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Author
Westheimer, Gerald

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Center-surround antagonism in spatial vision: Retinal or cortical locus?

Gerald Westheimer *

Division of Neurobiology, University of California, 565 Life Sciences Addition, Berkeley, CA 94720-3200, USA

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Abstract

Mach and Hering had early advanced a model of spatial visual processing featuring an antagonistic interaction between adjoining areas in the visual field. Spatial opponency was one of the first findings when single-unit studies of the retina were begun. Not long afterwards psychophysical experiments revealed a center-surround organization closely matching that found in the mammalian retina. It hinged on the demonstration of reduction of sensitivity in a small patch of the visual field when its surround was changed from dark to bright. Because such patterns inevitably produce borders, well-known phenomena of border interaction could be seen as providing alternative explanations, whose substrate would most likely be in the visual cortex. These competing viewpoints are discussed especially as they pertain to the recent demonstration of spatial differences in the center/surround organization between the normal and affected eyes of amblyopes. To the extent that most findings favor a retinal site for the psychophysically measured antagonism, and that evidence is accumulating for a direct effect on the mammalian retina of stimulus manipulation during visual development, the difference in spatial parameters of center/surround antagonism in amblyopia suggests that the dysfunction in amblyopia begins already in the retina.

Keywords: Center/surround antagonism; Spatial opponency; Desensitization/sensitization (Westheimer) function; Amblyopia; Retinal interaction; Visual cortex

1. Introduction

An abiding problem in vision concerns the conclusion about the location within the sensory and nervous system to which processing of a particular performance may be assigned. The issue, broadly speaking, is that of reductionism. The prototype of this kind of enterprise is the compelling association of rhodopsin with scotopic vision—its spectral absorption with the luminosity curve, and its kinetics with dark adaption. As knowledge of the working of the retina and the visual brain grows, so does the temptation to identify specific areas or structures as the site of operation underlying particular visual function.

Yet profuse interconnectivity is a pervasive feature of the nervous system. Feed forward, feedback, lateral interaction, top-down influences, re-entry—these are just a few concepts, usually based on anatomical and neurophysiological evidence, implying that paths from stimulus to response do not remain isolated. Hence a narrow program of site location would seem doomed to failure. The mammalian visual system does, however, happen to be provided with at least one sharp partition. Traffic of neural impulses between the retina and the rest of the nervous system is only one-way (Brindley, 1970), and some anatomical features (each hemiretina projects to a different cortical hemisphere) and disease incidences occasionally allow unambiguous distinction between retina and further stages of the visual stream.

A specific area of a vision lends itself particularly to this enquiry. Soon after Mach (1865) postulated that the strength of brightness sensation in a location de-

* Tel.: +1-510642-4828; fax: +1-510643-6791.
E-mail address: gwest@socrates.berkeley.edu (G. Westheimer).

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pends on the incident light level as well as its second spatial derivative, Hering (1874) gave an explicit physiological form to the proposition: "Light stimulation causes a reaction not only in the immediate region on which light impinges, but also in its surround, insofar as in the directly stimulated region there is increased activity and in the surround there is increased inhibition and in such a manner that the latter is highest in the immediate neighborhood, diminishing rapidly with distance."

Writing about mammalian retinal ganglion cells 79 years later, Kuffler (1953) stated "In all fields there exists a central region giving a discharge pattern which is the opposite from that obtained in the periphery... Functionally the center and surround regions are opposed, the one tending to suppress the other."

2. Neurophysiological research

The similarity between these verbatim quotes is so striking that it is tempting to think that Kuffler set about to give Hering's proposition a physiological, specifically retinal, underpinning. From personal conversation with Kuffler and members of his laboratory at the time, however, I have gained the impression that there was no conscious or overt connection between the two streams of research. Moreover, the trend to look for textured response properties at early stages of visual processing was gathering steam at the time, witness Barlow's (1953) contemporaneous observation that increasing the area of light exposure leads to a *decrease* in ganglion cell discharges in the frog retina, and the title of Hartline's (1949) abstract "Inhibition of activity of visual receptors by illuminating nearby retinal elements in the limulus eye."

In physiological experiments one records activity of a neural unit by varying size and position of retinal light stimuli, mapping the receptive field. For example, in Barlow's experiment, the discharge of a frog retinal ganglion cell is measured as a function of the diameter of the disk of light projected on the retina. The antagonistic organization is revealed by the fact that, for a fixed flux per unit retinal area, there is first an increase in activity with increasing disk diameter, and then, once a critical diameter has been exceeded, a reduction in impulses, revealing an antagonistic surround. In Kuffler's cat experiment, the opponency is in principle the same, but merely requires an extension into the ON–OFF regimen. The representation of this situation in the realm of psychophysics is a little less direct, because stimuli of increasing area cover an increasing number of responding units, making it difficult to assess any change in the response of a single unit.

3. The probing-spot psychophysical technique

This handicap can be overcome by resorting to a paradigm in which the activity level of a small retinal region (perhaps a single ganglion cell) is gauged by the increment threshold in a fixed location for a brief small probing spot. And, by turning this into a null experiment, i.e., keeping the light in the probing spot constant and varying the size and luminance of the background, an even closer concordance with a neurophysiological single-unit experiment can be achieved. It is based on the assumption that whenever the threshold for a small brief spot has a specific value the local neural activity is the same.

This experiment was implemented in the following manner. The probing spot, held at a fixed intensity, is flashed in a given retinal location superimposed on circular backgrounds of various sizes. The retinal illuminance of the latter is adjusted to set the probing spot to detection threshold. Backgrounds which have the same increment thresholds for the invariant probing spot can be regarded as equivalent, and in this manner an area-background function can be generated (Fig. 1). When it is compared with the corresponding neurophysiological experiment in the cat retina, a remarkable similarity emerges. In both experiments, for each background diameter a criterion luminance was determined. In the animal experiment, the criterion is a fixed impulse activity of a neuron, in the human psychophysical experiment it is the local retinal sensitivity as signalled by the fact that the probing spot is at threshold. The concordance between the two approaches extends even to the differences in curve shape that occur with different activity levels.

At the higher test spot intensities or neural discharge rates, there is an upturn in the luminance needed to reach criterion when the background is increased beyond a critical diameter. For background areas within a critical diameter there is areal summation of excitation: as the area is increased, less light per unit retinal area is needed to reach the criterion level at which the probe is at threshold. However, once the background is further increased and begins to cover the zone surrounding the critical diameter, stimulation in these locations engenders signals at the probing site of the opposite polarity, and there is then need to increase the background luminance to counteract these. The difference in the curve shape between high and low intensitites was interpreted by Barlow, Fitzhugh, and Kuffler (1957) as evidence that surround inhibition drops out at lower adaptation levels.

The phenomenon revealed in Fig. 1 can be more conveniently handled if, instead of the null procedure, one uses a reciprocal method, i.e., finds the detection threshold for a small probing spot superimposed on a background of constant luminance, as a function of the

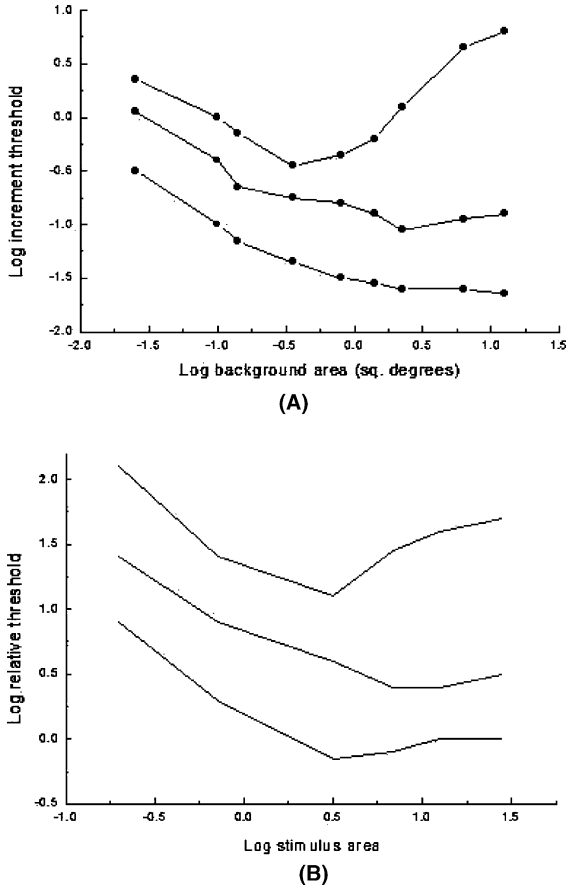

Fig. 1. Comparison of center/surround antagonism as measured psychophysically in the human and in single-unit activity from a retinal ganglion cell of the cat. (A) Retinal illuminance of circular backgrounds of various diameters required to bring a brief, small probing spot to detection threshold. Three different intensity levels of the probing spot. Scotopic conditions, peripheral vision (from Westheimer, 1965). (B) Threshold intensity for cat ganglion cell discharge as function of stimulus area at three adaptation levels (data redrawn from Barlow, Fitzhugh & Kuffler, 1958). The shape of the curves differs because surround inhibition drops out as the absolute threshold is approached.

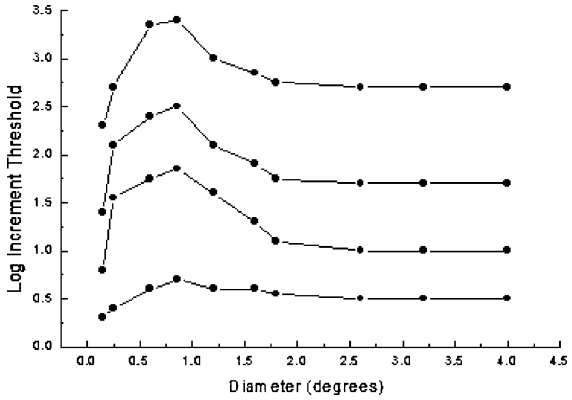

Fig. 2. Desensitization/sensitization (Westheimer function) under scotopic conditions in a single location in the human retinal periphery. Ordinates: Threshold intensity of a probing spot superimposed on uniform backgrounds of increasing retinal illuminance as function of their diameters. Beginning rise of probe threshold is interpreted as a summation of desensitizing signals in the receptive field of the probed unit; beyond a critical diameter, the surrounding area sends signals of opposite polarity which cause reduction in threshold (sensitization). Bottom curve: at very low background luminance there is no surround sensitization (from Westheimer, 1965).

diameter of the background. This yields the more familiar desensitization/sensitization curve (often called the Westheimer function) (Fig. 2), wherein the value of the test-spot's increment threshold is the indicator of the underlying state of excitation of the retina. As the background increases there is first a rise in threshold—reduced sensitivity or desensitization. After the background exceeds its critical diameter, the threshold now begins to fall (there is sensitization), indicating that the surround is sending signals of the opposite polarity. Here also, the absence of sensitization at low adaptation levels can be understood to mean that there is no surround inhibition in the deeply dark-adapted retina.

The pleasing match between retinal ganglion cell responses and the results of psychophysical experiments designed specifically to be their parallel was at the time regarded as convincing evidence that the rising and falling components of the desensitization/sensitation curve were indeed counterparts of the excitation/inhibition phases of ganglion cell receptive fields.

A series of psychophysical experiments consolidated this view. In any given location in the peripheral retina the critical diameter at which desensitization turns into sensitization is different depending whether vision is photopic or scotopic, analogous to the difference in summation areas and acuity in the cone and rod retinas. The concordance extends also the rate of increase of the spatial parameters with increasing retinal eccentricity which matches equivalent curves of retinal ganglion cell receptive field diameters in the primate (Oehler, 1985; Spillmann, Ransom-Hogg, & Oehler, 1987).

In a material extension of this work, Enoch and coworkers obtained measurements on patients with ophthalmic diseases affecting the retina. Only the sensitization phase of the desensitization/sensitization curve drops out reversibly during the progression and subsequent recovery in choroidal-retinal traumas (Campos, Bedell, Enoch, & Fitzgerald, 1978). On the other hand, the full desensitization/sensitization effect is observed at the edge of a hemianopia (Enoch, Berger, & Birns, 1970), showing that inhibition can emanate from a part of the retina whose own ganglion cells are not functioning. These two findings, among a variety of others, prompted Enoch and his group to assign an intra-retinal location (inner plexiform layer) to the interaction underlying the desensitization/sensitization phenomenon and to link it to the internal retinal circuitry elucidated from the intracellular recording from individual retinal elements in *necturus* by Werblin and

Dowling (1969) and Werblin and Copenhagen (1974). Small field elements contribute in a quasilinear, non-rectified manner separately to each of the two branches of the curves (Enoch & Johnson, 1976; Teller, Matter, & Phillips, 1970; Westheimer & Wiley, 1970). Surround sensitization is within and not between color system (McKee & Westheimer, 1970) and can therefore be regarded as a confirmation that what is being measured is at an early stage of visual processing, before color opponency is entrained. Some significant non-linearities (Westheimer & Wiley, 1970; Wyatt, 1972) do not as a whole detract from this view nor does the controversy about rod/cone independence (see MacLeod, 1978 for review). Some intraretinal studies of Werblin, concentrating on the amacrine cell responses which have prominent transients, led Enoch and his collaborators to introduce the "windmill" pattern (Enoch, Lazarus, & Johnson, 1976) in which the sensitization zone is stimulated by rotating wedges. "Transient" functions were compared with the more traditional "sustained" stimulus but, while there are occasional differences, this review will concentrate on the results with steady stimuli.

4. Spatial interaction and border inhibition

Seen from the purely psychophysical perspective, inquiry into the influence of background area on the sensation of brightness had a long history, preceding any attempts to make a sharp distinction between retinal and cortical processing. Blachowski (1913), who pioneered the test probe technique, measured the brightness discrimination of a 20′ circular disk in the presence of uniformly lit circular backgrounds of 2°, 8° and 16° diameter. He found that the larger the background, the lower the incremental threshold in its center. Steeped in Hering's teaching, he regarded the activity in the visual system underlying the subjective sense of brightness in any given location as a balance between the excitatory signals due to light falling on it and inhibitory signals arising from light impinging on neighboring regions: "Every point on the retina maintains a mutually antagonistic relationship with all others, at least within a certain region... Therefore every illuminated retinal location will tend to induce in its surround an influence which...has the consequence of reducing its brightness... Hence we must draw the conclusion that the excitation of a retinal region which corresponds to a larger area is lower than the equivalent one of a smaller." Blachowski's experiments were repeated and extended by Fry and Bartley (1935) who however posited quite a different explanation: "...whenever an activating border acts on the side of a test border...the effect is invariably an interference with the establishment of the border which raises the threshold." Delimited backgrounds necessarily have borders which, according to Fry and Bartley, interfere with the establishment of neighboring borders and therefore raise thresholds. But this effect decreases with increasing separation between the borders. They supported this contour-interaction hypothesis by an experiment in which the threshold was measured on a large uniform background with the addition of an annulus that could be given positive or negative contrast. In either case the test-field threshold was higher than in the absence of an annulus.

A thorough analysis of background diameter effect on the brightness discrimination threshold for a 1/2° test field was performed by Crawford (1940), both in the fovea and the 8° periphery He also demonstrated, as had Blachowski and Fry and Bartley, that thresholds decrease with background (or as he called it, conditioning) field diameter. Crawford also favored a contour-interference explanation—"the pattern of the conditioning field may interfere with the discrimination of the pattern of the test field, and such an interference will...raise the threshold." But when he employed backgrounds smaller than the test field he saw, for the first time, a lowering of thresholds.

Ratoosh and Graham (1951), using test flashes of 10′, 20′, 40′ and 100′ diameter, determined brightness discrimination thresholds against backgrounds of a similar range of diameters, at several luminances. For photopic luminance levels and 10′ foveal test fields, thresholds decreased by about 0.7 log units as the background diameter increased from 10′ to 100′. Ratoosh and Graham did not refer to the earlier research and their interpretation of the data was more in line with Blachowski's: "The improved brightness discrimination with large surrounds implies that a retinal area is made more sensitive, with regard to brightness discrimination, by an adjacent illuminated field." In a related experiment, Heinemann (1961) tested the increment threshold for a 10′ field on a 30′ background. When the latter was surrounded by a large annulus there was a threshold reduction. Battersby and Wagman (1962) found that the threshold for a 40′ test patch decreased progressively as the background was expanded from 40′ to 4°40′ and this held regardless of on and offset transients. The diameters of test and background stimuli used by these various investigators are summarized in Table 1.

Thus, by the time the desensitization/sensitization view emerged in the 1 ate 1960's the improvement of increment threshold with an increasing background field had been part of the literature and had been interpreted in one of two ways. Blachowski and Ratoosh and Graham took Hering's view of antagonistic interaction of neighboring regions, whereas Fry and Bartley and Crawford adopted a more perceptual explanation in terms of contour interaction: as the background expands, its edge (the border) recedes from the test zone, reducing the postulated threshold-raising contour interaction. Yet the overwhelming majority of the work

Table 1
Diameters of test and background stimuli used by various investigators

Investigator and condition	Test field	Background
Blachowski (1913) fovea	20′	2°–16°
Fry and Bartley (1935) fovea	45′	~1°–8°
Crawford (1940)		
fovea	30′	18′–10°
8° periphery	30′	18′–10°
Ratoosh and Graham (1949) fovea	10′	10′–80′
Heinemann (1961) fovea	10′	30′
Battersby and Wagman (1962) 7° periphery, photopic	40′	40′–4° 40′
Westheimer (1965) scotopic vision 10° periphery	6′	6′–4°
Westheimer (1967) fovea	1′	3′–15′

rested on the sensitization component of the phenomena. Only Crawford found any indication of a reduction when the background area was made *smaller* and because he used a 1/2° disk, which is large enough to be seen with prominent borders, it led him to a contour interaction interpretation.

To act as a true probe, a test spot should be only a few minutes in diameter rather than the much larger test flashes employed by Blachowski, Fry and Bartley, Crawford and Ratoosh and Graham. Only then does it become possible to reveal both the desensitization and sensitization phases of the threshold *vs* background diameter phases in a single experimental run. Basing the interpretation on the Hering conjecture, the initial rise is an expression of the areal summation of excitatory signals widely seen in such experiments as Ricco's (see for example, Barlow, 1958; Graham, Brown, & Mote, 1939). Beyond a critical background diameter, antagonistic surround signals begin to be fed into the test area whose threshold is explored by the small probe. The connection between the neural counterpart of these two phases as revealed in the retinal ganglion cell discharges reported in the experiments by Kuffler and by Barlow is strengthened by the researches described earlier on the influence of adaptation, peripheral location, retinal diseases and intraretinal recording.

But, however good the analogy between neural impulse traffic and psychophysical findings, when asking about the neural substrates of the latter one enters the realm of "psychophysical linking hypothesis" (Brindley, 1970; Teller, 1984). This is not a purely epistemological exercise but one that influences the design of subsequent rounds of experiments. In Fry and Bartley's time, and Crawford's, there was as yet no hint of the existence of neurons right at the beginning of cortical visual processing selective to edges, i.e., borders, in the visual field. Once these were demonstrated, however, the opposing views of border interference and center-surround opponency, could both call on neurophysiology to provide a substrate. Because spatial center-surround opponency has its base in the retina, whereas contours can rightly claim to be first explicitly represented in the cortex, the retina versus cortex dialogue began to be joined.

It was broached directly in the study of sensitization in photopic vision (Westheimer, 1967). Artificial borders were created by juxtaposing very a narrow concentric bright and a dark ring. They were clearly visible but their space-averaged luminance was that of the rest of the background. They induced no threshold change. A dichoptic experiment, in which an annulus surrounding the test region was shown either to the same or the other eye, showed sensitization only when the surround was in the same eye. Yet, there were subtle differences in a variety of experiments that led me to conclude: "Some of the findings. might, in fact be most easily understood as a demonstration that the presence of a border within a few minutes of arc of the area tested elevates the threshold by about 1/4 log unit." Lennie and MacLeod (1973), concentrating their attention on the annulus and some related experiments, favored a border desensitization hypothesis rather than antagonistic surround sensitization and raised an important new point. When the threshold in a given location is tested by a small probe as a function background area, could it be that different ganglion cell types were brought into play? The impetus was the "channel" concept in spatial vision according to which at every place in the visual field there are units of a range of receptive field diameters. The interpretation of sensitization in terms of size-selective channels was discussed by MacLeod (1978) and by Hayhow (1979). Further, supposing that there is a kind of ganglion cell whose receptive field is non-opponent but with properties that depend on the level of illumination, a gamut of psychophysical findings can be accounted for even without the need for a center/surround antagonism (Cornsweet & Yellott, 1985).

Summarizing the situation so far: the sensitivity for detecting an increment stimulus is increased (threshold decreased) when the background on which it is presented is enlarged beyond a critical diameter. This sensitization phenomenon has been variously interpreted as an expression of

(a) retinal center/surround antagonism;
(b) border interaction decreasing with receding edges of background; and
(c) size-selective channels with sensitivities depending on intensity and area of background.

The last of these was never developed in sufficient detail to become a significant concept. Evidence from physiology and findings from some cases of ocular pathology provide solid underpinning for the retinal center/surround antagonism as the origin of the effect, but some significant loose ends remain suggesting that edge or borders, per se, do play a role. The difference in the two concepts is also, basically, the difference in current views of processing at the level of the retina and the visual cortex. Retinal ganglion cell impulses are seen as reflecting summation, however nonlinear, of excitatory and inhibitory signals from spatial subunits of its receptive field. The response of cortical cells, on the other hand, is regarded as being predicated by the presence in their receptive field of specific non-uniformities. In the border interaction explanation of the sensitization phenomenon one would, therefore, regard the cortical excitation pattern that emerges when a border is shown, as reducing the conspicuity of the signal from a nearby probing flash. The masking of the latter would gradually subside with spatial separation of the border. Careful analysis of some sensitization data (Lennie & MacLeod, 1973; Westheimer, 1967) does indeed point to a non-trivial border component, especially where the interacting distances are small and where optical factors cannot be completely ruled out.

Many psychophysical findings with an undoubted cortical origin have some degree of similarity with what has been discussed: an adjoining pattern element causes a gradual increase in threshold and then a threshold reduction as it recedes from the test area. This process has been shown to be at work with vernier acuity (Westheimer & Hauske, 1975), line-orientation discrimination (Westheimer, Shimamura, & McKee, 1976) and stereoacuity (Butler & Westheimer, 1978). All these concern themselves with spatial relationships between identified features and not the detection of an increment stimulus, and one would naturally look to the cortex for this kind of processing. Vassilev (1973) performed a study that may be seen as a bridge between the probing-spot sensitization results and more frankly cortical processing. He mapped the threshold for a small disk and also for a small rectangle near a long straight border. The threshold for the rectangle increased much more than that for the disk as they approached the edge. It seems established now that neurons in the beginning of the cortical stream are attuned far better to lines or edges than to small spots. Hence experiments, like Vassilev's, with line, edge or Gabor patterns as the probe for testing sensitivity can be presumed to address cortical processing rather than retinal. This is likely to be the case for those of Polat and Sagi (1993) on sensitivity changes of Gabor patches, as a function of position, contrast, spatial frequency and orientation of nearby similar patterns.

A greater concordance with the phenomena described so far was achieved in the experiments of Yu and Essock (1996a, 1996b) and Yu and Levi (1997a). They used line or elongated Gabor stimuli as both background and test and studied the detection threshold of the latter in order to determine properties of spatial interaction, revealing distance effect with rising and falling phases reminiscent of the desensitization/sensitization curves found with small probing spots on circular backgrounds. The amount of sensitization is, however, considerably smaller than that found when the probe was a spot rather than a line; it has the same magnitude as the "border" effect in Westheimer (1967).

Interaction between neighboring elements in the visual field has also been implicated as playing a role in the Hermann grid illusion, subject to a recent in-depth review by Spillmann (1994). The concept of perceptive field is introduced (Spillmann, 1971), analogous to the physiologically measured receptive field, with a center and an antagonistic surround. Although results with dark adaptation and dichoptic presentation "point to a predominantly monocular origin...presumably in the retina" there is evidence for a post-retinal contribution, in particular an oblique effect. In the Hermann grid illusion, just as in the experiments by Yu and coworkers described above, lines are an essential component of the stimulus configuration. Because their processing has a defined cortical substrate, there is no disagreement that the interpretation of these experiments should involve interaction among cortical signals.

5. Amblyopia

On the basis of their own recent experiments, however, Yu and Levi (1997b) went further and argued for a cortical locus even for those experiments with a probing spot on a circular background that had been widely accepted as having its origin in retinal center/surround antagonism. The claim is based on two findings, a new attempt at demonstrating a dichoptic effect and a comparison of the difference in shape of the desensitization/sensitization curve between the normal and affected eyes of two amblyopes. Yu and Levi's monoptic/dichoptic experiments employed a 1.5′ probing spot on foveal backgrounds ranging in diameter from 3′ to 19′ and found thresholds peaking at around 9′ with a gentle decline by 0.1–0.2 log units for the largest backgrounds. In another experiment, there was on average a 0.1 log unit monocular threshold reduction when a

dichoptic annulus was added to a 9′ binocular disk background. These numbers may be compared with a threshold peaking with a 5′ background, a decline of up to 0.5 log units in the foveal data of Westheimer (1967) and a sensitization that was observed only with monoptic annuli, not dichoptic ones, suggesting that the procedures in the two experiments may have differed. Because, in dichoptic studies, problems of fixation disparity and convergence slip with attending rivalry have always to be faced, experiments in the retinal periphery might have been more revealing. Hence, the many demonstrations of either complete or at least substantial absence of a dichoptic sensitization effect (Battersby & Wagman, 1961; Johnson & Enoch, 1976; Markoff & Sturr, 1971; Sturr & Teller, 1973; Westheimer, 1967), several of them performed in scotopic vision where the critical diameter is several times larger, may not be as simply dismissed as Yu and Levi did.

On the other hand, Yu and Levi cover new ground with their amblyopia experiments. The finding that the desensitization/sensitization function peaks at wider background values in the amblyopic eye are convincing. Curiously, unlike in their monoptic/dichoptic experiments, said to have been performed with the same procedure, the normal eyes show a peak near 6′ and a sensitization of the order of 0.5 log units, a close match to the traditional values for foveal vision. Against this, when measured in the amblyopic eye, the curves are higher, peak near 10′ but still display sensitization of approximately 0.5 log units. The visual acuity in these eyes is about 1/4 of normal, and interestingly both the reduced acuity and stretched-out and shifted sensitization functions match that of a normal photopic retina about 4° from the fovea (Fig. 3). Hence Yu and Levi have adduced strong evidence that foveal vision in the affected eye of their two strabismic amblyopes has at least two of the spatial processing characteristics of the normal 4° periphery. On the other hand the data disagree with Miller's (1954) contention that the impairment in a strabismic amblyopic eye is due to "absence of inhibition…which leaves the spread of excitation unsubdued." The further claim by Yu and Levi that these data place sensitization in the cortex rests on the extent to which one can be certain that the spatial processing deficit in strabismic amblyopes is indeed confined to the cortex.

A thorough study of anatomical and physiological status of monkeys reared with unilateral blur and subsequent anisometropic amblyopia was conducted by Kiorpes et al. (1987), Hendrickson et al. (1987) and Movshon et al. (1987). No differences were found in histological sections of the retina. LGN parvocellular neurons from the affected eye were of the order of 20% smaller and cortical ocular dominance columns showed characteristic changes. There were marked differences in the spatial frequency tuning of cells in the visual cortex, favoring

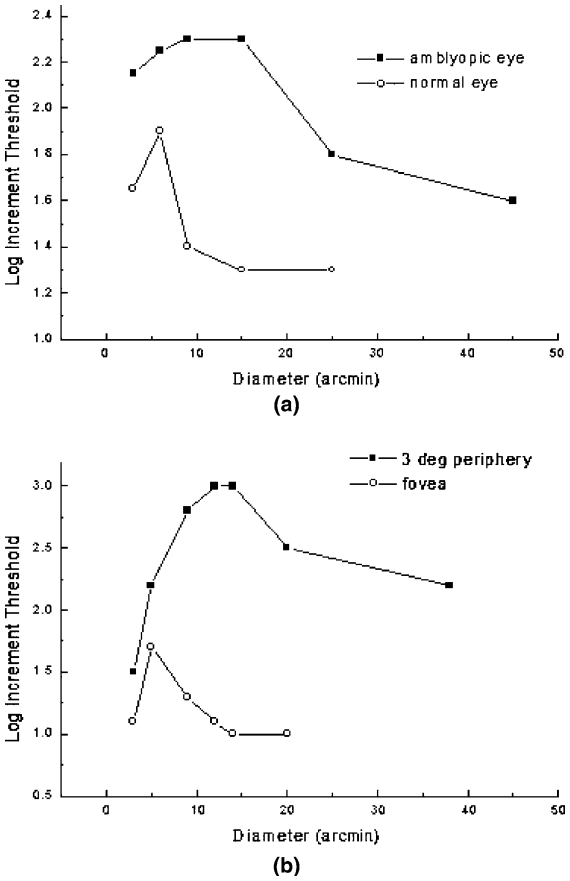

Fig. 3. Comparison of (top) desensitization/sensitization function in cone vision in the normal eye in the fovea and the near periphery (redrawn from Westheimer, 1967) and (bottom) curves under substantially identical conditions in the normal and affected eyes of amblyopes (representative data from Yu & Levi, 1997a).

the normal eye. Of particular interest is Fig. 5 of Movshon et al., illustrating how in some binocular cells in V1 the spatial frequency response band is quite different depending whether stimulation came through the normal or the affected eye. In the one monkey in which spatial frequency responses were recorded from LGN cells the affected eye was about 7% poorer. From this study it would seem that there are substantial differences in anatomy and neurophysiology of the cortex in anisometric amblyopic monkeys, and detectable ones in the LGN. Efforts to find differences in the retinal nerve-fiber layer between normal and affected eyes of amblyopes have not been successful.

One way of examining purely retinal function is electroretinography. Because even the near periphery of amblyopes may be normal, this needs ERG's from only the foveal regions, requiring restrictions of stimulation to a small zone of the retina and/or utilizing patterns with grain size of the order of foveal resolution. Some studies (Hess & Baker, 1984; Hess, Baker, Verhoeve, Keesey, & France, 1985) found no differences in pattern ERG's with gratings up to 3.2 cycles/° between

the normal and amblyopic eyes, although some of these patients also had no psychophysical deficits for such stimuli. On the other hand there are reports (Dahlke & Dodt, 1994; Fioretto et al., 1996; see also Hull & Thompson, 1989 for a review) in which differences were found in the pattern ERG in the normal and affected eyes. It is well recognized that there are many kinds of amblyopia. Strong conclusions in this area then obviously require application in the same eyes of the battery of tests.

This raises the possibility that optical blur during a critical period of development begins its influence on the visual system not at the cortex but already on the retinal circuitry. The changes would be subtle and confined to the regions of highest acuity, unlikely to be histologically visible in optical microscopy. Evidence is accumulating that unilateral manipulation of the stimulus reaching the mammalian retina can cause changes in the affected eye (Kiorpes & Wallman, 1995), sometimes even when deaffarented (Raviola & Wiesel, 1985). In the retina of the cat, postnatal light deprivation produces abnormalities in the ON and OFF pathways (Tian & Copenhagen, 2003). If it were to be firmly established that functional impairment in amblyopia can be found already in the retina, then the differences in sensitization found by Yu and Levi, instead of arguing for a cortical origin, would concord fully with all the other psychophysical results pointing to a retinal origin of the desensitization/sensitization phenomenon, in particular its photopic/scotopic dichotomy, the compelling findings from retinal physiology, and its loss with progression and subsequent recovery with resolution of retinal disease.

The strength of the case for a retinal origin of the body of findings described as the desensitization/sensitization effect does not by any means exclude quite similar phenomena in the cortex. Their examination, pioneered by Yu and Essock and by Polat and co-workers, is best accomplished by utilizing stimulus patterns matching the known operation of cortical mechanisms which, in contrast to retinal ones, are characterized by orientation-selectivity and influenced by a variety of factors such as context, attention and learning.

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