviations

GABA— γ -aminobutyric acid; IPSP—inhibitory postsynaptic potential; LGN—lateral geniculate nucleus.

sion of the cortex with either the excitotoxin, kainate, or the γ -aminobutyric acid (GABA) agonist, muscimol. These procedures eliminated the electrical signals produced by cortical cells, permitting the discrimination of the small spikes of geniculocortical afferent terminals. In most cases, afferent receptive fields recorded in a single penetration covered an elongated region of visual space, and the best-fit line through the centers of the afferent receptive fields generally paralleled the preferred orientation of the cortical cells previously recorded at the same site. Thus, the pattern of LGN input to a cortical column has an orientation preference similar to that of the cortical cells in that column, providing strong support for the Hubel and Wiesel model.

Cross-orientation inhibition

Past experimental tests of the cross-orientation inhibition model provided mixed results. Treatment of the visual cortex with pharmacological agents designed to remove intracortical inhibition does tend to decrease cortical cell orientation specificity [17,18]. However, the cross-orientation inhibition model suggests that intracellular recordings from oriented cortical cells would reveal inhibitory postsynaptic potentials (IPSPs) preferentially oriented orthogonal to the preferred orientation of the cell. Such cross-oriented IPSPs are not found [15]. Several studies have been published in the past year which again provide evidence for both sides of the controversy.

The earliest pharmacological studies providing evidence for cross-orientation inhibition can be criticized for failing to distinguish whether the broadening of cortical cell orientation tuning, in response to the pharmacological suppression of intracortical inhibition, was actually due to the removal of inhibitory inputs from cells of orthogonal orientation preference, or to the removal of iso-orientation inhibition from neighboring cells with incompletely overlapping receptive fields. The most recent in a series of experiments designed to specifically block only cross-orientation inhibition [19•] shows that the majority of cortical cells become less well oriented when neighboring areas of cortex with orthogonal orientation preference are silenced by iontophoretic application of GABA. This provides strong evidence that cross-orientation inhibition is involved in enhancing the orientation tuning of cortical cells.

On the other hand, using intracellular recording to show the absence of cross-oriented inhibitory potentials can be criticized because of the possibility that this method would not reveal cross-inhibition if such inhibition were shunting rather than hyperpolarizing. This criticism has been laid to rest by a study using whole-cell patch-clamp recording in cat area 17 *in vivo* [20••]. In this study there was no evidence of a visually-evoked shunting inhibition, the effects of which would have been visible as a preferential decrease in the amplitude of a test excitatory postsynaptic potential during phases of the visual response when the cell is hyperpolarized. The lack of shunting in-

hibition in response to cross-oriented stimuli confirms the earlier reported lack of specific cross-orientation inhibition.

These seemingly contradictory viewpoints and data may be reconcilable in light of a study designed to examine long-range inhibitory connections between cells of both similar and orthogonal orientation preference (JM Crook, ZF Kisvarday and UT Eysel: *Soc Neurosci Abstr* 1991, 17:177). GABA iontophoresis was used to inactivate cortical sites of known orientation preference while recording from a cortical cell 500–700 μm away. When cells in the inactivated site had orthogonal orientation preference to that of the recorded cell, the inactivation caused a broadening of orientation tuning, as had been reported earlier [19•]. When cells in the inactivated site had similar orientation preference to that of the recorded cell, no change was seen in orientation tuning, but there was frequently an increase in the amplitude of the recorded cell's response. In addition, in cases where there was similar orientation preference, direction selectivity was enhanced if the inactivated site had the same direction selectivity as the recorded cell, and decreased when there was opposite direction selectivity. These results are consistent with the hypothesis that intracortical inhibitory circuitry shows no specificity for cellular orientation preference, but rather interconnects cells of all preferences; removing inhibitory inputs to a cell from particular sites in the cortex had, in all cases, the expected effect of enhancing in that cell the attributes of the silenced region. Thus, inhibition from cells of orthogonal orientation is important in establishing orientation tuning, but at the same time there are no specific connections underlying cross-orientation inhibition, and thus no preponderance of inhibitory IPSPs is seen during null orientation stimulation in intracellular recordings. Anatomical findings also suggest that cortical inhibitory circuitry is non-specific: single biocytin-filled large basket cells (known to be inhibitory interneurons) send both axons and dendrites into regions of cortex subserving all orientation preferences (UT Eysel and ZF Kisvarday: *Soc Neurosci Abstr* 1991, 17:116).

Quantitative modeling of circuitry underlying orientation selectivity

Computational modeling represents another approach for testing whether proposed arrangements of neuronal circuitry could produce the orientation selectivity observed in primary visual cortex. A recently published model, which combines geniculocortical inputs covering an elongated region of visual space with various forms of inhibitory circuitry, shows that non-specific inhibitory mechanisms actually produce more realistic simulated cortical cell orientation tuning curves than does specific cross-orientation inhibition circuitry [21••]. It thus shows quantitatively that the circuitry proposed by the physiological experiments discussed above is sufficient to explain the observed cortical orientation tuning.

Development of orientation tuning

Many developmental processes in the nervous system, including the development of ocular dominance columns in primary visual cortex, are dependent on neuronal activity [13]. In the past year several reports have been published which suggest that the development of orientation selectivity is such an activity-dependent process. One recent report [22••] studied the development of orientation selectivity in the ferret, which has a visual system quite similar to that of the cat [23], but which is born approximately 3 weeks earlier in development [24]. Studies in the ferret therefore permit more stable recordings of cortical activity and allow manipulations of neuronal activity at developmental ages equivalent to day of birth in the cat. At the earliest ages in which cortical visual responses could be elicited in the ferret (p23, equivalent to day of birth in the cat), cortical cells were very poorly tuned for orientation. Increasingly well-tuned responses began to appear during postnatal week 6, and adult-like orientation tuning was seen by about p45. When cortical neuronal activity was blocked by infusing the Na⁺-channel blocker tetrodotoxin into the cortex during the time when orientation selectivity was normally developing, cortical cells remained in their poorly oriented immature state, showing that normal development of orientation selectivity does depend on the presence of neuronal activity.

Two recently published theoretical studies demonstrate that activity-dependent competition between on- and off-center geniculate inputs to cortical cells can produce orientation selectivity [25••,26••]. These models produce orientation-selective simulated cortical receptive fields with realistic subfields, as well as cortical orientation maps that are very similar to real maps seen in cat and monkey.

Development of corticocortical connections between orientation columns

Several new reports have investigated the activity-dependence of the development of patchy, presumably excitatory, intracortical connections that connect cortical areas with similar orientation preference. The development and refinement of these patchy connections, observed through retrograde tracer injections, has been studied in kittens deprived of vision by binocular lid suture [27••]. In these animals, the initial formation of crude clusters occurred normally, but the later refinement of connections did not take place. Thus, visually driven activity is necessary for the normal development of intracortical circuitry connecting cells with similar orientation preference. It is not known from these experiments whether the earlier emergence of crude clusters is dependent on spontaneous neuronal activity.

A second report also suggests that the establishment of connections between orientation columns of similar preference is activity dependent. In this study kittens were

raised with an artificially induced strabismus to eliminate correlations in neuronal activities driven by the two eyes [28••]. In these kittens, unlike normal animals, the patchy intracortical connections preferentially connected cortical regions driven by the same eye. The development of corticocortical connections may be viewed as preserving connections between areas of cortex that tend to be active simultaneously. In normal animals, binocular vision through properly aligned eyes correlates activity during the period of refinement so that connections between regions of cortex serving the two eyes are preserved, while connections between regions with different orientation selectivity are lost. In the strabismic animals, vision of objects in the world no longer correlated activity between the two eyes, and so these connections were lost as well, leaving connections only between regions of cortex preferring the same orientation and driven through the same eye.

Conclusion

Recent findings have provided a new understanding of the neuronal circuitry underlying orientation selectivity in the visual cortex. Strong evidence has been presented in support of Hubel and Wiesel's original hypothesis that input from LGN neurons with receptive fields covering an elongated region of visual space is important in establishing orientation preference in cortical simple cells. Intracortical inhibition has also been shown to be essential for cortical cell orientation tuning, but new evidence suggests that the cortical inhibitory circuitry is not specific for orientation. In addition, the normal development of cortical cell orientation specificity and the development of connections between areas of similar orientation have been shown to occur through an activity-dependent process, and testable models of this hypothesis have been proposed.

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