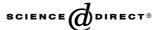


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## Age related changes in the characteristics of the near pupil response

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#### Abstract

Static and dynamic aspects of the near pupil response were studied in human subjects in the age range when accommodative amplitude steadily declines. Dynamic accommodative and pupillary responses to step stimuli were recorded in 66 subjects (ages: 14–45 years). Exponential fits to data provided amplitude, peak velocity and time constants. Accommodative amplitude decreased linearly with age (p < 0.05). Pupil constriction per diopter of accommodative response increased exponentially with age (p < 0.05). The amplitude of pupil constriction for a 2 D stimulus decreased linearly with age (p < 0.05) and for a 5 D stimulus did not change with age (p = 0.90). The latency of pupil constriction did not change with age (p = 0.65), while the mean peak velocity decreased linearly with age (p < 0.05). An increase in the amount of pupil constriction per diopter of accommodative response, but not per diopter of stimulus amplitude, suggests that the near effort per se does not increase with age. There is a slight reduction in the speed of near pupil response with age.

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Keywords: Accommodation; Main sequence; Pupillary reflex; Near triad; Presbyopia

## 1. Introduction

An attempt to focus on a near object includes accommodation, convergence eye movements and pupil constriction (Loewenfeld, 1999b; Myers & Stark, 1990; Wick & Currie, 1991). Accommodation results in an increase in the optical power of the eye to focus on the near object, convergence eye movements direct the eyes towards the near object and the pupil constriction increases depth of focus (Campbell, 1957; Campbell & Gubisch, 1966) and might thereby assist accommodation in providing a clear image of the near object on the retina. The ability to accommodate decreases with age resulting in the condition called presbyopia (Duane, 1912).

The pupil constriction with accommodation has been linked to the effort exerted when viewing a near target

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(Loewenfeld, 1999b). It has been suggested that an increased effort to accommodate due to reduced accommodative ability with age results in an increased near pupil constriction (Schaeffel, Wilhelm, & Zrenner, 1993). When maximum accommodation was stimulated, the amount of pupil constriction with accommodation increases with age, with almost no pupil constriction per diopter in children to approaching infinity in presbyopes (i.e., a strong pupil change with no accommodative change; Schaeffel et al., 1993). However, the increase in the ratio of pupil constriction to accommodation with age could be due to an increase in the pupil constriction, a decrease in the accommodative amplitude or a combination of the two. It has also been suggested previously that the magnitude of near pupil constriction, in fact, decreases with age between 10 and 74 years of age (Schafer & Weale, 1970) or remains constant after 20 years of age (Wilhelm, Schaeffel, & Wilhelm, 1993). The specific age related changes in the near pupil response with the progression of presbyopia are not clear. Quantifying the specific changes in the near pupil response with

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age will help understand any adaptive changes in the near response with the progression of presbyopia.

There are numerous age related changes in the shape and the activity of the pupil. The scotopic, mesopic and photopic pupil diameters decrease with age (Bitsios, Prettyman, & Szabadi, 1996; Loewenfeld, 1979; Netto, Ambrosio, & Wilson, 2004; Yang, Thompson, & Burns, 2002). The shape of the pupil changes from a regular circular form to an irregular form with age (Wyatt, 1995). The amplitude of light induced pupil constriction decreases with age (Bitsios et al., 1996; Loewenfeld, 1979). The pupil responsivity is influenced by the initial pupil diameter (Loewenfeld, 1979; Semmlow, Hansmann, & Stark, 1975; Sun, Tauchi, & Stark, 1983; Usui & Stark, 1978) and the relationship between pupil responsivity and initial pupil diameter changes with age, suggesting that the age related decline in the amplitude of light induced pupil constriction is not merely due to a change in the baseline pupil diameter with age (Loewenfeld, 1979). The dynamics of the pupil response have also been shown to slow down with age (Bitsios et al., 1996; Loewenfeld, 1979; Netto et al., 2004). The high frequency pupillary hippus reduces with age (Netto et al., 2004), the high frequency cut off of pupil responses occurs at a lower frequency in older individuals (Loewenfeld, 1979) and the maximum velocity of pupil constriction and dilation decreases with age (Bitsios et al., 1996). Given these age related changes in pupil responses, it is perhaps surprising that the near pupil response should increase with age.

There are two potential reasons to expect an increase in near pupil constriction with age based on its functional role associated with accommodation. The decrease in accommodation with age might result in an increased pupil constriction either to increase the depth of focus of the eye or from an increased effort to accommodate. Optically, a decrease in pupil diameter reduces the size of the blur circle of an out of focus image, providing an optimal modulation transfer function (MTF) at a 2-3 mm pupil diameter (Campbell & Gubisch, 1966). An increased near pupil constriction in presbyopes may reduce the blur on the retina caused by inadequate accommodation (Ostrin, Kasthurirangan, & Glasser, 2004). However, a direct association between accommodation and pupil constriction has been questioned in the past (Phillips, Winn, & Gilmartin, 1992; Stakenburg, 1991). It has been suggested that the near pupil constriction may be due to other factors such as target misalignment (Phillips et al., 1992; Stakenburg, 1991), proximal cues such as size (Phillips et al., 1992), fusional vergence (Backer & Ogle, 1964; Knoll, 1949) and near effort (rather than accommodation per se; Loewenfeld, 1999b; Schaeffel et al., 1993). Given the controversies regarding accommodation as a causal factor for the near pupil response, it is not clear if the decrease in accommodation with presbyopia necessarily causes an increase in pupil constriction. Alternately, if a near effort induces pupil constriction, presbyopia could result in the requirement for an increased effort to accommodate and thereby an increase in near pupil constriction.

The relationship between presbyopia and near effort is interesting in the context of two contradictory, but equally supported, theories that deal with the changes in near effort with presbyopia. The Hess-Gullstrand theory suggests that with increasing age, maximum accommodative response will be achieved with a lesser contraction of ciliary muscle (Atchison, 1995; Eskridge, 1984; Gullstrand, 1909) or with a similar effort (Ciuffreda, Rosenfield, & Chen, 1997; Gullstrand, 1909). The Duane–Fincham theory suggests that with increasing age, maximum accommodative response will be achieved at maximum ciliary muscle contraction (Atchison, 1995; Eskridge, 1984; Fincham, 1955) or with increasing effort (Ciuffreda et al., 1997). The Hess-Gullstrand theory is supported by the suggestion that ciliary muscle contraction increases beyond the maximum accommodative response amplitude (Saladin & Stark, 1975; Strenk et al., 1999; Strenk, Strenk, & Koretz, 2005; Swegmark, 1969). The Duane-Fincham theory is supported by the increase in accommodative convergence to accommodation ratio (AC/A) with age (Atchison, 1995; Baker & Gilmartin, 2002; Eskridge, 1984; Heron, Charman, & Schor, 2001), although other studies have shown no change in AC/A with onset of presbyopia (Ciuffreda et al., 1997) or suggest that changes in AC/A ratio with age need not support the Duane-Fincham theory of presbyopia (Bruce, Atchison, & Bhoola, 1995). Part of the controversy with AC/A could be because both accommodation and convergence can be controlled voluntarily (Ebenholtz & Citek, 1995; Provine & Enoch, 1975; Wick & Currie, 1991) and they can mutually affect each other in the form of AC/A or CA/C ratios (Schor & Kotulak, 1986). Pupil constriction is not under voluntary control and stimulating a puconstriction does not cause changes accommodation. It is of interest to study the accommodation-pupil constriction relationship as a function of age to understand which of the two theories is true with presbyopia, although it should be noted that the pupil response in itself may undergo age related changes. Given this caveat, an increase in the near pupil response with presbyopia may lend support to the Duane-Fincham theory of presbyopia and no change or decrease in near pupil response with age need not directly provide support for the Hess–Gullstrand theory of presbyopia.

In this study the static and dynamic characteristics of the near pupil responses were studied in 66 subjects 14–45 years of age. The magnitude and the dynamics, in terms of latency, peak velocity and time constants, of the near pupil constriction are reported as a function of age. The study was undertaken to understand the specific changes in the near pupil response with age related decline in accommodation.

## 2. Methods

## 2.1. Subjects

Eighty six (86) subjects were recruited for the study. Twenty (20) subjects were rejected at various stages (data collection through data analysis) for various reasons listed in the results section. Finally, data from 66 subjects, aged 14-45 years, are reported here. The age of the subjects were calculated in years including month [year + (month/12)]. The subjects were either emmetropes (n = 32) or myopes corrected with soft contact lenses (n = 33) or LASIK procedure (n = 1). Twenty eight (28) subjects had light irides (Grade A, B and C) and thirty eight (38) subjects had dark irides (Grade D and E; Seddon, Sahagian, Glynn, Sperduto, & Gragoudas, 1990). The subjects underwent a short optometric examination to ensure 20/20 Snellen visual acuity at distance and residual refractive error within  $\pm 0.50$  D. This preliminary screening was followed by dynamic measurement of accommodation and pupil responses from a far stimulus to stimuli at various near distances. The maximum accommodative amplitudes of the subjects were measured objectively with a Hartinger coincidence refractometer during a push-up task at the end of the experiment. The research was performed according to institutionally approved human subjects protocols with full informed consent and followed the tenets of the Declaration of Helsinki.

## 2.2. Dynamic experiment

The experimental set up is the same as that used in previous studies (Kasthurirangan & Glasser, 2005; Kasthurirangan, Vilupuru, & Glasser, 2003) and is further described briefly below. The 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 near distances from 1 m to 16.7 cm to create stimulus demands from 1 to 6 D in 1 D steps. Data was collected for one stimulus amplitude at a time, following which the stimulus amplitude was increased and data collected again. The far target at 6 m subtended 0.86° at the eye and the near target at 1 m subtended 1.66°. The angular size of the target increased approximately 1.5 times with each near target position or every diopter increase in accommodative demand.

The far and near 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. The room lights were turned off so that at any moment in time only one target, either at far or near, was visible. The switch in illumination between the far and near targets was instantaneous. The targets were matched in luminance to be 10 cd/m<sup>2</sup> on the white background. The luminance was measured with a light meter (LS 100, Konica Minolta, New Jersey, USA) through the apparatus from the subjects view. The left eye of the subject was covered with an eye patch and the subject's head was stabilized with a head and chin rest. The far and near targets were aligned with the right eye with the help of a beam splitter (Fig. 1). At each near target distance, subjects were asked to align the far and near targets by rotating the beam splitter about its vertical axis. 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.

## 2.3. Measurement of refraction and pupil diameter

Refraction and pupil diameter were measured with the PowerRefractor, a dynamic video based optometer that can measure refraction, pupil diameter and vergence simultaneously at 25 Hz (Allen, Radhakrishnan, & O'Leary, 2003; Kasthurirangan & Glasser, 2005; Kasthurirangan et al., 2003; Schaeffel, 2002; Schaeffel et al., 1993; Wolffsohn, Hunt, & Gilmartin, 2002). The PowerRefractor refraction measurement was calibrated for the spectacle plane on each subject as described previously (Kasthurirangan et al., 2003; Schaeffel et al., 1993). In short, PowerRefractor measurements were made through ophthalmic trial lenses of different powers held in front of the right eye covered with a visible block

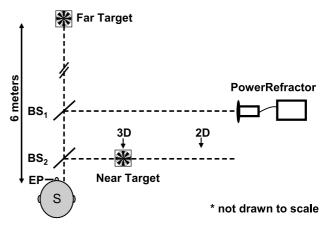


Fig. 1. The right eye of the subject (S) was aligned with the far target at 6 m. The near target was placed on a track to present a near target at stimulus demands from 1 D (1 m) to 6 D (16.7 cm). The far target, near target and the PowerRefractor camera were aligned with the subject's right eye with two beam splitters (BS $_1$  and BS $_2$ ). The subject viewed the far and near targets, monocularly 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.

infrared pass filter (Kodak Wratten filter # 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 linear calibration function for each subject. In a previous study the PowerRefractor pupil diameter measurements were found to be reliable albeit with an average underestimation of the pupil diameter by 0.50 mm (Kasthurirangan & Glasser, 2005). The raw unaltered PowerRefractor pupil diameter measurements are reported here.

## 2.4. Data analysis

For each subject, the accommodation and pupil data for each stimulus demand were averaged after removing the data during the latency period. The averaged accommodative and pupil responses for each stimulus demand were analyzed to determine the amplitude of accommodative and pupil responses, and the dynamics of pupil constriction in terms of peak velocity and time constants, as described previously (Kasthurirangan & Glasser, 2005).

## 2.4.1. Determination of the latency 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 to a new level (Fig. 2A). 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. Latency was determined individually for accommodation and pupil responses.

## 2.4.2. Amplitude of accommodation and pupil constriction

The amplitude and dynamics, in terms of time constants and peak velocity, of accommodative and pupil responses were determined by fitting the responses with exponential functions:

Accommodation: 
$$y = y_0 + a \times (1 - e^{-t/\tau}),$$
 (1)

Pupil constriction: 
$$y = y_0 - a \times (1 - e^{-t/\tau})$$
. (2)

Exponential functions were fit to 2 s of the averaged accommodative and pupil constriction responses (Fig. 2B) using the Levenburg–Marquadt algorithm

based on chi-squared reduction (Press, Teukolsky, Vetterling, & Flannery, 2002). Pupil responses have been shown to exhibit transient characteristics (Kasthurirangan & Glasser, 2005; Sun et al., 1983). In such cases, the exponential function was fit to the first 800 ms of the pupil data following the onset of the response. In general, the exponential functions provided excellent fits to the data. Only those responses that had no residuals greater than 1.0 D for accommodation and 0.50 mm for pupil responses were considered for further analyses. The exponential fits provided amplitude and time constant. The maximum value of the derivative of the exponential fits provided peak velocity. The dynamics of the accommodative responses in this population will be reported in a separate paper.

# 2.4.3. Amount of pupil constriction per diopter of accommodation (mm/D)

The amount of pupil constriction per diopter of accommodation was determined by two methods. In the first method, the pupil constriction amplitudes for various stimuli were plotted against the corresponding accommodative response amplitudes (Fig. 2C). A straight line was fit to the pupil constriction vs accommodation plot. The slopes of significant straight-line fits provided the magnitude of pupil constriction per diopter of accommodation. The relationship was not linear in all subjects (Fig. 2C), therefore, to include data from all the subjects, the second method considered the ratio of pupil constriction to accommodation for a maximum stimulus amplitude. It should be noted that in subjects that show a saturation of pupil responses at higher accommodative response amplitudes (Fig. 2C, left panel), a lower pupil constriction per diopter of accommodation will be measured. However, this metric provides the pupil constriction per diopter of response accommodation for a maximum stimulus amplitude. Both these numbers are reported in the manuscript as a function of age.

To understand the age related trends in near pupil responses for small and large stimulus amplitudes, a 2 and a 5 D stimulus were chosen. Reliable responses were not obtained for the 1 D stimulus in most subjects and therefore, the 2 D stimulus was chosen as the small stimulus amplitude, although even this stimulus was above the accommodative amplitude of three of the older subjects. The accommodative response amplitude and the ratio of pupil constriction to accommodation were compared across ages for a 5 D stimulus to understand the age related changes for a stimulus beyond the accommodative amplitude of the older subjects. This analysis was performed to understand if there are any changes in the effort involved for accommodation as a function of age.

## 2.4.4. Pupil transience

In an earlier study on young human subjects, it was found that the near pupil constriction was not sustained

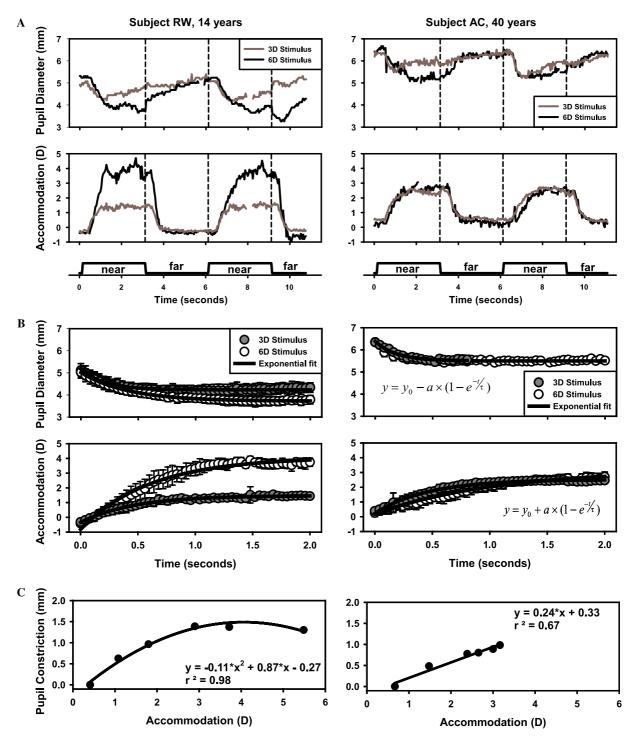


Fig. 2. (A) Two consecutive pupillary and accommodative responses from a 14-year-old (left panel) and a 40-year-old (right panel) subject are shown for a 6 D (black trace) and a 3 D (gray trace) stimulus. The onset of far and near stimuli is indicated below the figure. In this particular case, the young subject has a smaller baseline pupil diameter than the old subject. This reflects the normal individual differences in resting pupil diameter in the population. In this figure, the accommodative, disaccommodative and pupil responses have been truncated at 3 s (indicated by vertical dashed lines) to align the start of each response. (B) The accommodative and pupillary responses for each subject for each stimulus demand were averaged after removing latency. The averaged responses for a 3 D (gray filled symbols) and a 6 D stimulus (open symbols) demand are shown for the same subjects as in A. The error bars represent  $\pm 1$  SD. The averaged traces were fit with exponential functions (black lines) to calculate amplitude, time constant and peak velocity of responses (see Section 2). The exponential equations are shown in the right panels. The pupil response to a 3 D stimulus of the 40-year-old subject (right panel) showed transience and so the exponential function was only fit to 800 ms of the data. (C) The amplitude of pupil constriction is plotted against the accommodative amplitude for various stimulus demands for the same subjects in A. In the 14-year-old subject, the pupil constriction amplitude saturated at higher accommodative amplitudes (fit with a polynomial) and in the 40-year-old subject, pupil constriction increased linearly with accommodative amplitude.

and exhibited transient properties (Kasthurirangan & Glasser, 2005). This pupil transience has been reported in the past for light induced pupil responses (Sun et al., 1983) and can also be seen in Fig. 2A. It is possible that the near pupil constriction may become more sustained with presbyopia. To evaluate this, the transience of the near pupil response was calculated as the difference between the maximally constricted pupil diameter and the pupil diameter at the 2 s time point of the averaged response. In cases where the pupil response was transient, the maximally constricted pupil diameter was always within the 2 s time point. All responses to a stimulus were averaged and 2 s of the averaged data was considered. Responses less than 2 s long are also included in the averaged traces. This analysis was performed on the averaged pupil responses for each subject for each stimulus amplitude.

#### 3. Results

Out of the 86 subjects originally recruited, 20 were rejected due to various reasons such as uncorrected refractive errors (n = 3, aged 20, 22, and 32 years), very small baseline pupil diameters or high pupil constriction even for low ( $\sim$ 3 D) stimulus amplitudes (n=10, aged 21-31 years), inability to follow the dynamic far and near targets (n = 5, aged 21–36 years) and nonlinear PowerRefractor calibration functions (n = 2, aged 24 and 27 years). Although the present study is on the near pupil response, 10 subjects were rejected due to high pupil constriction, because of the inability of the PowerRefractor to record at pupil diameters smaller than 3.5 mm.

The objectively determined accommodative amplitude decreased linearly with age (Fig. 3A, slope = -0.26 D/ year, p < 0.05). The baseline pupil diameter was calculated as the average of ten successive data points (400 ms) from a continuous record of pupil diameter measurements during far fixation at the beginning of the dynamic experiment. The baseline pupil diameter also decreased with age (slope = -0.03 mm/year, p < 0.05; Fig. 3B). Although, if the two subjects aged 41.83 and 45 years with pupil diameters less than 5 mm are not considered in the linear regression, then there is no significant decreasing trend in the data (Fig. 3B).

The increase in pupil constriction with accommodation, calculated by two different methods (see Section 2), is shown in Figs. 4A and B. In either method, an age related exponential increase in the amount of pupil constriction with accommodation is seen. The increase in pupil constriction per diopter with age could be due to a true increase in pupil constriction or due to a reduction in accommodative response. Therefore the pupillary constriction amplitude and the accommodative response amplitudes to a low 2 D and a high 5 D stimu-

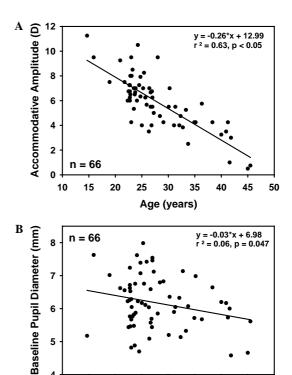


Fig. 3. The objectively measured maximum accommodative amplitude (A) and baseline pupil diameter (B) are plotted against age. The accommodative amplitude decreased linearly with age. From the linear regression, the calculated age for zero accommodation was 50 years. The baseline pupil diameter was highly variable between subjects. The decrease in baseline pupil diameter with age approached significance, although the linear regression was not significant if the data from two old subjects with the smallest pupil diameters were removed.

35

Age (years)

40 45 50

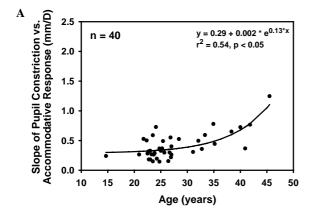
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10 15

lus amplitude were compared (Figs. 5A and B). The amplitude of near pupil constriction decreased linearly with age for the 2 D stimulus (slope = -0.02 mm/year, p < 0.05, Fig. 5A) and did not change systematically with age for the 5 D stimulus (p for straight line fit = 0.90, Fig. 5B). The accommodative response amplitude did not change with age for the 2 D stimulus (p for straight line fit = 0.14, data not shown) and decreased linearly with age for the 5 D stimulus (slope: -0.08 D/ year, p < 0.05, Fig. 5C). The pupil constriction to accommodation ratio did not show any systematic trends with age for the 2 D stimulus (data not shown) and increased exponentially with age for the 5 D stimulus (Fig. 5D). The age related increase in pupil constriction per diopter of accommodation for a maximum stimulus amplitude is therefore, merely due to a reduction in accommodative amplitude and not due to an increase in pupil constriction amplitude per se.

There was no age related change in the magnitude of pupil transience for any of the stimulus amplitudes (data not shown). The data from all subjects were combined for a subsequent analysis to compare magnitude of pupil transience and stimulus amplitude. In this analysis the



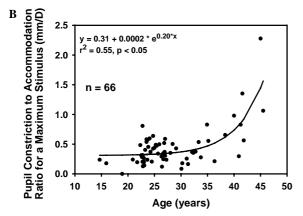


Fig. 4. The change in pupil diameter per diopter of accommodation obtained from the slope of significant linear fits to pupil constriction vs accommodation plots (A) and from the ratio of pupil constriction to accommodation for a maximum stimulus amplitude (B) are plotted against age. The number of subjects considered for each analysis is shown. In both cases the amount of pupil constriction with accommodation increased exponentially with age.

magnitude of pupil transience was averaged for each stimulus amplitude (Fig. 6). A one way ANOVA procedure revealed significant difference in pupil transience as a function of stimulus amplitude ( $F_{5,299} = 9.40$ ; p < 0.05). Post hoc *t*-tests with Tukey correction revealed that the pupil transience for the 1, 2 and 3 D stimuli were significantly different from the pupil transience for the 4, 5 and 6 D stimuli at the p < 0.05 level. In other words the pupil responses became more sustained at higher stimulus demands (Fig. 6). Interestingly, pupil transience was not related to pupil constriction amplitude (data not shown).

The latency of pupil constriction did not show any age related changes (p for straight line fit = 0.65, data not shown) and the mean  $\pm$  1 SD latency of the pupil constriction was  $357 \pm 82$  ms. There were no age related trends in accommodative latency either (data not shown) and the mean  $\pm$  1 SD latency of accommodative responses was  $256 \pm 67$  ms. Histograms of pupil and accommodative latencies from all the subjects are shown in Fig. 7. The accommodative latencies are generally shorter than the mean pupillary latencies. The

accommodative latency histogram has a Gaussian form, whereas the pupil latency histogram is skewed with a longer tail towards larger pupil latencies.

Time constants for pupil constriction increased with the amount of pupil constriction (slope = 0.13 s/mm, p < 0.05, Fig. 8A), as reported previously (Kasthurirangan & Glasser, 2005). Only in 32 out of the 66 subjects, significant linear fits were obtained for the time constant vs amount of pupil constriction relationship. The slopes of such significant linear relationships did not change significantly with age (p for straight line fit = 0.67, data not shown). The mean peak velocity of pupil constriction from each subject showed a slight but significant decline with age (slope:  $-0.08 \, \text{mm/s/year}$ , p < 0.05, Fig. 8B).

#### 4. Discussion

In this study, the characteristics of the near pupil response were studied in humans over an age range during which the accommodative amplitude progressively declines. An upper age limit of 45 years was chosen to ensure that some measurable accommodation was present. No attempt was made to test absolute presbyopes, although, accommodative stimulus amplitudes beyond the accommodative reserve of the older subjects were used to monitor the effort involved in accommodation. The finding that the magnitude of the near pupil constriction decreased with age for a 2 D stimulus corresponds to a decline in light induced pupil response with age (Loewenfeld, 1979; Schafer & Weale, 1970). It has been reported previously that the magnitude of near pupil constriction remains constant for stimulus amplitudes from 3 to 10 D over the age range 20–55 years (Wilhelm et al., 1993) or decreases for a 10 D stimulus amplitude over the age range 10-73 years (Schafer & Weale, 1970). In the present study, the magnitude of near pupil constriction for a 5 D stimulus did not change with age up to 45 years. It is possible that a decline in near pupil response to a 5 D stimulus may be observed if subjects older than 45 years were included, as reported by Schafer and Weale (1970).

The scotopic, mesopic, photopic and the accommodated pupil diameters are suggested to decrease with age (Bitsios et al., 1996; Kadlecova, Peleška, & Vaško, 1958; Loewenfeld, 1979; Schafer & Weale, 1970). A wide range spanning 10–100 years were considered in these studies. In the present study with a relatively restricted age range from 14 to 45 years, there was considerable variability in the baseline mesopic pupil diameter and no clear trend of decrease in pupil diameter with age was observed. The high individual variability in pupil diameter and response is a well characterized feature of the pupillary system (Brown, Khanani, & Xu, 2004; Loewenfeld, 1979). The variability in pupil diameter

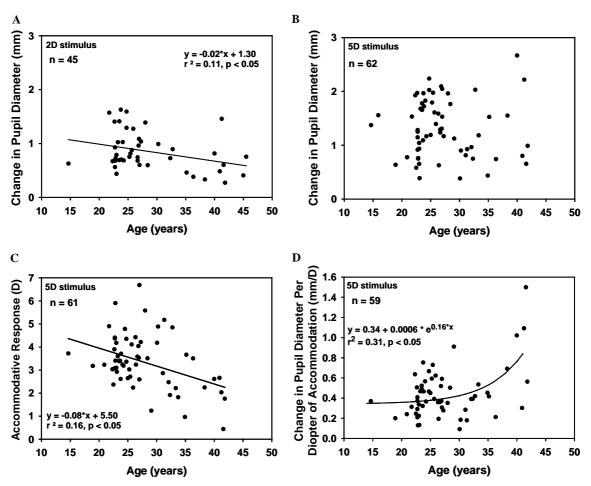


Fig. 5. The change in pupil diameter to 2 D (A) and 5 D (B) stimulus demands are plotted against age. The number of subjects considered for each analysis is given in the figures. These subjects represent those from whom reliable responses were obtained. The change in pupil diameter decreased linearly with age for the 2 D stimulus demand and had no relationship with age for the 5 D stimulus demand. The accommodative response to a 5 D stimulus decreased linearly with age (C). The change in pupil diameter per diopter of accommodation or the ratio of the pupil constriction to accommodative response increased exponentially with age (D).

and pupil response has been attributed to emotional factors (Loewenfeld, 1979), iris color (Bergamin, Schoetzau, Sugimoto, & Zulauf, 1998) and refractive errors (Chateau, de Brabander, Bouchard, & Molenaar, 1996; Schaeffel et al., 1993; Woung, Lue, & Shih, 1998; Yang et al., 2002). Dark irides have been shown to have a significantly greater constriction amplitude and velocity responses than light irides (Bergamin et al., 1998). The influence of refractive error on pupil responses is unclear, with two studies showing no effect (Chateau et al., 1996; Yang et al., 2002), one study showing greater pupil response in myopes (Woung et al., 1998) and another study showing diminished pupil response in myopes (Schaeffel et al., 1993). The emotional factors, iris color or refractive error were not controlled in this study.

It is commonly suggested that older individuals have smaller pupil diameters when focusing at closer targets (Chateau et al., 1996; Schafer & Weale, 1970). In this study, neither an increase in near pupil response nor any changes in the transience of the near pupil response was found in older individuals. With increasing age, the reduction in baseline pupil diameter will result in smaller accommodated pupil diameters for similar amplitude pupil constriction as in a younger individual. Therefore, the smaller accommodated pupil diameter in older individuals may be mainly due to a decline in baseline pupil diameter, as reported in other studies (Bitsios et al., 1996; Kadlecova et al., 1958; Loewenfeld, 1979; Schafer & Weale, 1970), and not due to an increase in near pupil constriction.

The near pupil constriction could potentially increase with age to increase the depth of field of the eye and thereby compensate the inadequate accommodation. No such increase in near pupil constriction is seen in the present study, although the smaller accommodated pupil diameter in older individuals will definitely help increase the depth of field. Therefore the older eye would have a greater depth of field at rest and therefore also a greater depth of field in the accommodated state, but

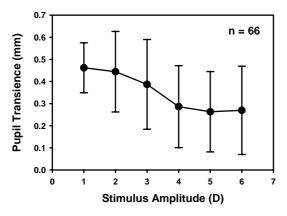


Fig. 6. The mean  $(\pm 1 \text{ SD})$  magnitude of pupil transience is plotted against the stimulus amplitude. Pupil transience was calculated as the difference between the maximally constricted pupil diameter and the pupil diameter at the 2 s time point of the averaged responses for each stimulus in each subject. The pupil response becomes more sustained at higher stimulus amplitudes.

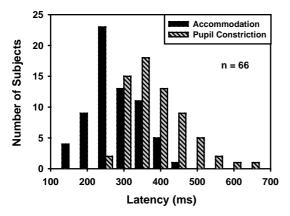
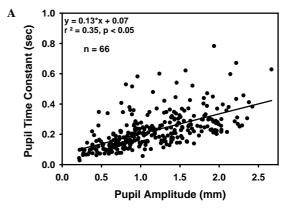


Fig. 7. The frequency distribution of accommodative and pupil constriction latencies are shown. The accommodative latencies resemble a Gaussian function and the pupil latencies are skewed towards longer latencies. On average, the accommodative latency is shorter than the pupil latency.

not because of a stronger pupil constriction. The primary function of the pupil is to control the light level within the eye (Loewenfeld, 1999a). The optical reasons for pupil constriction need further investigation. It seems likely that the optical benefits or depth of field effects of the pupil constriction are secondary and not the causal factor for near pupil constriction.

If the magnitude of near pupil constriction can be considered an indicator of accommodative effort (Loewenfeld, 1999b), then the results of the present study do not suggest a strong increase in effort to accommodate with age. The age related reduction in near pupil constriction for a 2 D stimulus may suggest subtle age related changes in the iris musculature, because it is unlikely that older individuals would exert less effort for a 2 D stimulus. Only a slight trend of decrease in baseline pupil diameter with age was seen, with all subjects having baseline pupil diameters greater than



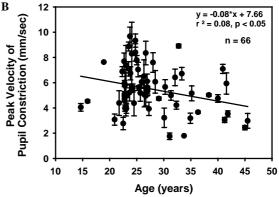


Fig. 8. Cumulatively the time constants of pupil constriction increased linearly with amplitude (A). The number of subjects considered for each analysis is shown. The mean peak velocity of pupil constriction ( $\pm 1$  SEM) from each subject showed a slight but significant decrease with age (B).

4.5 mm. This suggests that age related changes in iris function precede the gross structural changes such as change in pupil diameter and pupil shape. The age related decline in iris functionality may counteract any age related increases in near pupil response. The maximum accommodative amplitude of the oldest subjects was ten time less than that of the youngest subjects (Fig. 3A), with many older subjects having amplitudes well less than 5 D. The lack of any change in near pupil constriction for the 5 D stimulus argues against a significant increase in near pupil constriction, even after considering any age related changes in iris functionality or the marginal decrease in baseline pupil diameter. The magnitude of the near pupil constriction for a high 5 D stimulus may saturate and obscure age related trends. However, there was no age related increase in the near pupil constriction even for a low 2 D stimulus. Therefore, the present study does not lend support to the Duane–Fincham theory of presbyopia and supports the Hess-Gullstrand theory of presbyopia, which suggests that there is no increase in near effort to achieve maximum accommodative response in older individuals. If true, this would suggest that the human ciliary muscle does not lose the ability to contract with increasing age in accordance with MRI data which shows the persistence of ciliary body motility in presbyopes (Strenk et al., 1999, 2005).

The latency of pupil constriction found in the present study is similar to previous reports (Bergamin & Kardon, 2003; Hunter, Milton, Ludtke, Wilhelm, & Wilhelm, 2000; Kasthurirangan & Glasser, 2005). The mean latency of accommodation found in the present study (256 ms) is slightly lower than previous reports ranging from 285 to 370 ms (Heron, Charman, & Gray, 1999; Schor, Lott, Pope, & Graham, 1999; Shirachi et al., 1978). In the present study, the onset of far and near targets were randomized, although the subjects were aware of the far and near target positions and that the near target would be presented immediately following the far target and vice versa. Prediction, in terms of target positions, could have resulted in slightly lower latencies. The measurement frequency of the PowerRefractor was 25 Hz, which could have resulted in errors in the estimation of latency of about 40 ms, in part leading to the slightly smaller latencies found in the present study. The latency of near pupil constriction did not change with age in this age group. As reported previously, the pupil constriction latency is longer than the associated accommodative latency (Kasthurirangan & Glasser, 2005; Wilson, 1973). The peak velocity of pupil constriction shows a small but significant decrease with age, as has been shown previously (Bitsios et al., 1996). It has been reported that the dynamics of the pupil responses are influenced by the biomechanics of the iris muscle plant (Semmlow & Stark, 1973; Sun et al., 1983). The form of the pupil also shows age related change, presumably due to structural changes (Wyatt, 1995) such as changes in the contractility of the muscle fibers, stromal atrophy with loss of connective tissue and hyaline degeneration (Loewenfeld, 1979). It is plausible that the age related decrease in peak velocity also reflects the age related changes in the structure and the biomechanics of the iris muscle plant.

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#### References

Allen, P. M., Radhakrishnan, H., & O'Leary, D. J. (2003). Repeatability and validity of the PowerRefractor and the Nidek AR600-A

- in an adult population with healthy eyes. *Optometry and Vision Science*, 80, 245–251.
- Atchison, D. A. (1995). Accommodation and presbyopia. *Ophthalmic and Physiological Optics*, 15, 255–272.
- Backer, W. D., & Ogle, K. N. (1964). Pupillary response to fusional eye movements. American Journal of Ophthalmology, 58, 743–756.
- Baker, F. J., & Gilmartin, B. (2002). The effect of incipient presbyopia on the correspondence between accommodation and vergence. Graefe's Archives of Clinical and Experimental Ophthalmology, 240, 488–494.
- Bergamin, O., & Kardon, R. H. (2003). Latency of the pupil light reflex: sample rate, stimulus intensity, and variation in normal subjects. *Investigative Ophthalmology and Visual Science*, 44, 1546–1554.
- Bergamin, O., Schoetzau, A., Sugimoto, K., & Zulauf, M. (1998). The influence of iris color on the pupillary light reflex. *Graefe's Archives of Clinical and Experimental Ophthalmology*, 236, 567–570.
- Bitsios, P., Prettyman, R., & Szabadi, E. (1996). Changes in autonomic function with age: a study of pupillary kinetics in healthy young and old people. *Age Ageing*, 25, 432–438.
- Brown, S. M., Khanani, A. M., & Xu, K. T. (2004). Day to day variability of the dark-adapted pupil diameter. *Journal of Cataract* and Refractive Surgery, 30, 639–644.
- Bruce, A. S., Atchison, D. A., & Bhoola, H. (1995). Accommodation-convergence relationships and age. *Investigative Ophthalmology and Visual Science*, 36, 406–413.
- Campbell, F. W. (1957). The depth of field of the human eye. *Optica Acta*, 4, 157–164.
- Campbell, F. W., & Gubisch, R. W. (1966). Optical quality of the human eye. The Journal of Physiology, 186, 558–578.
- Chateau, N., de Brabander, J., Bouchard, F., & Molenaar, H. (1996).
  Infrared pupillometry in presbyopes fitted with soft contact lenses.
  Optometry and Vision Science, 73, 733–741.
- Ciuffreda, K. J., Rosenfield, M., & Chen, H. W. (1997). The AC/A ratio, age and presbyopia. *Ophthalmic and Physiological Optics*, 17, 307–315.
- Duane, A. (1912). Normal values of the accommodation at all ages. Journal of the American Medical Association, 1010–1013.
- Ebenholtz, S. M., & Citek, K. (1995). Absence of adaptive plasticity after voluntary vergence and accommodation. *Vision Research*, 35, 2773–2783.
- Eskridge, J. B. (1984). Review of ciliary muscle effort in presbyopia. *American Journal of Optometry, 61*, 133–138.
- Fincham, E. F. (1955). The proportion of ciliary muscular force required for accommodation. *The Journal of Physiology*, 128, 99–112.
- Gullstrand, A. (1909). The mechanism of accommodation. In J. P. C. Southall (Ed.), *Helmholtz's treatise on physiological optics* (pp. 382–415). New York: Dover.
- Heron, G., Charman, W. N., & Gray, L. S. (1999). Accommodation responses and ageing. *Investigative Ophthalmology and Visual Science*, 40, 2872–2883.
- Heron, G., Charman, W. N., & Schor, C. M. (2001). Age changes in the interactions between the accommodation and vergence systems. *Optometry and Vision Science*, 78, 754–762.
- Hunter, J. D., Milton, J. G., Ludtke, H., Wilhelm, B., & Wilhelm, H. (2000). Spontaneous fluctuations in pupil size are not triggered by lens accommodation. *Vision Research*, 40, 567–573.
- Kadlecova, V., Peleška, M., & Vaško, A. (1958). Dependence on age of the diameter of the pupil in the dark. *Nature*, 182, 1520–1521.
- Kasthurirangan, S., & Glasser, A. (2005). Characteristics of pupil responses during far-to-near and near-to-far accommodation. Ophthalmic and Physiological Optics, 25, 328–339.
- Kasthurirangan, S., Vilupuru, A. S., & Glasser, A. (2003). Amplitude dependent accommodative dynamics in humans. Vision Research, 43, 2945–2956.

- Knoll, H. A. (1949). Pupillary changes associated with accommodation and convergence. American Journal of Optometry and Archives of American Academy of Optometry, 26, 346–357.
- Loewenfeld, I. E. (1979). Pupillary changes related to age. In S. H. Thompson (Ed.), *Topics in neuro-ophthalmology* (pp. 124–150). Baltimore, USA: The Williams & Wilkins Company.
- Loewenfeld, I. E. (1999a). The light reflex. In *The pupil: Anatomy, physiology, and clinical applications* (pp. 83–272). Woburn, USA: Butterworth-Heinemann.
- Loewenfeld, I. E. (1999b). The reaction to near vision. In *The pupil: Anatomy, physiology, and clinical applications* (pp. 295–317).
  Woburn, USA: Butterworth-Heinemann.
- Myers, G. A., & Stark, L. (1990). Topology of the near response triad. *Ophthalmic and Physiological Optics*, 10, 175–181.
- Netto, M. V., Ambrosio, R., Jr., & Wilson, S. E. (2004). Pupil size in refractive surgery candidates. *Journal of Refractive Surgery*, 20, 337–342.
- Ostrin, L. A., Kasthurirangan, S., & Glasser, A. (2004). Evaluation of a satisfied bilateral scleral expansion band patient. *Journal of Cataract and Refractive Surgery*, 30, 1445–1453.
- Phillips, N. J., Winn, B., & Gilmartin, B. (1992). Absence of pupil response to blur-driven accommodation. Vision Research, 32, 1775–1779.
- Press, W. H., Teukolsky, S. A., Vetterling, W. T., & Flannery, B. P. (2002). Modeling of data. In *Numerical recipes in C. The art of scientific computing* (pp. 656–706). Cambridge: Cambridge University Press.
- Provine, R. R., & Enoch, J. M. (1975). On voluntary ocular accommodation. *Perception and Psychophysics*, 17, 209–212.
- Saladin, J. J., & Stark, L. (1975). Presbyopia: New evidence from impedance cyclography supporting the Hess–Gullstrand theory. Vision Research, 15, 537–541.
- Schaeffel, F. (2002). Kappa and Hirschberg ratio measured with an automated video gaze tracker. *Optometry and Vision Science*, 79, 329–334.
- Schaeffel, F., Wilhelm, H., & Zrenner, E. (1993). Inter-individual variability in the dynamics of natural accommodation in humans: relation to age and refractive errors. *The Journal of Physiology*, 461, 301–320.
- Schafer, W. D., & Weale, R. A. (1970). The influence of age and retinal illumination on the pupillary near reflex. Vision Research, 10, 179–191.
- Schor, C. M., & Kotulak, J. C. (1986). Dynamic interactions between accommodation and convergence are velocity sensitive. *Vision Research*, 26, 927–942.
- Schor, C. M., Lott, L. A., Pope, D., & Graham, A. D. (1999). Saccades reduce latency and increase velocity of ocular accommodation. *Vision Research*, 39, 3769–3795.

- Seddon, J., Sahagian, C., Glynn, R., Sperduto, R., & Gragoudas, E. (1990). Evaluation of an iris color classification system The Eye Disorders Case-Control Study Group. *Investigative Ophthalmology* and Visual Science, 31, 1592–1598.
- Semmlow, J., Hansmann, D., & Stark, L. (1975). Variation in pupillomotor responsiveness with mean pupil size. *Vision Research*, 15, 85–90.
- Semmlow, J., & Stark, L. (1973). Pupil movements to light and accommodative stimulation: a comparative study. Vision Research, 13, 1087–1100.
- Shirachi, D., Liu, J., Lee, M., Jang, J., Wong, J., & Stark, L. (1978).
  Accommodation dynamics I. Range nonlinearity. American Journal of Optometry and Physiological Optics, 55, 631–641.
- Stakenburg, M. (1991). Accommodation without pupillary constriction. *Vision Research*, 31, 267–273.
- Strenk, S. A., Semmlow, J. L., Strenk, L. M., Munoz, P., Gronlund-Jacob, J., & DeMarco, K. J. (1999). Age-related changes in human ciliary muscle and lens: a magnetic resonance imaging study. *Investigative Ophthalmology and Visual Science*, 40, 1162–1169.
- Strenk, S. A., Strenk, L. M., & Koretz, J. F. (2005). The mechanism of presbyopia. Progress in Retinal and Eye Research, 24, 379–393.
- Sun, F., Tauchi, P., & Stark, L. (1983). Dynamic pupillary response controlled by the pupil size effect. *Experimental Neurology*, 82, 313–324.
- Swegmark, G. (1969). Studies with impedance cyclography on human ocular accommodation at different ages. *Acta Ophthalmologica*, 47, 1186–1206.
- Usui, S., & Stark, L. (1978). Sensory and motor mechanisms interact to control amplitude of pupil noise. Vision Research, 18, 505–507.
- Wick, B., & Currie, D. (1991). Dynamic demonstration of proximal vergence and proximal accommodation. *Optometry and Vision Science*, 68, 163–167.
- Wilhelm, H., Schaeffel, F., & Wilhelm, B. (1993). Age dependence of pupillary near reflex. Klinische Monatsblatter fur Augenheilkunde, 203, 110–116.
- Wilson, D. (1973). A centre for accommodative vergence motor control. Vision Research, 13, 2491–2503.
- Wolffsohn, J. S., Hunt, O. A., & Gilmartin, B. (2002). Continuous measurement of accommodation in human factor applications. Ophthalmic and Physiological Optics, 22, 380–384.
- Woung, L. C., Lue, Y. F., & Shih, Y. F. (1998). Accommodation and pupillary response in early-onset myopia among schoolchildren. Optometry and Vision Science, 75, 611–616.
- Wyatt, H. J. (1995). The form of the human pupil. *Vision Research*, *35*, 2021–2036.
- Yang, Y., Thompson, K., & Burns, S. A. (2002). Pupil location under mesopic, photopic, and pharmacologically dilated conditions. *Investigative Ophthalmology and Visual Science*, 43, 2508–2512.