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Modulation sensitivity of ganglion cells in peripheral retina of macaque

Samuel G. Solomon [a], Paul R. Martin [a,*], Andrew J.R. White [a], Lukas Rüttiger [b,1], Barry B. Lee [b,c]

[a] *Department of Physiology, Institute for Biomedical Research, F13 University of Sydney, Sydney, NSW 2006, Australia*
[b] *Neurobiology Group, Max-Planck-Institute for Biophysical Chemistry, D37077 Göttingen, Germany*
[c] *State College of Optometry, SUNY, New York, NY 10036-8003, USA*

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Abstract

There is ample psychophysical evidence that flicker is more salient in the peripheral than the central visual field, but the physiological basis of this eccentricity-dependant change is unclear. Here, we compared responsivity to temporal modulation of ganglion cells in central and peripheral primate retina. Above 30 Hz modulation frequency, both magnocellular (MC) and parvocellular (PC) pathway cells are more responsive in peripheral retina. This suggests that an increase in high-frequency temporal responsiveness arises in outer retina before the MC and PC pathways diverge. In both central and peripheral retina, the critical fusion frequency of MC cells is higher than that of PC cells. This result is consistent with other evidence that psychophysical flicker sensitivity is mediated by the MC pathway.

Keywords: Contrast; Flicker; Parvocellular; Magnocellular; Temporal

1. Introduction

Porter's original observation (1902) that human sensitivity to flicker increases on passing from fovea to peripheral retina has been amply confirmed (Granit & Harper, 1930; Rovamo & Raninen, 1988; Seiple & Holopigian, 1996; Snowden & Hess, 1992; Tyler, 1985; Waugh & Hess, 1994), but the physiological substrate for this change is not known. The increased salience of flicker in the peripheral visual field is due to an increase in critical fusion frequency (CFF) rather than a broad increase in sensitivity to all temporal frequencies (Tyler, 1985). This suggests that the increase in CFF in the peripheral visual field is not simply due to a general increase in gain in peripheral retina. An outer retinal locus for the increase in CFF is implied by the correlation of CFF with electroretinogram amplitude (Seiple & Holopigian, 1996) and CFF has been correlated with the larger photoreceptor dimensions in peripheral compared to central retina (Tyler, 1985).

Responses of cells of the magnocellular (MC) pathway in foveal retina are consistent with their providing input to luminance flicker perception mechanisms (Lee, Pokorny, Smith, Martin, & Valberg, 1990). We here show that the CFF of MC pathway cells increases with increasing distance from the fovea, providing a basis for Porter's observation. The CFF of parvocellular (PC) pathway cells also increases in peripheral retina, which suggests an outer retinal locus for the more rapid retinal response.

2. Methods

Adult macaque monkeys (*M. fasicularis*, $n = 5$) were initially sedated with an intra-muscular injection of ketamine (10 mg kg^{-1}). Anesthesia was maintained with inhaled isoflourane (0.2%–2%) in a 70:30 N_2O:O_2 mixture. Intra-ocular recordings were made using standard techniques (Lee et al., 1990). All procedures were

* Corresponding author. Tel.: +61-2-9351-3928; fax: +61-2-9351-2058.
E-mail address: paulm@physiol.usyd.edu.au (P.R. Martin).
[1] Present address: Tübingen Hearing Research Center, University Clinic, Silcherstrasse 23, D-72076 Tübingen, Germany.

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approved by the State of Lower Saxony Animal Welfare Committee and conform to European Union guidelines for ethical care of animals.

Recordings were obtained from ventral peripheral retina. Luminance modulation sensitivity was measured using the combined light from diodes with dominant wavelengths of 639 and 554 nm, which gave a field of a dominant wavelength of ~590 nm and mean retinal illuminance 2000 td. Stimulus fields were viewed through Maxwellian optics (Lee et al., 1990). Under standard conditions, the entire stimulus field (4.7°) was modulated. Additional measurements were made for some cells with modulation of a smaller spot (0.59°–1.18°) within the 4.7° field. By using a second stimulus channel, the remainder of the field was held steady at the specified mean illuminance and chromaticity.

We recorded complete temporal modulation transfer functions (TMTFs) from 46 MC pathway cells and 20 PC pathway cells at eccentricities above 20°. Responses were obtained at modulation frequencies between 0.61 and 78 Hz at seven contrasts from 1.56% to 100%. First-harmonic response amplitudes were extracted by Fourier analysis of response histograms. Responses to high-contrast drifting sine gratings were measured for most cells and receptive field dimensions estimated by fitting a difference-of-Gaussians model (Derrington & Lennie, 1984). The TMTFs from 15 MC pathway and 20 PC pathway cells were obtained—using the same set of stimuli—predominantly from parafoveal retina in a previous study (Lee et al., 1990). Responses of the small number of cells recorded at overlapping eccentricities in the two studies showed no systematic differences, so data from the two sets were pooled for the present analysis.

3. Results

Responses of PC and MC cells to luminance modulation were recorded as a function of contrast and temporal frequency. First-harmonic response amplitudes as a function of contrast were fitted with Naka–Rushton functions (Naka & Rushton, 1966); examples of such fits may be found elsewhere (Lee et al., 1990). The initial slope of this function (the contrast gain) is plotted as a function of temporal frequency for on-centre MC and PC cells in Fig. 1A and B. Off-centre cells gave similar results, except that their low main-

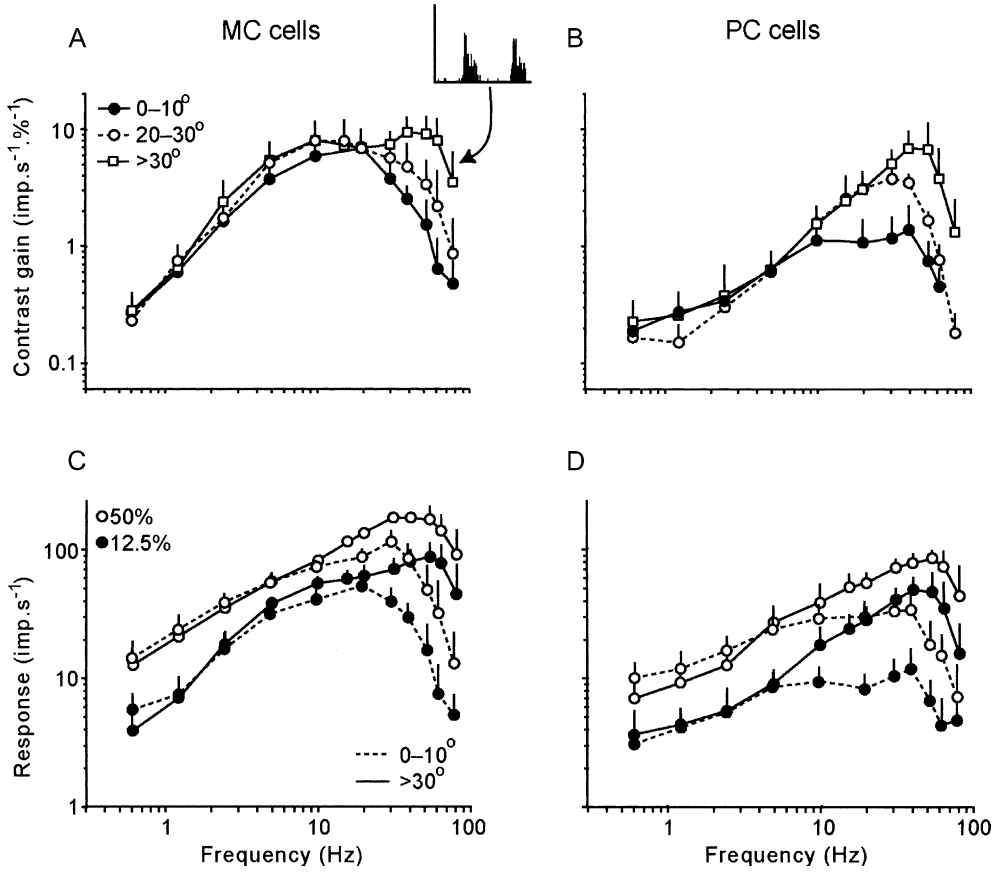

Fig. 1. Modulation transfer functions for on-centre MC pathway (A,C) and PC pathway (B,D) cells. Average data for at least seven cells for each eccentricity range are shown. Error bars are two standard errors of the mean. Inset in A shows peristimulus time histogram for one MC cell at 78 Hz, 100% contrast. Two cycles of stimulus modulation are shown. Vertical scale 300 imp s^{-1}. Data for 0°–10° eccentricity group are from Lee et al. (1990).

tained firing at the illuminance used caused contrast threshold effects in some cells. Cells are grouped into three eccentricity ranges (0°–10°, 20°–30°, >30° eccentricity). The most peripheral cell recorded was at 47° eccentricity. Below ~30 Hz responsivities at the different eccentricities are similar, but at 30 Hz and above responsivity is higher for the 20°–30° group than for the central retina cells, and is even higher for cells beyond 30° eccentricity. We showed elsewhere that PC cell responsivity to red–green chromatic modulation also extends to higher temporal frequencies in peripheral retina (see Martin, Lee, White, Solomon, & Ruttiger, 2001). Within each eccentricity group, the contrast gain of MC cells exceeds that of PC cells at all modulation frequencies tested (Fig. 1A and B).

For MC cells, the extension of responsivity to higher temporal frequencies in peripheral retina (>30°) is associated with the appearance of a resonance peak centred around 50 Hz (Fig. 1A). A similar peak was described in cat Y-cells (Frishman, Freeman, Troy, Schweitzer-Tong, & Enroth-Cugell, 1987). For the 0°–10° group, signs of resonance are not apparent in the contrast gain plot, but can be seen in response amplitude plots for high-contrast stimuli. Fig. 1C shows first-harmonic amplitude as a function of temporal frequency for 50% and 12.5% modulation contrast for on-centre MC cells. The responses of cells in the 20°–30° eccentricity group have been omitted for clarity. For central MC cells the peak response is seen to shift to higher temporal frequencies at 50% compared to 12.5% contrast, to form a shoulder around 30 Hz, beyond which responsivity falls abruptly.

The TMTFs of PC cells become more band-pass in shape at higher eccentricities (Fig. 1B) but there is little sign of a resonance peak as seen for MC cells. Response amplitude plots for 12.5% and 50% modulation contrast do not differ markedly in shape for PC cells (Fig. 1D). Some response compression is evident for peripheral PC cell responses above 10 Hz. This compression may be attributable to response rectification.

The shapes of chromatic and luminance TMTFs of central PC cells can be accounted for by vector summation of opponent cone mechanisms with a similar, linear temporal response and a latency difference of a few milliseconds (Benardete & Kaplan, 1997, 1999b; Lankheet, Lennie, & Krauskopf, 1998; Smith, Pokorny, Lee, Martin, & Valberg, 1990; Solomon et al., 2001). Responses of peripheral PC cells were also consistent with this model (data not shown).

The CFF for each cell was estimated by fitting a line to the descending slope of the 100% modulation contrast curve and extrapolating to 10 imp s^{-1}. The result is shown in Fig. 2. There is considerable inter-cell variability, but the increase in CFF in peripheral retina is clear. For three PC cells and two MC cells, responses at high frequencies were too variable to allow accurate

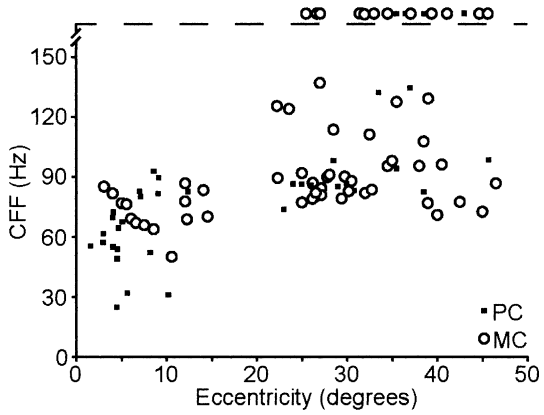

Fig. 2. CFF of PC ($n = 37$) and MC ($n = 59$) cells as a function of retinal eccentricity. It was not possible to estimate the CFF for cells above the dashed line. Data for cells under 20° eccentricity are from Lee et al. (1990).

estimation of the CFF. These cells are not included in the analysis. We asked whether, for each cell class, CFF in peripheral retina is higher than that in central retina. Cells were grouped into two eccentricity ranges (<15° and >15°) and their CFFs compared. For 12 peripheral MC cells and 4 peripheral PC cells, the temporal response extended to such high frequency that CFF could not be estimated from the descending limb of the response curve. These cells were assigned a CFF of 150 Hz for inclusion in the following analysis. The CFF of peripheral PC ($n = 17$) cells is higher than CFF of central PC ($n = 20$) cells ($P < 0.01$, Wilcoxin rank sum test; Bonferroni correction for multiple tests). The CFF of peripheral MC ($n = 45$) cells is higher than the CFF of central MC cells ($n = 14$; $P < 0.01$). The CFF of peripheral MC cells is higher than the CFF of peripheral PC cells ($P < 0.05$) and the CFF of central MC cells is higher than the CFF of central PC cells ($P < 0.05$).

The increase in CFF for both PC and MC cells is consistent with increased responsivity at a site prior to the divergence of these two pathways, i.e. in the cone receptors. Alternatively, the increase in CFF could be due to eccentricity-dependant changes in centre-surround interactions. Such interactions are known to contribute to the high temporal frequency sensitivity of MC and PC cells (Benardete & Kaplan, 1997; Derrington & Lennie, 1984). To establish whether centre-surround interactions contribute to the resonance peak and increased CFF in peripheral MC cells, responses to small spots (1.18° diameter) were compared with those to the full-field stimulus. Fig. 3 shows data from a subset of foveal and far peripheral (35°–47°) MC cells which were tested with both large field and small spot stimuli. Average diameters (peak sensitivity $\times 1/e$) of MC cells above 35° eccentricity is 0.99° (SD 0.30, $n = 9$) for the centre mechanism and 1.80 (SD 0.48, $n = 9$) for the surround. Thus, the small (“spot”) stimulus is substantially restricted to the receptive field

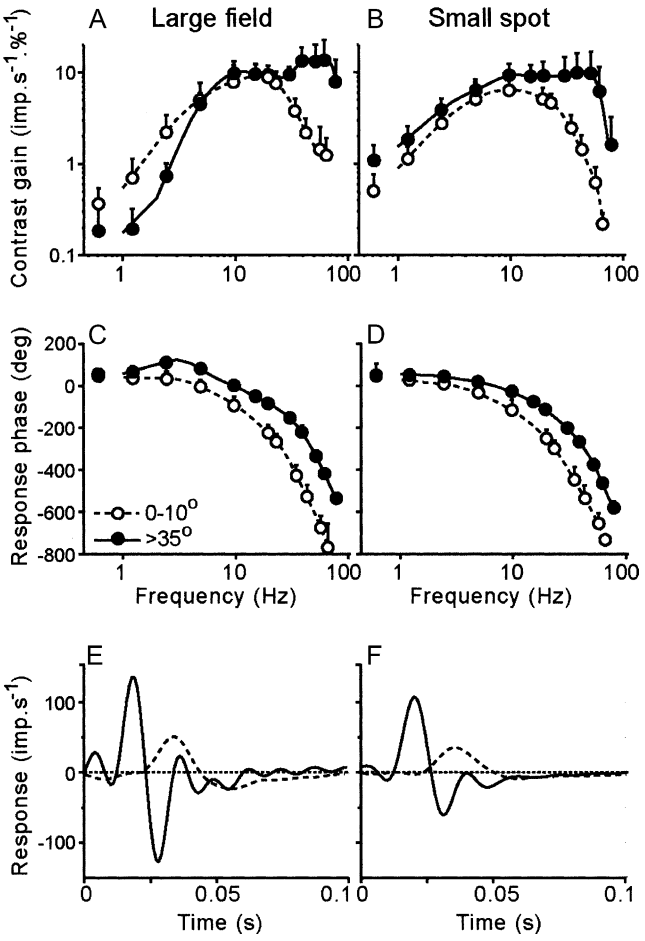

Fig. 3. IR functions of MC pathway cells for large (A,C,E) and small (B,D,F) fields. (A,B) modulation transfer functions (TMTFs). (C,D) response phase. (E,F) IR function for a 1 ms flash, Weber contrast of 1.0, calculated by inverse Fourier transformation of the TMTFs in A–D. Note shorter IR latency and resonance of peripheral MC cell response. Each data point in A–D is the mean of four cells (0°–10°) or six cells (>35°). Error bars are two standard errors of the mean. Continuous lines in A–D are the cubic splines (MATLAB v5.2, MathsWorks, Natick, MA), from which IRs shown in E–F were calculated.

centre. The contrast gain of these cells at 0.61 Hz (Fig. 3B) is a factor of five greater than the contrast gain for modulation of the whole field (Fig. 3A), suggesting that the influence of the surround mechanism has been largely removed. Nevertheless, the resonance peak in the far peripheral cells is still present with the spot stimulus and CFF decreases only slightly (by an average factor of 1.4). We conclude that the increase in CFF in peripheral retina cannot be attributed solely to centre-surround dynamics.

Responses of foveal MC cells become more transient at higher stimulus contrast. This is considered to be the result of contrast gain control; a mechanism which also produces an advance in response phase with increasing contrast (Benardete, Kaplan, & Knight, 1992; Lee, Pokorny, Smith, & Kremers, 1994). We observed that even at low contrasts, the responses of peripheral MC cells were more transient than those of their foveal counterparts. We therefore asked whether responses of peripheral MC cells to low-contrast stimuli show phase advance when compared to responses of foveal MC cells. Fig. 3C and D shows this comparison at a criterion response of 10 imp s^{-1}. At this response amplitude, phase advance due to contrast gain control is not apparent in foveal MC cells. A phase advance at higher temporal frequencies is evident for peripheral MC cells compared to central cells (Fig. 3C and D, for large field and small spot respectively). Phase advance at high temporal frequencies was also seen for PC cells of peripheral retina, when compared to the responses of foveal PC cells (data not shown).

The gain and phase data were used to derive the impulse-response (IR) function for these stimulus conditions (Lee et al., 1994); these are shown in Fig. 3E and F. The IR for each eccentricity group is biphasic. For peripheral MC cells, the peak of the IR is higher and occurs at a shorter latency than that for central MC cells. These data predict that responses to pulse or step stimuli in peripheral MC cells should be more transient than responses of foveal MC cells. Preliminary measurements of responses of MC cells to brief flashes confirmed this prediction (data not shown) but quantitative comparison is made difficult by contrast-related changes in pulse response latency and gain (Benardete & Kaplan, 1999a; Lee et al., 1994).

4. Discussion

Responses of foveal MC cells can account for psychophysical aspects of flicker detection, including the TMTF (Lee et al., 1990), spectral sensitivity in heterochromatic flicker photometry (Lee, Martin, & Valberg, 1988) and phase-dependent sensitivity to heterochromatic modulation (Lindsey, Pokorny, & Smith, 1986; Smith, Lee, Pokorny, Martin, & Valberg, 1992). Further data are in support of the hypothesis that the MC pathway determines CFF. The responses of MC cells (but not PC cells) conform to the Ferry–Porter law, and the dependence of psychophysical CFF on chromaticity can be accounted for by MC cell, but not PC cell, behaviour (Pokorny, Smith, Lee, & Yeh, 2001). There is also evidence that high-frequency PC cell responses are not perceptually utilized (Lee et al., 1990).

Here we show that both MC and PC pathway cells show eccentricity-dependent increases in CFF. The sensitivity of PC cells to high-frequency modulation comes close to that of MC cells in far peripheral retina. Nevertheless, the contrast gain and response amplitude of MC cells at any eccentricity exceeds that of PC cells (Fig. 1).

The TMTF of peripheral MC cells has a complex shape, with a resonance peak centred around 50 Hz.

Central MC cells show evidence of contrast gain controls (Benardete et al., 1992). We also found this to be the case in our peripheral recordings (Figs. 1 and 3). We suggest that the resonance peak seen in peripheral retina is the same as the high-contrast 'knee' in the response plot of central cells. Such a resonance or knee is difficult to capture using first-order filters. The data suggest that the change in TMTF shapes of MC cells in peripheral retina cannot be accounted for by centre-surround interactions, because these changes persist even when small spots are used (Fig. 3).

It is unlikely that rods contribute to the responses observed, since their responses are saturated at the high retinal illuminance used. There is increased convergence of cone photoreceptors to bipolar cells, and bipolar cells to ganglion cells, in peripheral primate retina. However, it is unclear why this should affect temporal response. Eccentricity-dependant changes in cone convergence are quite different for MC and PC cells (Goodchild, Ghosh, & Martin, 1996), yet MC and PC cells show a similar increase in CFF. Our observations are thus consistent with an enhanced high frequency response in outer retina before the PC and MC pathways diverge. A possible basis for the increase in high frequency sensitivity is in the cones themselves, as proposed by Tyler (1985).

Below 30 Hz modulation frequency, the TMTFs of ganglion cells are similar in central and peripheral retina, in conformity with human psychophysical data (Tyler, 1985). However, at higher frequencies TMTFs of macaque ganglion cells differ from human psychophysical TMTFs in two respects. Firstly, the TMTFs of PC and MC cells in both central and peripheral retina show higher CFFs than in human psychophysics. Part of this difference may reflect a species difference; psychophysical measurements of TMTFs in macaques viewing foveal targets have yielded a slightly higher CFF than human observers (Harwerth & Smith, 1985). Further, the resonance peak in peripheral MC cells is not obvious in human psychophysical measurements (Tyler, 1985). Lee et al. (1990) proposed that a cortical low-pass filter with a corner frequency of $\sim$20 Hz operates on the MC pathway. Application of such a filter to the measurements of Fig. 1A (data not shown) eliminates the resonance peak of MC cells and reduces their CFF to close to 40 Hz in foveal retina and 65 Hz at 30°–47° eccentricity, consistent with the psychophysical measurements of Tyler (1985).

The dependence of CFF on stimulus size (the Granit–Harper law) extends to diameters larger than a ganglion cell receptive field, implicating spatial summation at a cortical site. Nevertheless, the properties of retinal ganglion cells must constrain the input to central mechanisms of flicker perception. The eccentricity-dependant changes in behaviour of individual ganglion cells, together with eccentricity-dependant changes in receptor properties may be prove to be more important than the spatial density of neuronal populations (Rovamo & Raninen, 1988) as limiting factors for flicker sensitivity.

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