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Vernier acuity of neurones in cat visual cortex

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The ability of human observers to detect Vernier breaks of as little as 5 s of arc has been termed hyperacuity[1] as this distance is substantially less than the angular separation of the bars of the highest spatial frequency of grating (~1 arc min) that can be detected. Although the visual cortex is a likely candidate for the location of detectors involved in this performance[2], it is not known whether there are cells sensitive enough to detect deviations from co-linearity that are small compared with their spatial resolution (defined in terms of the highest spatial frequency that the cell can detect). We report here the results of physiological experiments on single units in area 17 of the cat visual cortex in which we studied the effect of introducing a Vernier break into a bar stimulus moved across the receptive field of the cell at a constant velocity. Our results show that the responses of most simple and complex cells are significantly reduced by the introduction of a Vernier break that is substantially smaller than the spatial resolution of the cell. The most sensitive cells in our sample could discriminate Vernier offsets of 3–6 arc min with a reliability of ~70%. This was much smaller than their spatial resolution, which was in the range 25–30 arc min. We interpret these results in terms of mechanisms that could underly the orientation selectivity of cortical neurones and suggest how our results relate to human Vernier acuity.

We made recordings with extracellar platinum–iridium microelectrodes in area 17 of the cortex of 13 normal adult cats. Anaesthesia was induced with intravenous pentothal and subsequently maintained by respiration with 70% N_2O and 30% O_2. The animals were paralysed with Flaxedil, and the eyes were refracted using contact lenses with 3 mm artificial pupils onto a tangent screen 137 cm away. Two moving-bar stimuli, one from each of two computer-controlled optic benches, were projected onto the screen[3]. Each bar was typically between 1/10 and 1/4° wide and 1 and 2° long. The bars were oriented parallel with each other at the preferred orientation of the cell, and were normally placed end to end with no intervening gap. The total length of the bars was usually about the same as the length of the receptive field. In most experiments we moved the bars across the receptive field in the preferred direction of the cell and at a constant velocity close to the preferred velocity of the cell, normally between 0.5 and 3° s^{-1}. The stimuli were presented monocularly to the dominant eye. Vernier offsets of from −30 arc min to +30 arc min in 6-arc min steps were introduced, providing 11 different stimulus conditions; in a further 2 conditions each bar moved on its own through the receptive field. We normally tried to centre the stimulus in the receptive field so that each of the two bars moving on its own produced a similar response, although precise centering turned out to be unimportant. Responses were averaged over 8–16 presentations of each particular stimulus, given in random order. We often made other quantitative measurements, including a line-weighting function and orientation- and velocity-tuning curves. We measured spatial resolution either by listening to an audiomonitor or by examining computer-averaged responses from the cell as high-contrast grating stimuli of varied spatial frequency were moved across the receptive field. The bars of the gratings were the same length as that of the stimulus used to determine the Vernier acuity of the cell. All the cells in our sample had receptive fields that lay 3–15° from the area centralis. Of the 82 cells studied, 27 were classified as simple and 47 as complex; 8 could not be classified.

In most cells, the response, measured either in terms of peak firing rate or as total number of spikes per presentation, was reduced by the presence of a Vernier break (Figs 1, 2). Simple cells did not seem to differ from complex cells in this respect, and were among the most and the least sensitive cells in our sample. We found examples of cells with Vernier sensitivity in all laminae. Typically, responses were reduced by 20–50% of maximum for a Vernier offset of 30 arc min, although in the most sensitive cells the average response could be halved by a change in Vernier offset of 6 arc min.

We used an approach similar to that recently adopted by Parker and Hawken[4] to estimate the ability of a single neurone reliably to signal information about the presence of a Vernier offset. We compared the responses of a cell (measured in terms of the total number of impulses evoked) to presentations of a pair of stimuli differing in Vernier offset by a given amount. A correct response was scored if the responses of the cell differed in the expected direction, that is, if the response was greater for a smaller Vernier offset. An incorrect response was scored if the response was in the opposite direction. This comparison was carried out for all pairs of presentations in a series that took from 5 to 10 min to complete. As a means of describing the Vernier acuity of a cell this method has the advantage of taking into account the reliability of the response to a change in Vernier offset. This could be a better way to describe its performance than measuring the slope of the Vernier tuning curve averaged over many presentations.

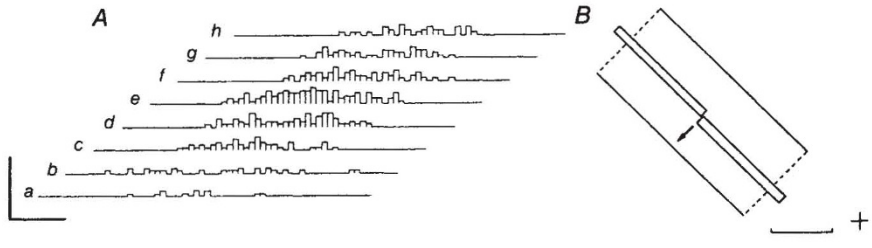

Fig. 1 *A*, *a–h*, Impulse frequency histograms from an experiment on a complex cell located in layer V of area 17; the cell had a receptive field ~3° from the area centralis. *B*, The stimulus configuration and the shape of the receptive field are drawn to scale relative to the location of the area centralis (cross). Arrow, direction of movement of the stimulus; bars are offset by ~6 arc min. Responses *a–h* are to Vernier offsets of −18, −12, −6, 0, 6, 12, 18 and 24 arc min, respectively. Each histogram shows the response to a single presentation of the stimulus. The presentations were in random order and made every 4 s. The velocity of the bars was 1° s^{-1}. Scale bars: *A*, 500 s^{-1} (vertical); 500 ms (horizontal). *B*, 1°.

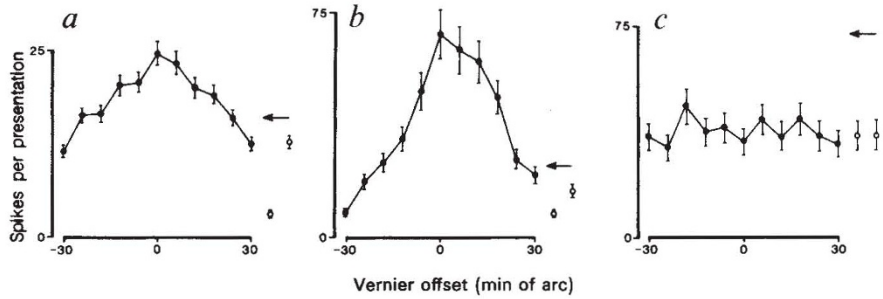

Fig. 2 Total number of impulses evoked plotted against Vernier offset for three different units. *a*, Simple; *b*, *c*, complex. The final two points in each graph (open circles) are the response to each bar presented separately. Arrow, linear sum of these responses. *a*, From a layer IV simple cell with an odd symmetrical receptive field 5° from the area centralis. The receptive field is 2° across, each bar is 0.2 × 1.1°, each response is the average of 16 presentations. *b*, From a complex cell located at the layer V/VI boundary; *c*, from a complex cell located in the upper layers of area 17 with a receptive field 10° from the area centralis. Each response is the average of eight presentations. Standard error bars are shown.

This method of analysis showed that many cells could discriminate 6–12 arc min of Vernier offset with >70% reliability. Some cells did better than this (Fig. 3); the most sensitive cell in our sample (Figs 1, 3) achieved 88% correct performance for a 6 arc min Vernier offset, implying a Vernier threshold of ~3 arc min for a 70% criterion of reliability. Figure 3 also shows one other such Vernier-discrimination curve from a cell that could detect 6 arc min of Vernier offset with 77% reliability. The spatial resolution of this cell was measured and found to be between 25 and 30 arc min. Its Vernier discrimination is thus an example of neuronal hyperacuity.

Inhibitory and, to a more variable extent, excitatory interactions between the component bars of the stimulus seem to be involved in producing these effects. In cells with good Vernier tuning, the response to the bars in the aligned condition was often greater than the sum of the responses to each bar alone (Fig. 2*a*, *b*). As Vernier offset was increased, the response decreased to a value less than this sum. The changeover from excitation to inhibition occurred typically for offsets of ~12–24 arc min. In other cells, including both simple and complex types, length summation was approximately linear, although the cells nevertheless showed good Vernier tuning. The reduction in the response caused by Vernier offset in these cells was presumably entirely caused by inhibition.

In a few cells (2 simple and 14 complex) the response was unaffected by the presence of a Vernier break. In these units, the response to the bars in the aligned condition was always similar to the response to each bar on its own (Fig. 2*c*). It was never possible to induce Vernier sensitivity in these cells by changing the stimulus properties, for example, bar length, separation, contrast or brightness of the stimulus. We recorded several cells showing some intermediate degree of Vernier sensitivity, so it could be that there are not two distinct classes of Vernier sensitivity, but rather a continuum.

We found evidence that the interaction producing the Vernier sensitivity has features in common with that responsible for the orientation selectivity of the cell. A Vernier stimulus can be approximated by a single bar of the same overall length, with an orientation the same as a line connecting the midpoints of the two component bars (Fig. 4*c*). Two observations suggest

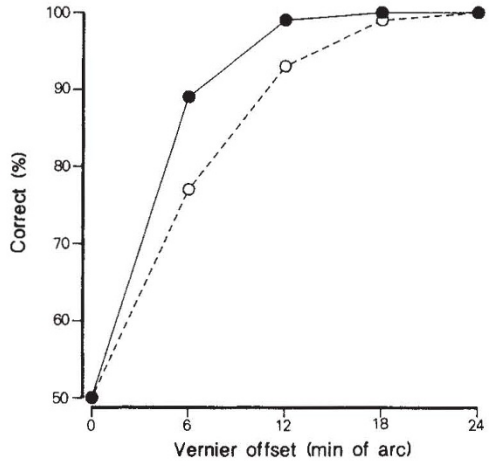

Fig. 3 Correct discriminations (%) plotted against Vernier offset for two of the most sensitive cells in our sample. A percenage discrimination of 70% for a Vernier offset of 6 arc min means that on 70% of presentations differing in Vernier offset by 6 arc min (for example, stimuli with offsets of 12 and 18 arc min), the response of the cell, measured in terms of the total number of impulses evoked, was greater for the smaller Vernier offset. Each point is based on many comparisons, for example, an experiment in which a set of nine Vernier offsets differing in 6-arc min steps were presented 16 times would yield $(9-1)\times 16^2 = 2{,}048$ comparisons for the 6 arc min point on the graph. Filled circles, results from the cell shown in Fig. 1; open circles, results from a complex cell in layer III.

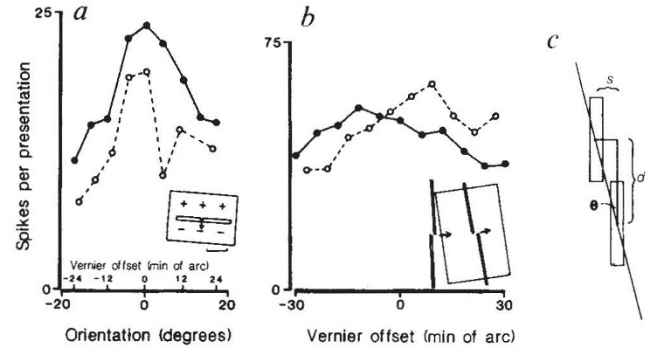

Fig. 4 *a*, Comparison between a Vernier tuning curve (filled circles) with Vernier offset re-expressed as equivalent orientation (defined in *c*), and an orientation-tuning curve (open circles) obtained for a bar of the same overall length as the Vernier stimulus. The sizes of the receptive field and the stimulus are shown. The difference in the height of the two curves is probably caused by a change in the responsiveness of the cell between experiments. Scale bar, 1°. *b*, Effect of changing the overall orientation of the Vernier stimulus on the tuning curve. Filled and open circles are for stimuli (drawn to scale relative to the receptive field size) whose overall orientation differed by 8°. The separation between the bar centres is 2.6°; the change in the orientation of the stimulus is 8° so the tuning curve should shift by 2.6° tan(8°) = 22 arc min, which is close to the shift actually observed. *c*, The definition of equivalent orientation used here; the equivalent orientation of two bars whose centres are separated by a distance *d*, and with a Vernier offset of *s*, is $\theta = \tan^{-1}(s/d)$.

that cells were treating both the Vernier stimulus and this approximation to it as equivalent. First, in several cells for which we made a quantitative measure of the orientation tuning curve (using a bar of the same overall length as the Vernier stimulus), re-expressing the Vernier tuning in terms of an equivalent orientation tuning gave a curve that was comparable in shape (Fig. 4*a*). This relationship was found to hold true for cells with both poor and good Vernier tuning. Second, changing the overall orientation of the Vernier stimulus shifted the position of the peak of the Vernier tuning curve (Fig. 4*b*). The size of this shift, re-expressed as an equivalent orientation, matched the change in the overall orientation of the stimulus.

Our results may be relevant to an understanding of Vernier acuity as measured in psychophysical experiments. Although other factors are probably involved, detection of orientation differences close to the Vernier break seems to be an important cue in Vernier tasks[5,6]. Thus, detection of Vernier offset, alignment of dots along a vertical axis, curvature or chevron distortions all have thresholds that, expressed in terms of the orientation cues available, are comparable with the ability to detect the deviation of a straight line from vertical[7,8]. This angle varies from ~1/3 to 1° (depending to some extent on the skill of the observer)[7]. Because the orientation-tuning curves of cortical cells (in monkeys) have a half-width at half-height of rather more than this (~5°), Westheimer[1] concluded that they cannot be involved in hyperacuity-type tasks. However it is arguable that the output from any kind of detector whose response is a smoothly varying function of the position or configuration of a retinal stimulus and is sufficiently noise -free, could, in principle, serve as a basis for hyperacuity-type discrimination. Thus, if two stimuli merely give rise to a statistically significant difference in the firing rate of a neurone they could, as a direct consequence, be discriminable in a behavioural task.

If this is true then a signal from a cortical cell with an orientation-tuning curve with a half-width at half-height of 5° might well subserve an orientation discrimination of ≤1°. This performance could be improved on if the outputs from several cells with similar properties were averaged, although the number of cells over which an average of this sort could be taken is uncertain. Parker and Hawken[4] have recently studied the performance of neurones in monkey visual cortex and found cells with resolution and contrast sensitivity thresholds, and a predicted sensitivity to positional displacement in the hyperacuity range which is similar to that shown behaviourally by monkeys. This is evidence that the nervous system either does not average the outputs of several cortical neurones to improve its performance, or that an averaged response is degraded by noise elsewhere in the nervous system, perhaps at the level of some subsequent decision-making process. The ability of the nervous system to interpret fractional changes in the firing rates of neurones in this way, either above threshold (as we have suggested) or close to it (as Parker and Hawken[4] suggest) would eliminate the need for a fine-grain representation of positional information as hypothesized elsewhere[9,10].

Our present data show that some cells, recorded at a retinal eccentricity of 3-5°, were able to discriminate 3-6 arc min of Vernier offset with ≥70% reliability. This was substantially less than their spatial resolution, which lay in the range 25-30 arc min. It is also less than the best resolution of retinal ganglion cells at this eccentricity, which is in the range of 15-25 arc min (ref. 11), and limits the maximum possible resolution of cortical neurones to which they provide inputs. One can extrapolate from these data to estimate the likely Vernier acuity of cells with receptive fields in the area centralis, where spatial resolution is about half that at the eccentricity from which our data came[11]. On the basis that Vernier acuity increases in proportion to resolution, some cells with receptive fields in the area centralis could be expected to have Vernier acuities as high as 1.5 arc min. This is better than the threshold of 5 arc min measured in behavioural experiments by Berkley and Sprague[2]; however, a different behavioural method shows a threshold of 1.2 arc min, which is similar to the postulated neural threshold (K. Murphy and D. E. Mitchell, personal communication). When compared with a behavioural grating resolution of ~7-8 arc min (ref. 12), the behavioural Vernier acuity of the cat is, like that of humans, well within the hyperacuity range. Berkley and Sprague's finding[2] (confirmed by Mitchell and Murphy) that lesions in area 17, but not in other visual areas, drastically reduce Vernier acuity, also supports the notion that the performance of cells with properties similar to those we have studied could be the limiting factor in the achievement of a high Vernier acuity in both cats and humans.

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Reciprocal changes in corticotropin-releasing factor (CRF)-like immunoreactivity and CRF receptors in cerebral cortex of Alzheimer's disease

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Alzheimer's disease is a progressive degenerative disease of the nervous system characterized neuropathologically by the presence of senile plaques and neurofibrillary tangles in amygdala, hippocampus and neocortex[1-4]. Dysfunction and death of basal forebrain cholinergic neurones projecting to forebrain targets[5,6] are associated with marked decreases in cholinergic markers, including the activity of choline acetyltransferase (ChAT)[2,3,7-9]. Although cortical levels of somatostatin[10-12] and somatostatin receptors[13] are reduced in Alzheimer's, no consistent changes have been reported in other neuropeptide systems[12,14-17]. We have now examined in control and Alzheimer's brain tissues pre- and postsynaptic markers of corticotropin-releasing factor (CRF), a hypothalamic peptide regulating pituitary–adrenocortical secretion[18,19] which also seems to act as a neurotransmitter in the central nervous system (CNS) (reviewed in refs 20, 21). We have found that in Alzheimer's, the concentrations of CRF-like immunoreactivity (CRF-IR) are reduced and that there are reciprocal increases in CRF receptor binding in affected cortical areas. These changes are significantly correlated with decrements in ChAT activity. Our results strongly support a neurotransmitter role for CRF in brain and demonstrate, for the first time, a modulation of CNS CRF receptors associated with altered CRF content. These observations further suggest a possible role for CRF in the pathophysiology of the dementia. Future therapies directed at increasing CRF levels in brain may prove useful for treatment.