

Characteristics of pupil responses during far-to-near and near-to-far accommodation

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Abstract

The static and dynamic aspects of the pupil response associated with various amplitudes of far-to-near (accommodation) and near-to-far (disaccommodation) focusing responses were evaluated in this study. Dynamic refractive and pupillary changes were measured simultaneously during focusing responses to targets at real distances in 12 young (23–26 years) emmetropic subjects. The targets were presented alternately at far (6 m) and at one of six near positions from 1 D (1 m) to 6 D (16.7 cm) in 1 D steps. The latency, magnitude and peak velocity of pupil changes associated with accommodation and disaccommodation responses were calculated. The latency of refractive changes was shorter than that of pupillary changes. In general, the pupil constricted with accommodation and started dilating while accommodation was still maintained, resulting in reduced pupil dilation with disaccommodation. The magnitude of the pupil response increased linearly with that of accommodation and disaccommodation. The amount of pupil change per dioptre of refractive change was invariant with various amplitudes of refractive change. The peak velocity of pupil constriction was greater than that of pupil dilation for corresponding amplitudes. The pupil response is more closely associated with accommodation than with disaccommodation.

Keywords: accommodation, main sequence, near triad, presbyopia, pupillary reflex

Introduction

The act of focusing the eye to different distances is usually associated with a concurrent change in pupil diameter. The pupil diameter decreases when focusing from far to near (accommodation) and increases when focusing from near-to-far (disaccommodation). It has been shown previously that the pupil response is negligible for small amplitudes of accommodation (≤ 1 D) and increases linearly with higher amplitudes of accommodation (Marg and Morgan, 1949, 1950). The pupil responses during disaccommodation have not been systematically studied in the past. The dynamics of accommodative and disaccommodative responses have been described as a function of amplitude (Ciuffreda and Kruger, 1988; Vilupuru and Glasser, 2002;

Kasthurirangan *et al.*, 2003; Bharadwaj and Schor, 2005). Differences between the amplitude dependent dynamic properties of accommodative and disaccommodative refractive changes have been shown in the past (Yamada and Ukai, 1997; Vilupuru and Glasser, 2002; Kasthurirangan *et al.*, 2003). The differences between accommodation and disaccommodation, at least in terms of dynamics, suggest that properties of pupil responses associated with accommodation and disaccommodation should be examined individually.

Age-related decreases in pupil diameter in the dark and an increase in the extent of the near pupil reflex have been reported (Kadlecova *et al.*, 1958; Schaeffel *et al.*, 1993). The increase in the near pupil response with age might suggest an increased effort to accommodate because of reduced accommodative ability with increasing age. Age-related changes in the dynamics of the pupil response have not been quantified in the past. It is important to quantify the magnitude and dynamics of the pupil change associated with various amplitudes of accommodation and disaccommodation in a normal young adult population prior to studying age related changes in the near pupil response. This study is mainly directed at this goal.

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The dynamics of the pupil response have received relatively little attention. It has been suggested that the latency of the accommodative response is shorter than the latency of the associated pupil response (Wilson, 1973; Takagi *et al.*, 1993; Hunter *et al.*, 2000) and that disaccommodation occurs later than the associated pupil response (Hunter *et al.*, 2000). Wilson has shown that, in the near triad, convergence latency is shorter than the accommodative latency which in turn is shorter than the pupil constriction latency (Wilson, 1973). The longer latency of accommodative and pupillary responses compared with convergence eye movements suggests that the accommodative and pupillary dynamics are constrained by the biomechanics of the intraocular tissues (Wilson, 1973). The dynamics of the pupil responses have been shown to be dominated by the biomechanics of the iris plant (Semmlow and Stark, 1973; Semmlow *et al.*, 1975; Usui and Stark, 1978) and the dynamics of the accommodative responses have been shown to be influenced by the biomechanics of the lens/ciliary muscle plant (Fisher, 1969a,b, 1971, 1977). It is of interest to understand the similarities and differences in the dynamics, such as latency and speed of responses, of two plant dominated systems, namely accommodation and the pupil response.

The velocity of the near pupil response for different amplitudes of pupil response is not known. Semmlow and Stark (1973) have shown that the maximum velocity of near pupillary constriction is three times greater than dilation. They suggest that this difference in dynamics suggests a nonlinearity and precludes application of simple linear systems analysis (Semmlow and Stark, 1973). However, it is not clear if they compared similar amplitude pupillary constrictions and dilations or if there is any relationship between amplitude and the speed of pupil responses. It is of interest to compare the velocity of constricting and dilating pupil responses as a function of amplitude to address questions raised in the Semmlow and Stark (1973) study. Understanding the dynamics of the pupil response has implications for a better understanding of the neural control of the pupil as well as the biomechanical constraints on the accommodative and pupillary mechanisms.

Marg and Morgan (1950) studied the near pupil response under a variety of conditions and concluded that the near pupil response is essentially elicited by accommodation and not by vergence eye movements. However, the influence of other factors such as fusional vergence (Knoll, 1949; Backer and Ogle, 1964), target alignment (Stakenburg, 1991; Phillips *et al.*, 1992), proximal factors (Phillips *et al.*, 1992), retinal illuminance (Roth, 1969) and starting pupil diameter (Semmlow *et al.*, 1975) on the pupil responses cannot be ignored.

In this study we stimulated focusing responses with targets in real space and measured the corresponding changes in refraction and pupil diameter dynamically in a

group of young subjects. We report the latency, magnitude, per dioptre change and dynamics of the pupil response associated with accommodative and disaccommodative responses. The present study is an attempt to describe the characteristics of the pupil responses when presenting targets at far and near. The viewing conditions in the present study were designed to provide a compelling stimulus for accommodation and elicit robust accommodative and pupillary responses. No attempt has been made to discern the factors causing the near pupil response, although, for the sake of convenience, the pupil response during far-to-near focusing is referred to as accommodative pupil response and the pupil response during near-to-far focusing is referred to as disaccommodative pupil response in the manuscript.

Methods

Subjects

This study was performed on 12 young emmetropic (+0.50 to -0.50 D) subjects, aged 23–26. Four subjects had light irides (grade A or B) and eight subjects had dark irides (grade D) (Seddon *et al.*, 1990). All subjects had at least 20/20 Snellen visual acuity at distance. The subjects underwent a short optometric examination to ensure refractive error within ± 0.50 D, and normal phoria, near point of convergence, and push-up accommodative amplitude measured subjectively and objectively with a Hartinger coincidence refractometer (Zeiss, Jena, Germany). The accommodative amplitude measurements were performed after the experiment in order not to induce any accommodative fatigue or in any way influence the experiment. The research followed the tenets of the Declaration of Helsinki. All subjects signed an informed consent document prior to participation in the experiment. The research was performed according to institutionally approved human subject protocols.

Stimuli

Subjects were required to look at black on white, printed, star-like targets presented at far and near real distances. The far target was placed at 6 m and the near target was placed at one of six near distances from 1 m to 16.7 cm to create stimulus demands from 1 to 6 D in 1 D steps. The star-like target consisted of eight triangular spokes and concentric rings (*Figure 1*). The far target at 6 m subtended 0.86 degrees at the eye and the near target at 1 m subtended 1.66 degrees. A two-dimensional Fast Fourier Transform (Matlab, The Mathworks, Natick, MA, USA) indicated that the target was spatially broadband consisting of multiple spatial frequencies from 1 to 30 cpd, with predominantly < 9 cpd, at 6 m. The angular size of the target

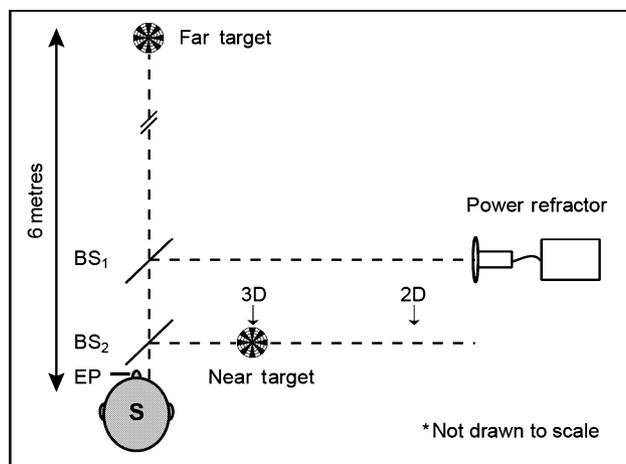


Figure 1. The right eye of the subject (S) was aligned with the far target at 6 m. The near target was placed on a track to present a fixed amplitude accommodative stimulus from 1 D (1 m) to 6 D (16.7 cm). The far target, near target and the PowerRefractor camera were aligned with the subject's right eye with two beam splitters (BS₁ and BS₂). The subject monocularly viewed the far and near targets with the right eye while the left eye was covered with an eye patch (EP). The PowerRefractor measured refraction and pupil diameter simultaneously in the right eye, continuously at 25 Hz.

increased and the spatial frequency content decreased approximately 1.5 times with each near target position or every dioptre increase in accommodative demand.

For each stimulus amplitude, the targets were alternately illuminated by ultra-bright white LEDs under the control of a computer for randomly variable durations from 1.5 to 6 s in 500 ms steps. At any moment in time only one target, either at far or at one near distance, was visible. The switch in illumination between the far and near targets was instantaneous. The targets were matched in luminance and had a luminance of 10 cd m⁻² on the white background. The left eye of the subject was covered with an eye patch and the subject's head was stabilized with a headrest and a chin rest. The far and near targets were aligned with the right eye with the help of a beam splitter (*Figure 1*). For each near target distance, subjects were asked to align the far and near targets by rotating the beam splitter about its vertical axis. During this alignment procedure, the far target was illuminated constantly and the near target was flashed briefly for 100 ms at 1 s intervals. During the experiment, the subjects were instructed to focus on the illuminated target and keep it clear as long as it remained illuminated. The room light was switched off so that the only objects visible were the targets used in the experiment and a dim red glow from the measuring instrument (PowerRefractor). It was also necessary to turn the room lights off to ensure a large baseline pupil diameter in order to obtain reliable data from the PowerRefractor during accommodation. The baseline pupil diameter represents a mesopic pupil diameter and was not the same diameter across the

subjects. For each stimulus demand about 10–15 dynamic responses of refraction and pupil diameter were recorded. The near stimulus was moved to the next near distance, and the process repeated.

Measurement of refraction and pupil diameter

Refraction and pupil diameter were measured with a PowerRefractor (MultiChannel Systems, Reutlingen, Germany). This is a dynamic video-based optometer that can measure refraction, pupil diameter and vergence simultaneously at 25 Hz (Schaeffel *et al.*, 1993; Schaeffel, 2002; Wolffsohn *et al.*, 2002; Allen *et al.*, 2003; Kasthurirangan *et al.*, 2003). Prior to the experiment, the PowerRefractor refraction measurement was calibrated for the spectacle plane on each subject as described previously (Schaeffel *et al.*, 1993; Kasthurirangan *et al.*, 2003). In short, PowerRefractor measurements were made through ophthalmic trial lenses of different powers held in front of the right eye while the eye was covered with a visible block infrared pass filter (Kodak Wratten filter no. 89b, high pass at 700 nm). The uncovered left eye looked at a far target at 6 m. The PowerRefractor measurements were plotted against the induced refractive error to obtain an individual calibration function for each subject.

The accuracy of the PowerRefractor in measuring pupil diameter was tested by using model pupils (white paper behind an aperture on a black card). Model pupils of various diameters were made by drilling holes of specific diameters between 3 and 7 mm. The holes were measured with the PowerRefractor, a vernier calliper and a loupe. The PowerRefractor pupil measurement correlated linearly with the artificial pupil diameter measurements with the vernier calliper ($y = 1.09x + 0.09$) or the loupe ($y = 1.11x + 0.02$). Bland–Altman analysis (Bland and Altman, 1986) showed a mean difference of 0.52 ± 0.16 mm (mean \pm S.D.) and a maximum difference of 0.86 mm between PowerRefractor and vernier calliper measurements. The mean difference between the PowerRefractor and the loupe was 0.48 ± 0.16 mm (mean \pm S.D.) and the maximum difference was 0.76 mm. Although systematic differences between the PowerRefractor and the other two measurements exist, the change in diameter from one artificial pupil to another measured by the three methods was comparable (slopes of 1.09 and 1.11). The raw, uncorrected PowerRefractor measured pupil data are reported in this study.

Data analysis

The accommodation and pupil data were objectively analysed with custom computer software to determine the latency and termination of responses, amplitudes of refractive and pupillary responses and amount of pupil

response per dioptre change in refraction. These analyses were carried out independently for accommodation and disaccommodation. In addition, the peak velocity of pupil responses and time constants of pupil constriction were calculated analytically by fitting equations (see below).

Latency and termination of response. Both the accommodative and pupil responses show a typical pattern. Following stimulus onset, there is an initial delay in the response (latency), followed by a response period, which in turn is followed by a steady-state response for refraction (Figure 2). The start of the response was determined as described previously (Kasthurirangan *et al.*, 2003). In short, custom software developed for the PowerRefractor data searched for three consecutively increasing values, followed by five consecutive values in which no two consecutive decreases occurred. When these criteria were met, the first data point in the sequence was recorded as the start of the response (Kasthurirangan *et al.*, 2003). This algorithm was verified, by visual inspection, to reliably detect the start of a response. If a start of the response could not be identified in the first 1 s of the response following stimulus onset, then that particular response was discarded. The termination of a response (i.e. when the steady-state was achieved) was determined as the last increasing value in a set of 10 data points in which less than six increasing intervals were observed. The algorithm started from the data point corresponding to the start of a response and incremented by one data point until the termination condition was satisfied. If a termination of the response could not be identified before the start of the next event i.e. near/far stimulus, then the data from that particular response were discarded. Latency and termination of responses were determined individually for accommodation, disaccommodation, accommodative pupil response and disaccommodative pupil response.

Identifying pupil responses associated with accommodation and disaccommodation. In many cases, especially for low accommodative amplitude responses, pupil changes unrelated to refractive changes were observed. In the case of disaccommodation, in many cases, a clear pupil response could not be identified. To extract only those pupillary responses that were associated with a change in refraction, only pupillary responses recorded during the response period of refraction were considered (Figure 2b). This algorithm enabled reliable, objective identification of pupil responses associated with accommodative and disaccommodative responses.

Amplitude of refractive and pupillary change. Amplitudes for both pupil and refractive responses were

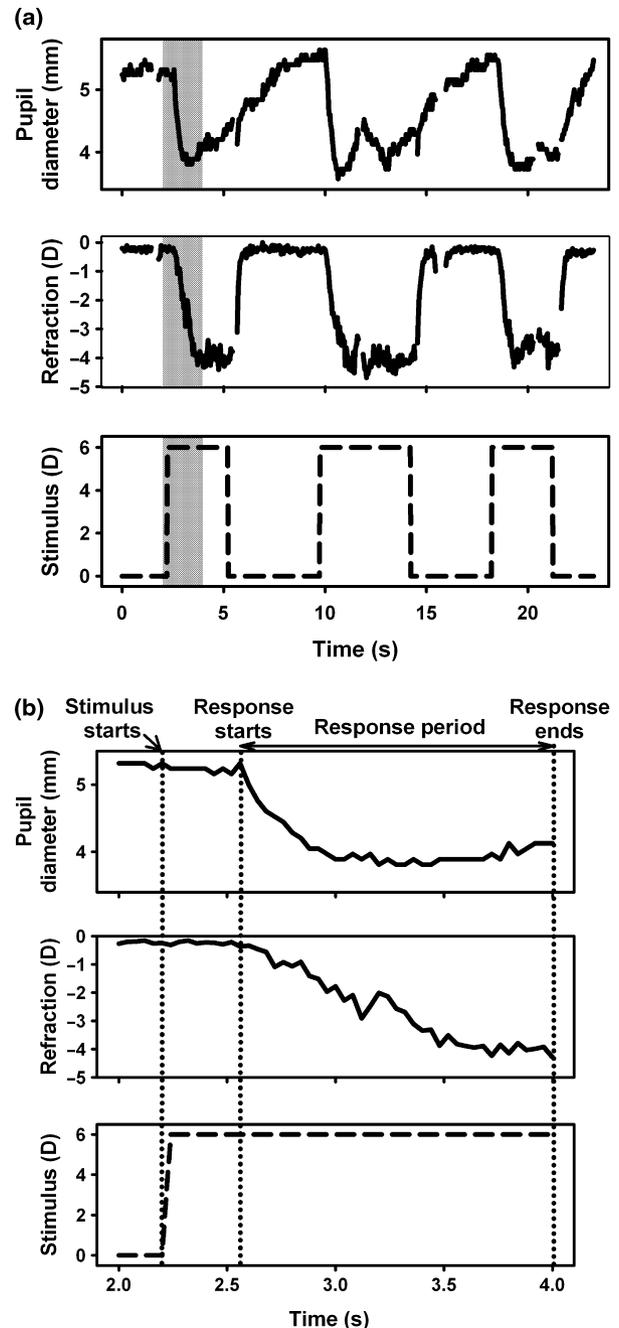


Figure 2. (a) Three successive pupillary (top) and refractive responses (middle) to a 6 D stimulus (bottom) in one subject are shown. The duration of the near stimulus presentation was randomly varied between 1.5 and 6 s in 500 ms steps. The accommodative responses to a 6 D stimulus are relatively consistent, but the associated pupil responses are variable and exhibit transient properties. The data from a single accommodative response (the grayed regions) are shown in (b). (b) The figure illustrates three events for the refractive response (vertical dashed lines); (1) the start of the stimulus, (2) the start of the response and (3) the termination of the response. The period between start and termination of the response when the response changes from one level to another is termed 'response period'. The start and termination of the responses were identified by custom computer algorithms (see Methods).

determined as the difference between the first and last data value in the response period (*Figure 2b*). The amplitude of a response was determined for refractive and pupillary responses associated with accommodation and disaccommodation individually.

Amount of pupil change per dioptre of refractive change (mm D^{-1}). The amount of change in pupil diameter per dioptre change in refraction was determined by plotting the pupil data against the refraction data recorded during the response period (*Figure 3*). A linear regression was fitted to this data and a significant linear regression ($p < 0.05$, based on r^2 value) indicated that there was a change in pupil diameter with refraction. The slopes of the significant linear regression lines provided the amount of pupil change per dioptre of refractive change (mm D^{-1}).

Comparison of accommodative and pupillary dynamics. It has been shown previously that time constants increase linearly with the amplitude of accommodation (Kasthurirangan *et al.*, 2003). To compare the dynamic properties of pupil constriction and accommodation, the pupil constriction responses were fitted with exponential functions as was done with accommodative responses in the previous study. Exponential functions were fitted to each individual pupil constriction response, after removing latency, using the Levenburg–Marquadt algorithm based on chi-squared reduction (Press *et al.*, 2002). In general, the exponential functions provided excellent fits to the data. Only those responses that had no residuals > 0.50 mm were considered for further analyses. The exponential fits provided time constant and amplitude, which were plotted against each other as was done in the previous study with accommodation.

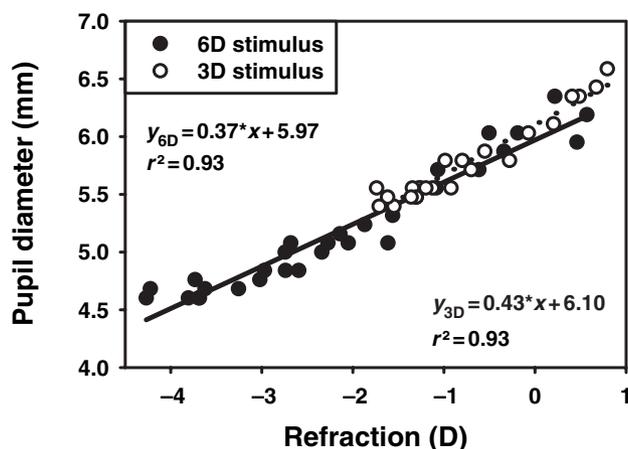


Figure 3. The pupillary and refractive data from the response period of accommodation (see *Figure 2*) are plotted against each other for a 6 D (filled circle) and a 3 D (open circle) stimulus demand. The slope of the linear regressions provides pupil changes per dioptre of refractive change.

Comparison of the dynamics of constricting and dilating responses. The PowerRefractor measurement frequency was 25 Hz and the individual pupil responses showed considerable fluctuations. To reduce noise and extract a dynamic metric, analytical equations, such as exponential functions, have been fitted to physiological responses in the past (Beers and Van Der Heijde, 1994; Vilupuru and Glasser, 2002; Kasthurirangan *et al.*, 2003). Pupil constriction responses were well fitted with exponential functions, however, it was found that most of the dilation responses could not be reliably fitted with an exponential function. Therefore, to allow a direct comparison, both constriction and dilation responses were fitted with fifth order polynomial functions (*Figure 4*). The polynomial functions were fitted to 2 s of the averaged data. The derivative of these polynomial functions provided velocities (*Figure 4b*). The maximum value of the derivative is the peak velocity of the response. Polynomial functions were fitted to the average of the constricting and the average of the dilating pupil responses for each stimulus demand, after removing the latency, for each subject individually.

Results

Subjectively it was observed that, in general, the pupil constricted with accommodation and started dilating while accommodation was still maintained (*Figure 2a*). This transient characteristic of the near pupil response resulted in a reduced amplitude of pupillary dilation during disaccommodation. In many cases, a clear pupil dilation could not be identified with disaccommodation.

Latency and termination of responses

The data included for this analysis are only those responses for which a clear latency and termination of refractive and pupillary changes could be identified. The percentage of data considered for the analysis was 57% (566 of 986 responses) for accommodation and 48% (474 of 986 responses) for disaccommodation. The individual percentage of data extracted ranged from 14 to 80% with a median of 64% for accommodation and 11 to 70% with a median of 50% for disaccommodation. On average, the start and end of a response could be clearly identified in 94% of the accommodative responses, 57% of the accommodative pupil response, 92% of the disaccommodative responses and 48% of the disaccommodative pupil responses. Clear refractive responses could not be identified for 1 D stimulus demands and the rest of the discarded data were because of blinks during the initial 1 s after target onset when no data was collected by the PowerRefractor. Clear pupillary responses could not be identified for low stimulus amplitudes (1 and 2 D). In general the pupil responses

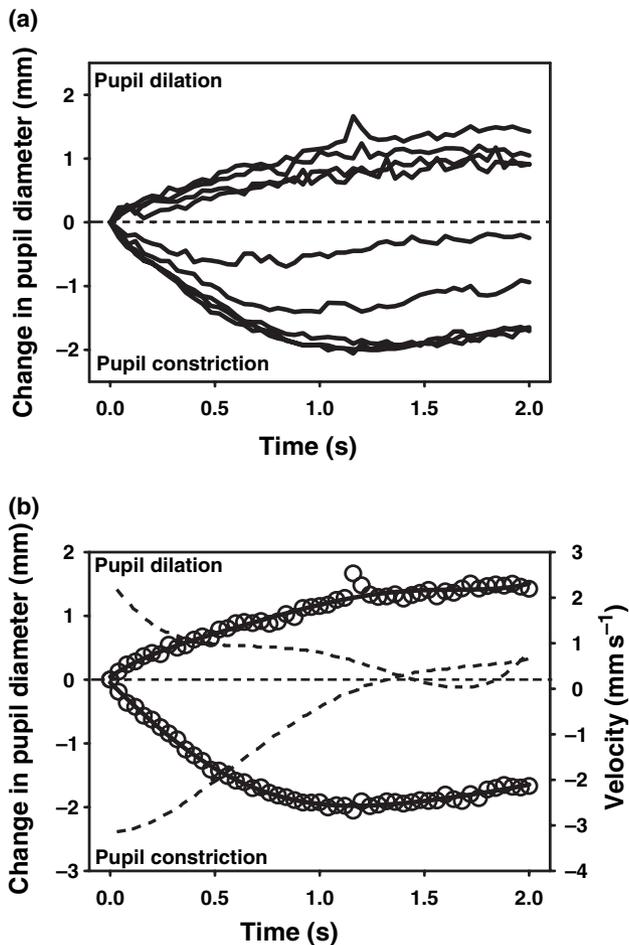


Figure 4. (a) Averaged pupil dilation (above dashed horizontal zero line) and constriction (below dashed horizontal zero line) responses to different stimulus demands are shown for one subject. The responses for a single stimulus demand were averaged after removing latency and are shown as change in pupil diameter from baseline level. (b) Two seconds of the averaged pupil responses (open circles) were fit with fifth order polynomial equations (solid black lines). The derivatives of the polynomial functions (dashed lines with y -axis at right) were calculated to obtain velocities. The maximum value of the derivative provides the peak velocity.

were variable from trial to trial with some trials eliciting no pupil response.

No systematic trend was seen between the latency and amplitude of accommodative and disaccommodative refractive and pupillary responses ($r^2 < 0.1$ for respective linear regressions). Therefore for each subject, average latencies of refractive and pupillary responses were calculated for all stimulus demands combined. A grand mean latency of refractive and pupillary responses was then calculated from each subject's mean latency. The average latency of the accommodative responses was 225.72 ± 42.88 ms (mean \pm S.D.) and that of pupillary responses was 310.72 ± 47.81 ms (mean \pm S.D.). Accommodative latency was significantly shorter than the pupillary latency (paired t -test, $t = 4.55$,

d.f.: 11, $p < 0.05$), with accommodation occurring on average 85 ± 45.76 ms (mean \pm S.D.) earlier than the pupil response. The average termination times for accommodation and pupil responses are not given as the termination times are influenced by the amplitude of the response. However, considering each individual response, the accommodation and pupil termination times were significantly different (paired t -test, $t = 3.89$, d.f. = 11, $p < 0.05$) with accommodation terminating 153.59 ± 96.71 ms (mean \pm S.D.) after termination of the pupil response. On average, the accommodative response started before the pupil response and terminated after the pupil response had terminated.

The average latency of disaccommodation was 231.32 ± 33.99 ms (mean \pm S.D.) and that of the associated pupil dilation was 491.02 ± 61.18 ms (mean \pm S.D.). The disaccommodative latency was significantly shorter than the pupillary latency (paired t -test, $t = 11.90$, d.f. = 11, $p < 0.05$), with disaccommodation starting 259.70 ± 75.58 ms (mean \pm S.D.) earlier than the pupil response. As with accommodation, the termination times may be influenced by the amplitude of disaccommodation and pupil amplitudes and so average termination times are not given. However, considering each individual response, the difference between disaccommodation and pupil termination times was not significantly different (paired t -test, $t = 1.17$, d.f. = 11, $p = 0.27$). On average, the disaccommodative response started before the pupil response and terminated with the associated pupil response.

Amplitude of pupil and refractive change

For this analysis only those accommodative and disaccommodative refractive responses for which a clear start and termination could be determined were included. The data here represents 94% (926 of 986 responses) of the responses obtained for accommodation and 92% (911 of 986 responses) of the responses obtained for disaccommodation. The individual percentage of data extracted ranged from 87 to 98% with a median of 95% for accommodation and from 85 to 100% with a median of 91% for disaccommodation.

The amplitude of the pupil response increased linearly with the amplitude of accommodation and disaccommodation in all 12 subjects. The cumulative data is shown in *Figure 5* along with linear regressions based on the mean slope and mean intercept calculated from the linear fits to individual subject data. The slope of the relationship provides the per dioptre change in pupil diameter with accommodation or disaccommodation. Pupil diameter changed 0.39 mm D^{-1} with accommodation (individual subject slopes ranged from 0.20 to 0.76 mm D^{-1}) and 0.17 mm D^{-1} with disaccommodation (individual subject slopes ranged from 0.11 to

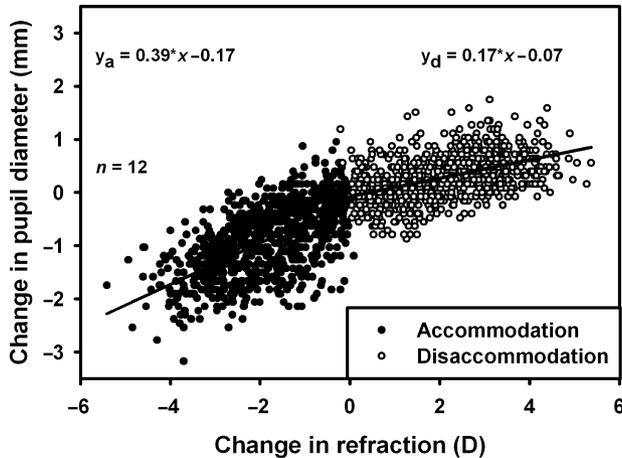


Figure 5. Change in pupil diameter is plotted against change in refraction for accommodation (solid circles) and disaccommodation (open circles) for all amplitudes from 12 subjects. Linear regression lines based on the mean slope and mean intercept from individual significant linear regression fits are shown ($n = 12$ for constriction and dilation responses). The magnitude of the change in pupil diameter was significantly different between accommodation and disaccommodation (paired t -test based on individual subject slopes; $p < 0.05$).

0.25 mm D^{-1}). The slope of the pupil diameter vs accommodation relationship was significantly greater than the slope of pupil diameter vs disaccommodation relationship (paired t -test for comparison of individual slopes, $t = 5.57$, d.f. = 11, $p < 0.05$). No differences in the magnitude of pupil response between subjects with light or dark irides were found for accommodation (ANOVA, $F_{1,10} = 0.08$, $p = 0.80$) or disaccommodation (ANOVA, $F_{1,10} = 0.38$, $p = 0.58$).

Amount of pupil change per dioptre refractive change

To determine if the amount of the pupil change with refraction, differs with the amplitude of the refractive change, the slope of the pupil vs refraction relationship for each individual response (see *Figure 3*) was plotted against the amplitude of the refractive change of each response (*Figure 6*). At low amplitudes, both the accommodation and disaccommodation data show considerable variability. This is because there can be relatively large changes in pupil diameter with small changes in refraction, so the slope of the pupil vs refraction relationship varies widely when refractive changes are small. For greater refractive changes, the amount of pupil change is constant. Straight line fits to accommodative and disaccommodative data yielded weak r^2 values of 0.05 and 0.08, respectively. The average amount of pupil change with accommodation was 0.58 mm D^{-1} and with disaccommodation was 0.08 mm D^{-1} . This difference between the amount of pupil change with accommodation and disaccommodation was statistically

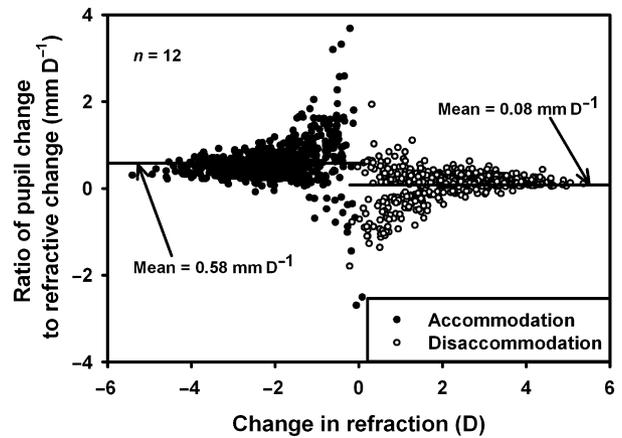


Figure 6. The amount of pupil change per dioptre of refractive change (the slope of pupil vs refraction plots – see *Figure 3*), for each response is plotted against amplitude of accommodation (solid circles) and disaccommodation (open circles). The amount of pupil change is highly variable at low amplitudes ($\leq 1 \text{ D}$) and relatively more consistent at higher amplitudes of accommodation and disaccommodation. The horizontal black lines indicate the mean amount of pupil change.

significant (paired t -test of individual means, $t = 7.40$, d.f. = 11, $p < 0.05$).

Time constants of pupil constriction

The time constant and amplitude of each constriction response, obtained by fitting exponential functions, were plotted against each other. Time constants increased linearly with amplitude of pupil constriction in 10 of 12 subjects. The cumulative data are shown in *Figure 7* along with a linear regression based on the mean slope and mean intercept from the 10 significant linear fits to the individual subject data. Disaccommodative pupil dilations were not well fit with exponential functions, so no time constant data for pupil dilations are available.

Peak velocity of pupil constriction and dilation

The peak velocity of pupil change, obtained by fitting polynomial functions to constricting and dilating responses (see *Figure 4*), were plotted against the amplitude of the pupil change (*Figure 8a*). It can be seen that most of the peak velocities for dilating responses (open circles) are below those of the constricting responses (solid circles) of similar amplitude. To directly compare the peak velocity of constricting and dilating responses, the amplitude data were divided into 0.1 mm bins, for example 1.0–1.09, 1.1–1.19 mm etc. Then, the mean peak velocity for each amplitude bin was calculated. The mean peak velocity of corresponding amplitude bins of constriction and dilation responses are plotted against each other in *Figure 8b*. All the data

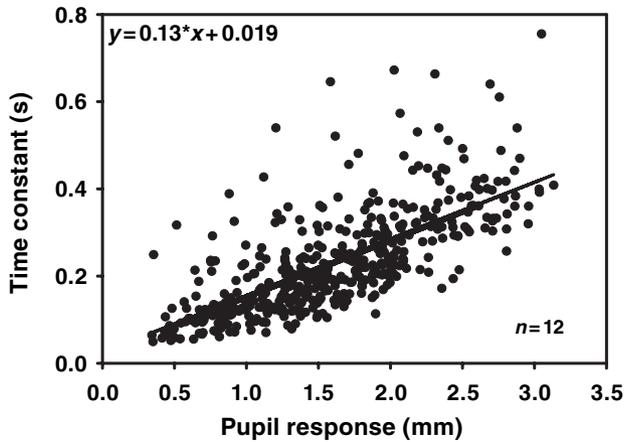


Figure 7. Time constants and amplitude of pupil constriction, obtained by fitting exponential functions are plotted against each other. The time constants increased linearly with the amplitude in 10 of the 12 subjects. A linear regression based on the mean slope and mean intercept calculated from only the 10 individual significant linear regression fits is shown. Disaccommodative pupil responses could not be reliably fit with exponential functions.

lie above the 1:1 line demonstrating that the peak velocities of constriction responses are greater than those of dilation responses.

Discussion

Proportion of good data and criteria for rejection

The pupillary responses were variable from trial to trial and were not as robust as the associated refractive responses in many instances. Therefore specific criteria were established to isolate clearly identifiable pupillary and refractive responses, independently for each analysis exploring a particular aspect of the pupil response. The comparison of the latency and termination of pupillary and refractive responses was performed only on those responses for which a clear onset and termination could be identified for both the refractive and associated pupil response. If the onset could not be identified either because of the lack of a response or because of an eye blink, the response was rejected. Most rejections resulted from the lack of a pupil response. At low stimulus amplitudes (1 and 2 D) pupil constriction was virtually absent with accommodation. The proportion of data included for this analysis was 57% for accommodation and 48% for disaccommodation. A greater proportion of the disaccommodative data was discarded because the pupil started to dilate while the eye was still accommodated resulting in little or no further dilation during the subsequent disaccommodation. The comparison of the amplitude of refractive and pupillary responses (Figure 5) included only those responses for which a clear onset and termination of

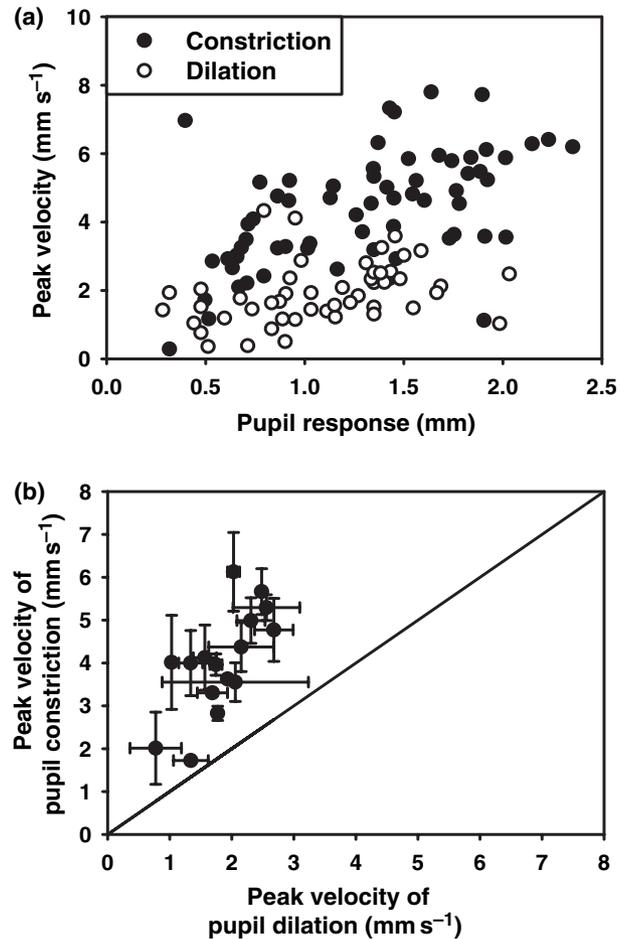


Figure 8. (a) The peak velocity of pupil constriction (solid circles) and pupil dilation (open circles) are plotted against the corresponding amplitude. Peak velocities of dilation responses are generally lower than the constriction responses for corresponding amplitudes. (b) To demonstrate the differences in the peak velocities of constriction and dilation responses, the data were grouped into 0.1 mm amplitude bins. The mean \pm 1 S.E. of the peak velocities from corresponding amplitude bins of constricting and dilating responses are shown. Note that the peak velocities of constriction responses lie above the 1:1 line (black line) indicating that the constriction responses are faster than the dilation responses.

the refractive responses could be identified. Rejection criteria for this analysis were based only on the refractive responses and not pupil responses. The proportion of data included for this analysis was 94% for accommodation and 92% for disaccommodation. The comparison of the amount of pupil response per dioptre of refractive response (Figure 6) included only those responses for which a clear onset and termination of the refractive responses could be identified and for which a significant linear relationship, based on r^2 statistic, between refractive and pupil responses was obtained. The proportion of data included for this analysis was 73% for accommodation and 56% for disaccommodation. The comparison of the time

constant and amplitude of pupil constriction (*Figure 7*) included only those pupil constriction responses for which a clear start could be identified and the exponential fit to 2 s of data resulted in no residuals >0.50 mm. The proportion of data included for this analysis was 46% of the pupil constriction responses. The analysis comparing peak velocity of constricting and dilating pupil responses (*Figure 8*) included only those pupil responses for which a clear start could be identified. The proportion of data included for this analysis was 81% for constriction and 53% for dilation responses. Although the criteria for good responses employed in the various analyses resulted in the rejection of a considerable number of responses in some cases, it ensured that only clearly identifiable refractive and pupillary responses were considered for further analysis.

Latency of refractive and pupillary changes

The latency of accommodation was shorter than that of the associated pupillary change. This agrees with findings from other studies, which have shown that accommodation precedes pupillary responses (Takagi *et al.*, 1993; Hunter *et al.*, 2000). It was also found that the latency of disaccommodation was shorter than the latency of the associated pupillary response. Hunter *et al.* (2000), found that disaccommodation latency was longer than pupillary latency. They report data from one subject for one stimulus amplitude only. Therefore no general trends are available from that study. The present study is the first study, to our knowledge, that has directly compared latencies of refractive and pupillary responses for multiple amplitudes in a group of subjects. In general, refractive changes precede pupillary changes.

Termination of refractive and pupillary changes

Accommodation and disaccommodation start before the pupil response and terminate together with (in the case of disaccommodation) or after (in the case of accommodation) the associated pupil response in this group of subjects aged 23–26 years. It will be of interest to determine if this relationship will hold in older subjects, as pupil responses increase while refractive changes decrease with ageing. The analysis used to estimate the amplitude of a response considered data from the start to the end of the refractive change. On average, this method included the full extent of the refractive and pupil change. This method was used in preference to considering individual pupillary and refractive responses, because there are instances when there are changes in pupil diameter that are unrelated to accommodative changes.

Correlation between refractive and pupil changes

It was found that the change in pupil diameter was well correlated with the refractive change for both accommodation and disaccommodation. Accommodation resulted in a greater change in pupil diameter than disaccommodation. The change in pupil diameter per dioptre for accommodation (0.39 mm D^{-1}) was greater than that for disaccommodation (0.17 mm D^{-1}) because of transient characteristics of the accommodative pupil response (*Figure 2*). A similar transient characteristic of the pupil response called ‘pupillary escape’ has been reported in the past for light-induced pupil responses (Sun *et al.*, 1983). Sun *et al.* have also shown that the pupillary escape phenomenon is influenced by the starting pupil diameter. The similarity between accommodative and light induced pupil responses and the influence of starting point on the pupillary escape may suggest that the cause of this transient pupillary response may be of a peripheral mechanical, rather than central neurological, origin.

The pupillary escape associated with accommodation may also possibly be due to two other factors. The far and near targets were matched in luminance so a pupil constriction causes a reduction in retinal illuminance. Therefore, pupil constriction associated with accommodation could be antagonized by the pupil dilation resulting from reduced retinal illuminance (Roth, 1969). This could result in pupil dilation immediately following accommodative pupil constriction. Secondly, the near pupil response could be initiated by the phasic component of the accommodative system, as has been suggested for accommodative–vergence interactions (Schor and Kotulak, 1986; Schor, 1992; Jiang, 1996). The phasic component of the accommodative response could have caused the pupillary response and then the tonic component of accommodation that follows may fail to maintain the pupillary constriction, causing the pupil diameter to return towards baseline. At this point it is not clear which of these three mechanisms, or a combination thereof, results in the transient pupil response with accommodation.

The amount of pupil change per dioptre of accommodation determined in this study was 0.39 mm D^{-1} . In a previous study Marg and Morgan (1949) determined the amount of pupil change per dioptre of accommodation to range from 0.12 to 0.53 mm D^{-1} , with a mean value of 0.30 mm D^{-1} . In a subsequent study they replicated this result (Marg and Morgan, 1950). For a similar age group, Schaeffel *et al.* (1993) found pupil response to range from approximately 0 to 0.50 mm D^{-1} . The range of pupil response obtained in the present study (0.20 – 0.76 mm D^{-1}) is comparable with the previous studies (Marg and Morgan, 1949, 1950; Schaeffel *et al.*, 1993). The differences in the

amount of pupil response between the subjects could not be attributed to iris colour, refractive error, or predictability of the temporal characteristics of the stimulus. The present study was designed to elicit robust accommodative and pupillary responses. Therefore, no attempt was made to eliminate proximal or perceptual cues to accommodation or pupil responses. The inter-individual variability may potentially arise from individual susceptibility to such proximal or perceptual cues (Stark and Atchison, 1994). No previous study has, to our knowledge, systematically determined the amount of pupil change during disaccommodation. The amount of pupil change with disaccommodation determined in the present study was 0.17 mm D^{-1} .

In the present study, at low amplitudes, highly variable pupil changes with refraction occurred (Figure 6). The variable results at low amplitudes are probably because of relatively large pupillary fluctuations during low amplitude refractive changes. Beyond the first 1 D of refractive change, the data become more consistent and show no systematic change in the ratio of pupil change to refractive change as a function of amplitude of refractive change. Marg and Morgan (1949) report a linear change in pupil diameter with accommodation after the first 1 D of accommodation similar to the present study (Figure 5).

Dynamics of constricting and dilating responses

The speed of accommodative pupil constriction and dilation are suggested either to be similar (Terdiman *et al.*, 1969) or constriction is suggested to be up to three times faster than dilation (Semmlow and Stark, 1973). The latter do not provide cumulative data, but base their results on representative phase plots (Semmlow and Stark, 1973). It is not clear if similar amplitude constriction and dilation pupil responses were compared, as their phase plots show slight differences in amplitudes. This factor is important considering that for a given near response, the amplitude of constriction is greater than the amplitude of dilation (Figure 5). In other words, if constriction and dilation responses for the same amplitude of target vergence are compared, different amplitudes of pupil response will be compared. To avoid this confound, the peak velocity of similar amplitude constriction and dilation responses were compared in this study (Figure 8). This analysis shows that constriction responses are faster than similar amplitude dilation responses, confirming the findings of Semmlow and Stark, 1973.

The difference in dynamics between constriction and dilation responses may suggest that the pupil constriction during accommodation is more actively driven than the pupil dilation during disaccommodation. Therefore, the differences in the magnitude of pupil response

associated with accommodation and disaccommodation could be due to neurophysiological factors. The fast dynamics and step response of the accommodative system are dominated by parasympathetic input (Ruskell, 1973; Gilmartin, 1986; Gilmartin *et al.*, 2002). In the case of the pupil, constriction is caused by parasympathetic input and dilation by sympathetic input (Loewy, 1979). Therefore, strong accommodative pupil responses might result from concurrent parasympathetic activity during accommodation and reduced pupil responses with disaccommodation may be the result of termination of the parasympathetic response and an absence of sympathetic activity during step disaccommodative responses (Gilmartin, 1986).

The static and dynamic aspects of pupil responses and the dynamics of accommodation have been shown to be influenced by the operating range (Semmlow *et al.*, 1975; Shirachi *et al.*, 1978; Usui and Stark, 1978). In the present study accommodation always started from a far position of 6 m and disaccommodation started from various near positions. The static and dynamic aspects of the pupil responses may indeed be influenced by the differences in starting point and operating range of accommodation and disaccommodation or that of the pupil response. No attempt was made in the present study to determine the influence of operating range on the pupillary dynamics. However, future studies exploring the influence of operating range will help better understand the differences between accommodative and disaccommodative pupil responses.

Comparison of accommodative and pupillary dynamics

The static and dynamic properties of pupil responses have been shown to be strongly influenced by the biomechanics of the iris plant (Loewenfeld and Newsome, 1971; Semmlow and Stark, 1973; Usui and Stark, 1978). In the case of accommodation it has been suggested that dynamics are determined by the biomechanics of the lens/ciliary muscle plant (Ejiri *et al.*, 1969; Fisher, 1969a,b, 1977; Beers and Van Der Heijde, 1994) or by the firing rate of the neurons in the midbrain (Schor *et al.*, 1992; Gamlin *et al.*, 1994). It is of interest to compare the dynamics of the iris plant influenced pupillary system and the accommodative system to better understand the factors influencing the dynamics of the accommodative system. In the present study and in a previous study (Wilson, 1973), it was found that the latency of accommodation is shorter than that of pupil constriction. Wilson further showed that the third aspect of the near triad, namely convergence, has a shorter latency than accommodation and pupil constriction. He suggested that the longer latency of accommodative and pupil response are because of the mechanical constraints of intraocular tissues such as the lens/ciliary muscle

tissues in the case of accommodation and iris musculature in the case of the pupil response. In the present study, when the pupil constriction responses were fitted with a first order exponential function, it was found that the time constant of pupil constriction increases with amplitude (*Figure 7*). A similar trend of time constants of accommodation increasing with amplitude has been reported previously (Kasthurirangan *et al.*, 2003). Based on the suggestion by Wilson that the dynamics of accommodation and pupil constriction are influenced by mechanical constraints, it is possible that the dynamic trend of time constants increasing with amplitude may reflect the dynamics of the biomechanical factors associated with accommodation and pupil constriction.

Age-related changes in near pupil response

The pupil changes determined in this study ranged from 0.20 to 0.76 mm D⁻¹ for accommodation and 0.11–0.25 mm D⁻¹ for disaccommodation. Schaeffel *et al.* (1993), have shown that the amount of pupil change with accommodation increases with age, with almost no pupil constriction per dioptre in children to approaching infinity (i.e. a strong pupil change with no refractive change) in presbyopes. Therefore, the amount of pupil change reported in the present study may be applicable only to a young population between 23 and 26 years of age.

The near pupil response (mm D⁻¹) may be an index of the accommodative effort exerted, similar to the accommodative convergence to accommodation (AC/A) ratio (Bruce *et al.*, 1995; Ciuffreda *et al.*, 1997; Francis *et al.*, 2003). The present study shows that there is no change in the amount of pupil change per dioptre of accommodation for various amplitudes of accommodation in young subjects.

It will be of interest to study the amount of pupil change per dioptre of accommodation, the dynamics of the near pupil response and the transient nature of the accommodative pupil response with ageing. With ageing, as the accommodative ability decreases, pupil constriction plays an increasingly important role in increasing the depth of field of the eye. Therefore, it is possible that the accommodative pupil constriction seen in young subjects may become more sustained in older subjects.

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