WHAT IS ODD ABOUT THE SHORT-WAVELENGTH MECHANISM AND WHY IS IT DISPROPORTIONATELY VULNERABLE TO ACQUIRED DAMAGE? REPORT OF A DISCUSSION

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After the formal papers on the short-wavelength mechanism, a panel discussion was held on the problems raised. The Chairman was Dr. R.M. Boynton and the panel consisted of Dr. A.J. Adams, Dr. P. Grützner, Dr. M. Marré, Dr. J. Mollon, Dr. A. Pinckers, Dr. D. van Norren, Dr. B. Wooten, Dr. F. Zisman and Dr. E. Zrenner. The report and commentary given below are based on a tape recording of the discussion. Occasional references have been inserted for the convenience of the reader.

The site at which long- and short-wave signals interact

Dr. Boynton prompted a discussion of the relationship between the model of the blue mechanism proposed by Pugh and Mollon (1979) and that advanced at the present meeting by Dr. Zrenner (see this volume). One difference, Dr. Zrenner suggested, is that Pugh and Mollon postulate only a single site of interaction between long- and short-wavelength signals, whereas he and Gouras postulate (a) an interaction in the outer plexiform layer (which is responsible for transient tritanopia, for example) and (b) a further site, later than the retinal ganglion cell, at which a positive yellow signal is introduced (Gouras and Zrenner, 1981). He pointed out to the near absence of blue OFF-centre retinal ganglion cells in the macaque (e.g. Gouras and Zrenner 1978; Malpeli and Schiller 1978; de Monasterio 1978) and suggested that the yellow-blue opponent channel was constructed only at a post-retinal level, where a signal derived from the long- and middle-wavelength cones is combined with the short-wavelength signal. Commenting on this suggestion, Dr. Mollon recalled that in the account given by Polden and Mollon (1980) the 'blue-yellow' channel was deliberately assumed to be asymmetric, in that a greater dynamic range was postulated between the signal produced by white light and that produced by blue than between the former signal and that produced by monochromatic yellow light. One reason for assuming this asymmetry was the small number of just-noticeable differences (jnd's) between white and a monochromatic light of 570 nm in

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comparison to the number of jnd's between white and the short-wavelength end of the spectrum; there are only about 5 jnd's in the former case and more than 20 in the latter (Wyszecki and Stiles, 1967, p. 510). Given that only a very limited range of psychophysical discrimination has to be explained, is it necessary to postulate introduction of a 'yellow' signal at a post-retinal site? Could not yellowness be adequately represented by decrements in the activity of blue ON-centre cells, decrements below the level of response produced by white light? In response, Dr. Zrenner agreed that inhibition could in principle carry the positive signal about a given attribute but he doubted whether the necessary dynamic range was available in the present case. Very small amounts of yellow light suppress the type of ganglion cell that receives its excitatory centre input from the short-wavelength receptors. Since the cell is then silent, subsequent sites cannot discriminate between amounts of yellow light.

Dr. van Norren noted that Dr. Zrenner's model required that transient tritanopia should occur at the receptor level; but Valeton and van Norren (1979) had shown that it was not present at that level. In reply, Dr. Zrenner said that Valeton and van Norren's results did show a small effect in the a-wave of the ERG (at the two shortest wavelengths), as well as the larger one in the b-wave. (In subsequent correspondence, Dr. Zrenner writes (a): 'GABA is involved as a neurotransmitter in the feedback loop which modulates the blue cone signal as revealed by experiments in the arterially perfused eye with the GABA-antagonist bicuculline (Schuurmans and Zrenner, 1981); this again points to a horizontal cell loop back on to the blue cone's pedicle.' And (b): 'the model would work as well (with a sign reversal) if the interaction occurred between the horizontal cell, fed by long-wavelength sensitive cones, and the on-centre bipolar cell, fed by blue-sensitive cones. This interaction would take place most probably in the blue cone's pedicle, and thereby – strictly speaking – in the receptor layer without affecting the electrical responses in the outer segment'.)

The use of long-wavelength fields in studies of the short-wavelength mechanism

Dr. Boynton drew attention to the growing evidence that bright long-wavelength adapting fields placed the visual system in an abnormal state. Yet in investigations of the psychophysically defined 'blue mechanism', such fields were commonly used in order to eliminate the response of the long- and middle-wavelength receptors. For example, bright long-wavelength fields were typically present during measurements of the spatial and temporal characteristics of the blue mechanism. Dr. Mollon took up this point and drew attention to an apparent contradiction in the literature on acquired colour deficiencies. If increment thresholds are measured for monochromatic targets, as for example in studies by Drs. Marré, Adams, King-Smith and their collaborators, then impairments of the short-wavelength mechanisms seem to predominate in many disorders, whether of the retina or the optic nerve; tritanopia crops up everywhere. But if classification is based on, say, the Farnsworth-Munsell 100-hue test, then red-green disorders or general impairments of colour discrimination are frequent; and Koellner's Rule, very

broadly, holds. Other discussants made related points. Thus, Drs. Adams and Zisman, in response to a question from Dr. Wooten, reported that in diabetic patients a large loss could occur in π_1 without a corresponding loss on clinical colour vision tests. A 2-log-unit drop in the sensitivity of π_1 could occur before a patient volunteered that there was anything unusual about his or her colour vision. Similarly, Dr. van Norren, describing a new tritan test in which the patient must detect a flickering blue target on a yellow field, reported the existence of patients who showed a 2-log-unit drop in sensitivity and yet passed other tritan tests.

How are these discrepancies to be explained? The model of Pugh and Mollon (1979) suggests two distinct ways in which performance might come to be impaired when short-wavelengths targets are presented on long-wavelength fields. Firstly, the short-wavelength receptors might be selectively damaged, as classically proposed; no doubt, patients of this kind exist and they would be the ones who were consistently tritan on other tests. Secondly, the abnormality might occur at the 'second site' of the model, the site at which short- and long-wavelength signals interact. The model supposes that this chromatically opponent site becomes most sensitive to input perturbations (i.e. small changes in chromaticity) when it is in the middle of its response range; when it is *polarized,* that is, driven to one or other extreme of its operating range by a strongly coloured field, its sensitivity is reduced. However, if the coloured adapting field is maintained, a restoring force acts to bring the channel back towards the centre of its operating range. Two pathological malfunctions of this system could occur: firstly, the operating range of the opponent channel might be reduced, and secondly, the restoring force might be inadequate and 'normalization' of the operating range might not occur. Now, malfunctions of this type might affect all colour-opponent channels equally and yet, if increment thresholds were measured on coloured fields, it would appear that the short-wavelength mechanism was disproportionately impaired. This is because signals originating in the short-wavelength receptors are probably confined to colour-opponent channels (see Boynton, Zrenner, Mollon, this volume), whereas incremental stimuli detected by the long- and middle-wavelength cones enjoy access to a variety of post-receptoral channels some of which are not chromatically opponent; the latter, owing to differences in size, morphology or biochemistry, may be relatively spared by a given disease, or it may be that under the conditions of observation the non-opponent channels are not placed at the extremes of their response ranges. Patients with a disorder of post-receptoral colour-opponent systems would be those who showed a large loss for short-wavelength increments on a yellow field but were not so clearly tritan on other tests. It might also be expected that their detection performance for short-wavelength targets would improve if the adapting field were neutral rather than monochromatic; that is to say, they would show in an exaggerated form the *combinative euchromatopsia* (Polden and Mollon 1980) of the normal eye, since the neutral field would place colour channels in favoured parts of their dynamic ranges. A phenomenon of this type has been explicitly described by King-Smith and his collaborators (see, for example, Alvarez, King-Smith and Bhargava, this volume) and we could perhaps call it the *Manchester sign*, to acknowledge its discoverers.

Why is little impairment seen on clinical tests in the case of some patients who show large losses of π_1 when increment thresholds are measured on long-wavelength fields? Perhaps the explanation lies in the fact that the chromaticities used in clinical tests are never close to the spectrum locus and so do not test chromatic channels at the extremes of their operating ranges.

Dr. Boynton pointed out that it was possible to study the isolated short-wavelength mechanism without using the traditional long-wavelength adapting field. One could require the observer to detect an alternation between lights that were confusable by a tritanope (e.g. Wisowaty and Boynton 1980). It was thereby possible to produce a large modulation of the short-wavelength receptors without modulating the long- and middle-wavelength receptors. Dr. Boynton suggested that such a technique might be useful clinically.

Why is the blue mechanism more vulberable to acquired deficiencies of colour vision? A summary of possibilities

Owing to limitation of time, the Group's discussion had to end before this central question had been fully discussed. Nevertheless, a number of possible hypotheses emerged in the course of the discussion. These are summarised below and this checklist may possibly be useful when the Group next discusses the question.

(1) *The problem is a pseudoproblem.* Dr. Hansen asked whether there was firm proof that the blue mechanism is more liable to acquired disorders. Certainly there were exceptions. He had seen cases where there was very good blue sensitivity and where red-green sensitivity had been lost. Dr. Verriest added that the predominance of blue defects was in part artificial. For the 100-hue test and the D-15 have an intrinsic bias towards giving tritan results. Often a red-green defect would be seen on the HRR plates when a blue-yellow defect was seen on the 100-hue. Dr. Pinckers raised the possibly related question of why plate tests, such as the HRR, show no age-dependent changes whereas others, such as the Farnsworth-Munsell 100-hue test, the D-15, and the Lanthony New Colour Test, do show changes with age. Are the plate tests not sensitive enough or, he wondered, does a marginal small-field tritanopia come into play in the case of tests such as the 100-hue?

(2) *The short-wavelength receptors are not individually more vulnerable than other receptors, but are rare.* It is conceivable that a disease that affects all receptors equally may appear to affect first the short-wavelength receptors simply because they are widely spaced in the retina to begin with.

(3) *The short-wavelength receptors are more fragile than others.* Several hypotheses might be distinguished. (a) the membranes of the short-wavelength receptors may be more permeable to toxins, as suggested by De Monasterio *et al.* (1981); or (b) synthesis of the opsin of the short-wavelength pigment may require amino acids that are in short supply; or (c) the short-wavelength receptors may be shorter than others and thus in less secure contact with the pigment epithelium. A further possibility is considered by Zrenner elsewhere in this volume.

pigment epithelium. A further possibility (d) is considered by Zrenner elsewhere in this volume. He suggests that blue cones are morphologically similar

to rods in that their outer segment membranes are more disc- than sac-like. Therefore it may be more difficult for blue cones to dispose of calcium than it is for other cones and this would make them more vulnerable to changes in their metabolism.

(4) *Signals originating in short-wavelength receptors are transmitted only by colour-opponent channels and thus, if such channels are impaired but the task allows non-opponent channels to be used for discrimination, sensitivity will appear to be lost disproportionately at short-wavelengths.* This is probably the case when increment thresholds are used to study (what are misleadingly called) 'colour vision mechanisms'. Measurements of sensitivity to short-wavelength targets on long-wave fields will not, on their own, distinguish between true tritanopia and a general impairment of opponent channels; but the 'Manchester sign' may prove to be a good indicator of damage to post receptoral opponent channels. Disease and toxins may (a) reduce the dynamic range of such channels or (b) impair the restoring forces that serve to centre the operating range on the chromaticity of the background illuminant. If, as Dr. Zrenner suggests (this volume), an asymmetric interaction occurs between cone types in the outer plexiform layer, a further complication is introduced.

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