



Interocular differences in visual latency induced by reduced-aperture monovision

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Abstract

Purpose: To explore the interocular differences in the temporal responses of the eyes induced by the monocular use of small-aperture optics designed to aid presbyopes by increasing their depth-of-focus.

Methods: Monocular and binocular pattern-reversal visual evoked potentials (VEPs) were measured at a mean photopic field luminance of 30 cd/m² in seven normal subjects with either natural pupils or when the non-dominant eye wore a small-aperture contact lens (aperture diameter 1.5, 2.5 or 3.5 mm, or an annular opaque stop of inner and outer diameters 1.5 and 4.0 mm respectively). Responses were also measured with varying stimulus luminance (5, 13.9, 27.2 and 45 cd/m²) and a fixed 3.0 mm artificial pupil.

Results: Mean natural pupil diameters were 4.7 and 4.4 mm under monocular and binocular conditions respectively. The small-aperture contact lenses reduced the amplitude of the P100 component of the VEP and increased its latency. Interocular differences in latency rose to about 20–25 ms when the pupil diameter of the non-dominant eye was reduced to 1.5 mm. The measurements with fixed pupil and varying luminance suggested that the observed effects were explicable in terms of the changes in retinal illuminance produced by the restrictions in pupil area.

Conclusions: The anisocoria induced by small-aperture approaches to aid presbyopes produces marked interocular differences in visual latency. The literature of the Pulfrich effect suggests that such differences can lead to distortions in the perception of relative movement and, in some cases, to possible hazard.

Introduction

It has long been known that ocular depth-of focus increases as pupil diameter decreases (e.g. Atchison & Smith).¹ This led to the suggestion that the intermediate and near vision of emmetropic presbyopes could be improved by artificially reducing the pupil diameter in one eye. Originally this was considered for contact-lens corrections but the idea never found favour, largely because of the associated reduction in retinal illuminance in the lens-wearing eye and the restriction of visual field.^{2,3} More recently, however, the concept has been applied to corneal inlays.^{4,5} The Kamra (originally

Acufocus) inlay (www.acufocus.com) consists of a thin, quasi-opaque disc with an outer diameter of 3.8 mm and a central clear aperture 1.6 mm in diameter.^{4,6} The inner diameter represents a compromise between improved depth-of-focus, light loss and optical quality, since diffraction with smaller diameters degrades retinal image quality and acuity.⁷ The outer diameter was presumably selected on the basis of minimising any obstruction of nutrients and waste products through the cornea, allied to the desire to increase retinal illuminance under dim lighting conditions when the natural pupil dilates. The inlay is usually implanted monocularly in the non-dominant eye. Clinical

reports suggest good levels of patient satisfaction and useful improvements in intermediate vision, near vision and reading performance, the effects being stable for up to 4 years.^{8–12} A laboratory study confirms that binocular acuity at near is similar to that achieved monocularly by the eye with the inlay.¹³ It is claimed that inlays have the advantage of being minimally invasive and easily reversible.

Assessment of visual performance purely in terms of acuity or reading ability may, however, give a limited indication of the advantages and disadvantages of any method of presbyopic correction. Here we consider one aspect of this type of corneal inlay, the reduction that it produces in the light reaching the retina. It is well known that marked differences in retinal illuminance between the two eyes can induce the Pulfrich effect, the distortion of the path of moving objects. This effect (the provoked Pulfrich effect) is best known for the way it distorts the apparent path of a simple pendulum swinging in a fronto-parallel plane so that the pendulum bob appears to follow an elliptical path in depth rather than moving in a plane. This distortion occurs largely as a result of the interocular difference in visual latency arising as a result of the difference in retinal illuminance between the two eyes.^{14–16} Clinically, illuminance differences and the Pulfrich effect can arise as a result of unilateral cataract.^{17,18} Unilateral wear of such light-absorbing devices as the X-Chrom lens, or unilateral mydriasis.^{14,19} The Pulfrich effect (the spontaneous Pulfrich effect) is also found in patients suffering increased latency in one eye due to pathology or trauma^{19–24} or reduced-aperture monovision.¹⁶ In practical terms these motion-related spatial distortions mean that patients may experience difficulties in moving about their environment at home, at work or when driving.^{17,20}

If we assume that the natural pupils of both eyes have equal diameter but that the pupil of one eye is partially obstructed by the concentric inlay, the ratio of their retinal illuminances is nominally the ratio of the effective pupil areas. *Figure 1* shows the retinal illuminance in the eye with the artificially-restricted Kamra-type pupil divided by that of the normal eye, as a function of the natural pupil diameter: it is assumed that the natural pupils of the two eyes are equal in diameter. If required, allowance can be made for the reduction in effective pupil area due to Stiles-Crawford effect under photopic conditions (see, e.g. Atchison and Smith, pp. 124–126¹), but this has only minor impact for the normal range of natural photopic pupil diameters (*Figure 1*). The effective illuminance in the eye with the inlay can fall to a minimum of about 20% of that of the eye with the unobstructed natural pupil, equivalent to putting a 0.7 neutral density filter in front of the eye. This is well above the density required to provoke the Pulfrich effect in normal observers.¹⁴ We would, then, predict that interocular differences in visual latency and the Pulfrich effect might

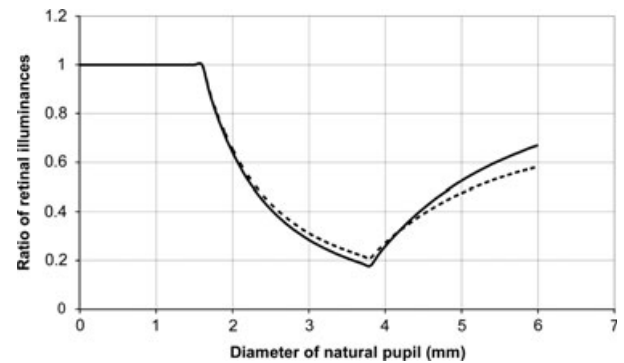


Figure 1. Theoretical factor by which the retinal illuminance in an eye with an ideally-centered Kamra implant differs from that in the normal eye, as a function of the pupil diameter in the normal eye. The full line is based on the actual clear areas of the pupils and the dashed curve is corrected for the photopic Stiles-Crawford effect.

occur under some lighting conditions in patients with this type of corneal implant.

The above reasoning depends upon the assumption that a reduction in pupil area acts in the same way as a neutral filter in producing interocular differences in visual latency. To demonstrate that this is the case, we first explored the effects of pupil anisocoria on the latency and amplitude of pattern-reversal Visual Evoked Potentials (VEP) under monocular and binocular conditions. The monocular experiments were then repeated under conditions where the pupil diameter was kept constant but retinal illuminance was varied by changing the test luminance, rather than by using different pupil diameters with constant test luminance.

Methods

Participants

Seven volunteers (five females, two males) with an average age of 29 ± 5 years (range: 25–40 years) participated in the study. Exclusion criteria included: spectacle-corrected visual acuity worse than 0.00 logMAR in each eye (Snellen 6/6, 20/20), anisometropia >0.50 D, abnormal phorias and any history of refractive or other ocular surgery. Average spherical equivalent was -0.95 ± 0.95 D (range: plano to -2.25 D). Verbal consent was obtained from all participants after they had received an oral explanation of the nature of the study. The study was conducted in adherence to the tenets of the Declaration of Helsinki and followed a protocol approved by the University of Crete Research Board.

Pupils

The effects of reduced-aperture corneal inlays were simulated by using afocal, hand-painted opaque soft contact

lenses (74% water content), supplied by Cantor & Nissel Ltd (www.cantor-nissel.co.uk). Three of these had clear, circular, central apertures 1.5, 2.5 and 3.5 mm in diameter. The outer diameter of the opaque region was 8.0 mm. A fourth lens had a smaller annular opaque zone with outer and inner diameters of 4.0 and 1.5 mm respectively. The latter approximately simulated the geometry of the Kamra inlay. The lenses were inserted in the non-dominant eye to create the required anisocoria. Although the lenses were placed on the anterior surface of the cornea rather than within the cornea, this small difference in axial position would be expected to have only minor effects on the associated visual performance.

Procedure

VEPs recording

Recordings of visual evoked potentials (VEPs) took place in low photopic ambient lighting conditions (illuminance approximately 5 lux), in a sound-attenuated room. VEPs were elicited using reversing 10 arcmin checks (nominal dominant spatial frequency 3 c/deg) at a rate of 4 reversals per second (2 Hz) with square-wave temporal modulation. The stimulus was displayed on a Sony GDM F-520 CRT monitor by means of a VSG 2/5 stimulus generator card (www.crsLtd.com). At the 1.0 m testing distance, the stimulus subtended a circular field of 15 degrees with 100% contrast and a constant time- and space-averaged luminance of 30 cd/m². The circular test field was surrounded by a constant background of the same mean luminance. Fixation was achieved using a centrally-placed cross.

Visual evoked potentials were recorded using silver-silver chloride electrodes. An active electrode was positioned 10% of the distance between the inion and the nasion over the vertex and referenced to an electrode placed at Fz with a ground electrode placed on the forehead. The active and reference electrodes were applied to the head with electrode paste after the area had been thoroughly cleaned. Trigger synchronisation was achieved using a CED 1401 'micro' (www.ced.co.uk). The waveforms were amplified (gain = 10K) using the CED 1902 (www.ced.co.uk). Amplifier bandwidth was set at 0.5–30 Hz (together with a 50 Hz notch filter) and signals were sampled at a rate of 1024 Hz with an analysis time of 0.970 s. Data acquisition and averaging were controlled using the SIGNAL software (vs 3.1, CED, UK). Each VEP trace was the average of 64 epochs of 1 s duration each, as suggested by the International Society of Clinical Electrophysiology of Vision (ISCEV).²⁵ Computerized artifact rejection was performed before signal-averaging, according to standard ISCEV guidelines, in order to discard epochs in which deviations in eye position, blinks, or amplifier blocking occurred.

P100 peak amplitude and latency were derived from the average waveform. This required manual definition of the lowest negative peak (N75) prior to the P100 peak. Amplitude was scored as the voltage difference between these two points and latency as the time difference between the P100 peak and stimulus onset (*Figure 2*).

Effect of pupil diameter at constant test luminance

Visual evoked potentials measurements were performed binocularly and monocularly, with best sphero-cylindrical spectacle correction. During the binocular measurements, the pupil geometry of the non-dominant eye was manipulated, while the dominant eye retained its natural pupil. Eye dominance was determined by looking through a central hole in an A4 card, held by the participant in both hands away from the body. The monocular measurements were made on the lens-wearing, non-dominant eye with the dominant eye being covered with an eye patch, and on the dominant eye with the non-dominant eye being patched.

Visual evoked potentials were measured (a) with natural pupils, when the average pupil diameters (measured with head-mounted infrared cameras, EyeLink II, www.sr-research.com) were 4.7 ± 0.3 mm and 4.4 ± 0.4 mm under monocular and binocular viewing, respectively and (b) with the four artificial pupils inducing anisocoria.

Effect of test luminance at constant pupil diameter

To investigate whether any observed changes in VEP characteristics for the lens-wearing, non-dominant eye were the result of changes in retinal illuminance, rather than, for example, changes in retinal image quality associated with

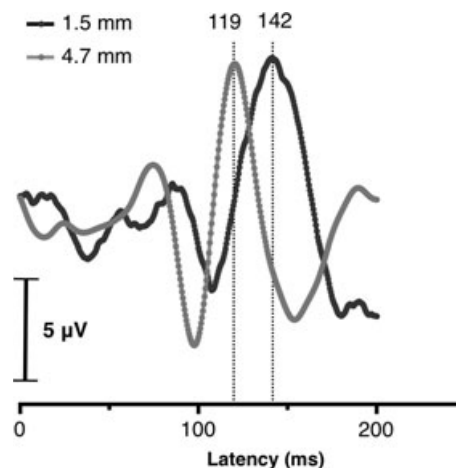


Figure 2. Grand-averaged (64 epochs) monocular VEP waveforms from one subject elicited using 2 Hz-reversing 10 arcmin checks of 100% contrast for a pupil diameter of 1.5 mm (black line) and 4.9 mm (grey line). The responses were recorded from electrode position Oz referenced at Fz. P100 latency is indicated in ms.

the varying effects of diffraction and aberration for the different pupil diameters, the monocular VEP measurements were repeated using a constant pupil diameter (3.0 mm) for both the dominant and the non-dominant eye but varying space- and time-averaged screen (stimulus) luminance (5, 13.9, 27.2 and 45 cd/m²). The successive values of this sequence bear the same ratios to one another as the areas of the circular apertures in the contact lens and the natural pupil diameter in the first experiment (i.e. 1.5², 2.5², 3.5², 4.5²).

Results

Effect of varying pupil diameter

Figure 3 shows the effect of pupil diameter on the P100 component of the Visual Evoked Potential (VEP).

Under monocular viewing with the non-dominant eye, P100 amplitude with the circular pupils increased with increasing pupil diameter (R^2 for a second-order fit equals 0.991). P100 latency also increased with pupil diameter: a linear fit to the data gave $R^2 = 0.996$. For the contact lens having the annular opaque zone (A in Figure 3), VEP amplitude and latency were approximately the same as those found with a 3 mm circular pupil. This appears reasonable, since assuming that the annular opaque zone was concentric with the natural pupil and that the latter had a diameter of about 4.7 mm, the area of unobstructed pupil was about the same as that of a circular aperture of 2.9 mm in diameter.

With binocular viewing, amplitudes increased and latencies reduced as compared with the monocular results ($p < 0.01$ for all apertures except for the amplitude with the 2.5 mm pupil, Students t -test). There was, however, still a tendency for amplitude to increase and latency to reduce as the pupil diameter and area were increased in the

non-dominant eye, although the trends were not as marked as in the monocular case.

The monocular VEP responses of the two eyes are compared in Figure 4. The left-hand plot shows the interocular P100 amplitude ratios, i.e. the amplitudes of the monocular VEPs of the non-dominant eye (without and with the four lens apertures) divided by the monocular VEP of the dominant eye with its natural pupil, as a function of the non-dominant pupil diameter. The mean interocular ratio (the ratio of dominant to non-dominant amplitude) in the P100 amplitude decreases from 0.93 (SD \pm 0.20) with the equal 4.7 mm natural pupils to 0.66 (SD \pm 0.23) when the pupil of the non-dominant eye is reduced to 1.5 mm.

Also shown in Figure 4 (right) are the differences between the monocular latencies of the non-dominant eye under the different pupil conditions and the dominant eye with its natural pupil. The latency difference increases from 5.4 ± 2.5 ms when both eyes have 4.7 mm pupils to 22.2 ± 6.1 ms with the 1.5 mm aperture lenses.

Both the interocular ratio in VEP amplitude and difference in VEP latency correlations with pupil aperture are best-fitted with a second order polynomial (R^2 equals 0.99 and 1.00, respectively).

Note that the interocular amplitude ratios and latency differences with the non-dominant eye wearing the 'annular' (A) lens are again comparable to those that would be expected for a circular pupil of similar area, having a diameter of about 2.9 mm.

Effect of varying the stimulus luminance on monocular VEPs at constant pupil diameter

The effect of varying the stimulus luminance (and hence the retinal illuminance) on the VEPs in the non-dominant eye with the fixed pupil was found to be very similar to that

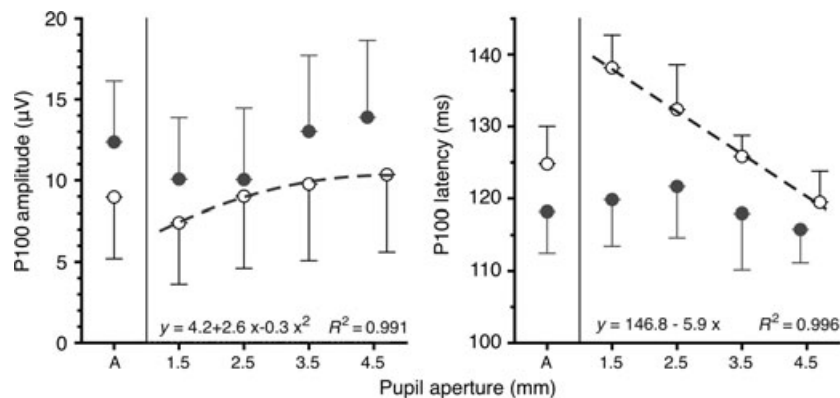


Figure 3. Mean amplitude (left) and mean latency (right) of the VEP P100 component from seven subjects as a function of the central aperture of the contact lens (used in the non-dominant eye) under binocular (filled circles) and monocular (open circles) stimulation. The data for the largest pupil aperture is for the unobstructed natural pupil condition. The bars indicate \pm 1 SD. The dashed lines form second order (left) and linear (right) regressions. The 'A' in x-axis represents the 'annular' lens (4.0 mm diameter opaque pupil with a central 1.5 mm aperture).

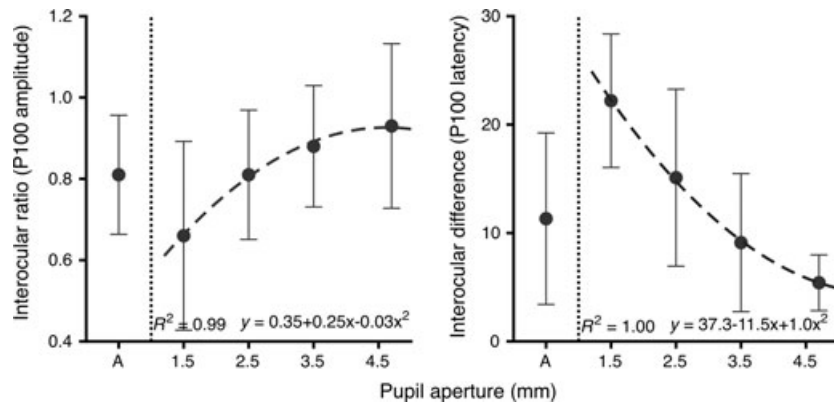


Figure 4. Mean interocular amplitude ratio (left) and mean interocular latency difference in milliseconds (right) in the VEP P100 component from seven participants as a function of the central aperture of the contact lens (used in the non-dominant eye) under monocular stimulation. The dominant eye had its full, unobstructed natural pupil (mean diameter about 4.7 mm). The bars indicate ± 1 SD. The dashed lines form second-order regressions. The 'A' in x-axis represents the 'annular' lens (4.0 mm diameter opaque pupil with a central 1.5 mm aperture).

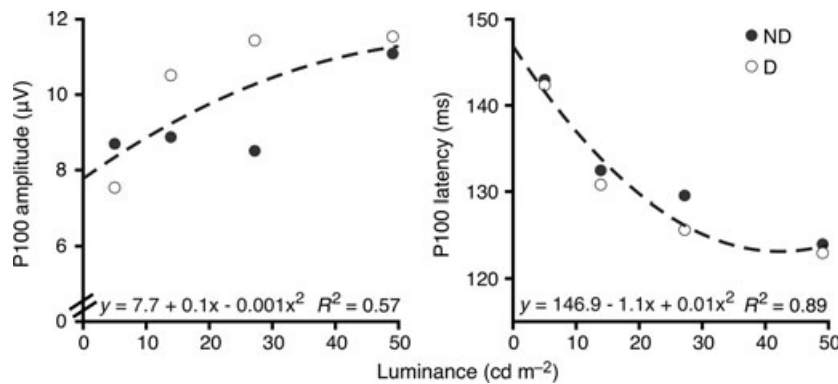


Figure 5. The effect of varying screen luminance on P100 amplitude and latency when the pupil diameter was kept fixed at 3.0 mm. Average data from three participants from both dominant (D) and non-dominant (ND) eyes are shown. The dashed lines form second-order regressions.

found when a constant stimulus luminance was used but retinal illuminance varied as a result of changes in the pupil size. *Figure 5* shows plots of the mean P100 amplitude and latency when relative retinal illuminance was varied by changes in the stimulus luminance. Amplitude increases and latency decreases as the stimulus luminance is increased.

Note that *Figure 5* is qualitative very similar to *Figure 3*. If we assume that in both cases the VEP characteristics depend only on retinal illuminance we can replot the VEP data for the two experiments and the same subset of 3 subjects in terms of retinal illuminance, where retinal illuminance in trolands is simply the product of pupil area (mm) and field luminance (cd/m²). The result is shown in *Figure 6*. The combined data agree quite well with the hypothesis that the VEP variation in both experiments is due to the changes in retinal illuminance, and is independent of whether such illuminance variation is produced by changes in pupil diameter or stimulus luminance. This

finding implies that the interocular differences in retinal image quality associated with anisocoria had little influence on the relevant VEPs.

Discussion

The present results confirm that artificial reduction in the pupil diameter of one eye and the consequent induced interocular differences in retinal illuminance cause interocular differences in visual latency as determined by VEP. The magnitudes of the VEP latency changes are similar to that found by earlier authors using neutral density filters to create the illuminance differences.¹⁹ Differences in visual latency are known to be capable of causing distortions in the perception of the position and path of moving objects, although the interocular differences in latency deduced from the Pulfrich effect are usually smaller than those determined from P100 peak latencies.¹⁷ Our subjects all experienced binocular distortions in the path of a Pulfrich

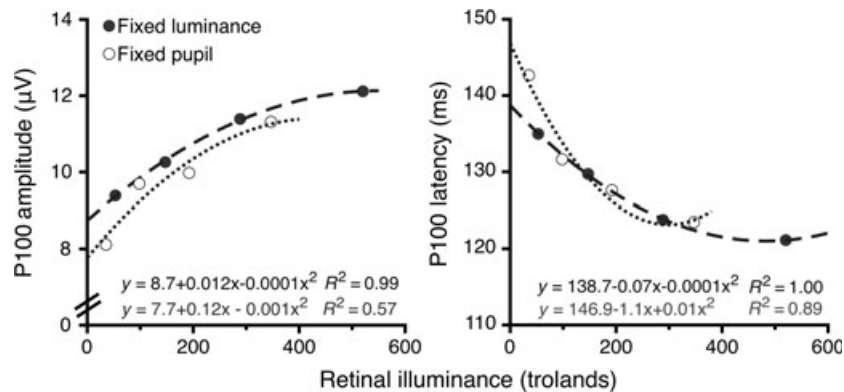


Figure 6. Changes in VEP amplitude and latency as a function of retinal illuminance for three subjects. Changes in retinal illuminance were produced combinations of either variable pupil diameter and fixed luminance (filled symbols) or variable luminance and fixed pupil diameter (open symbols). The dashed and dotted lines are second-order regressions to each data set.

pendulum during monocular wear of any of the small-aperture lenses.¹⁶ These distortions in perception may lead to hazard in some everyday tasks, such as driving or moving through a congested environment.^{19,20,24} Such effects may therefore constitute a significant disadvantage of devices like the Kamra inlay for presbyopes, even though the inlays may be helpful in improving vision in for static binocular acuity tasks.

Clearly the exact effects are likely to vary with such factors as the scene luminance,^{15,26} the pupil diameter¹⁶ and Stiles-Crawford function of the individual, and the centration of the inlay or contact lens. There is evidence that long-term neural adaptation effects can reduce interocular differences in latency.²⁷ This possibility deserves further exploration, although clinical experience with the spontaneous Pulfrich effect suggests that adaptation is unlikely to ameliorate such differences.²⁰ With one eye having a fixed artificial pupil, adaptation is likely to be difficult since, as the diameter of the natural pupil of the other eye changes with ambient lighting level and other factors, the relationship between the retinal illuminances of the two eyes will be continuously changing.

We suggest that presbyopic patients should be made aware of the possible visual problems in movement perception associated with the unilateral use of 'pinhole' type inlays or lenses and that active steps should be taken to ascertain their impact, if any.

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Disclosure

Ioannis G Pallikaris is the medical director of the Flexivue corneal inlay (Presbia). Sotiris Plainis, Dionysia Petratou, Trisevgeni Giannakopoulou, Hema Radhakrishnan and W Neil Charman have no proprietary or commercial interest in any material discussed. The authors did not receive any financial support from any public or private sources.

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