

Age related changes in accommodative dynamics in humans

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Abstract

Age related changes in the dynamics of accommodation (far to near focus) and disaccommodation (near to far focus) are reported in this study. Dynamic responses to step stimulus demands from 1 D to 6 D, in 1 D steps, were recorded with a PowerRefractor in 66 subjects in the age range 14–45 years. The accommodative and disaccommodative responses were fit with exponential functions to calculate response amplitude, time constant and peak velocity. The latency of accommodation did not change and the latency of disaccommodation increased with age. For accommodation, time constant increased and peak velocity decreased with age. For disaccommodation, no change in time constant or peak velocity was found with age. The form of the peak velocity vs response amplitude relationship (main sequence) of accommodation changed with age. The differences in the dynamics of accommodation and disaccommodation with age are discussed with reference to the age related changes in the eye leading to presbyopia.

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1. Introduction

An effort to focus on a near object results in an increase in the optical power of the eye called accommodation. Focusing from far to near (accommodation) is brought about by the contraction of the ciliary muscle and increase in the lens surface curvatures, while focusing from near to far (disaccommodation) is brought about by relaxation of the ciliary muscle and the lens being pulled, via the zonular fibers and lens capsule into an unaccommodated state (Glasser & Kaufman, 1999; Helmholtz von, 1909). As a person ages, the ability to accommodate diminishes (Duane, 1912) resulting in the condition called presbyopia (Atchison, 1995; Beers & Van Der Heijde, 1996; Glasser & Campbell, 1999; Glasser & Campbell, 1998; Strenk, Strenk, & Koretz, 2005; Weale, 1989). Accommodation has been studied for more than a century (see (Loewenfeld, 1999) and (Schneider, Bacsukulin, & Guthoff, 2001) for reviews of the history of accommodation research). However, there is still considerable debate over the accommodative mech-

anism and the changes that occur with presbyopia (Atchison, 1995; Beers & Van Der Heijde, 1996; Glasser & Campbell, 1998; Schachar, Black, Kash, Cudmore, & Schanzlin, 1995; Strenk et al., 2005). Accommodation and presbyopia are topics of active research in part because presbyopia affects 100% of the population over 50 years of age (Duane, 1912; Weale, 2003) and there is no satisfactory treatment for presbyopia. The age related changes that underlie presbyopia are not fully understood. Many different theories of presbyopia exist. There is considerable evidence suggesting that presbyopia results from a hardening of the crystalline lens (Fisher, 1973; Glasser & Campbell, 1999; Heys, Cram, & Truscott, 2004; van Alphen & Graebel, 1991; Weeber et al., 2005; Wyatt, 1993). However, other theories suggest that the predominant cause is due to lenticular geometric factors such as an increase in the lens thickness and diameter with age (Strenk et al., 2005) or extralenticular factors such as age related changes in the angle of the zonular attachments to the lens (Farnsworth & Shyne, 1979; Koretz & Handelman, 1986; Koretz & Handelman, 1988), age related decrease in the ciliary body movement (Croft et al., 1998; Tamm, Croft, Jungkunz, Lütjen-Drecoll, & Kaufman,

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1992; Tamm, Lütjen-Drecoll, Jungkunz, & Rohen, 1991) or reduced elasticity of the choroid (van Alphen & Graebel, 1991; Wyatt, 1993).

It is well characterized that the accommodative amplitude decreases with age (Duane, 1912; Hamasaki, Ong, & Marg, 1956). The changes in accommodative dynamics with age are less clear. Studies of accommodative dynamics provide insight into the mechanism and the factors that influence the accommodative responses (Beers & Van Der Heijde, 1994; Bharadwaj & Schor, 2005a; Kasthurirangan, Vilupuru, & Glasser, 2003; Schor & Bharadwaj, 2005). Dynamics of the accommodative system can be used as a tool to understand the age related changes leading to presbyopia (Beers & Van Der Heijde, 1996; Schor & Bharadwaj, 2005; Weeber et al., 2005). Differences between accommodation and disaccommodation, in terms of dynamics, have been shown in humans (Kasthurirangan et al., 2003) and in rhesus monkeys when accommodation was elicited by stimulating the Edinger–Westphal nucleus (Vilupuru & Glasser, 2002). These differences may largely be due to the differences in the mechanism and the biomechanics of the structures that underlie accommodation and disaccommodation (Beers & Van Der Heijde, 1994; Kasthurirangan et al., 2003). The dynamics of accommodation and disaccommodation can be compared as a function of age to gain insight into the specific age related changes in the accommodative system leading to presbyopia.

Past studies on the age related changes in accommodative dynamics have provided equivocal results. Descriptions of age-related changes in accommodative dynamics include a decrease in speed of both accommodation and disaccommodation (Beers & Van Der Heijde, 1996; Schaefel, Wilhelm, & Zrenner, 1993), speed of accommodation only (Sun et al., 1988; Temme & Morris, 1989), speed of disaccommodation only (Heron & Winn, 1989) or no change in either the speed of accommodation or disaccommodation (Heron, Charman, & Gray, 1999; Heron, Charman, & Gray, 2002; Heron, Charman, & Schor, 2001). It is possible that the age related changes reported in some studies may be due to the comparison of disproportionate amplitudes between young and old individuals (Kasthurirangan et al., 2003; Vilupuru & Glasser, 2002). A response of the same amplitude may involve a different effort in a young and an old person. If the maximum available amplitude is considered, it may require the same amount of effort between young and old. However, the stimulus amplitude will be large in young subjects and small in older subjects and therefore different response amplitudes, with different dynamics, would then be compared between young and old. If a fixed amplitude available to both young and old is considered, this would represent a greater proportion of the available accommodative amplitude for an older individual than for a younger individual. Therefore, it may be necessary to study dynamics over a wide range of response amplitudes to truly understand age related changes in the dynamics.

Accommodative responses have been shown to be inherently variable between individuals and in an individual from trial to trial (Heron et al., 1999; Kasthurirangan et al., 2003; Schaefel et al., 1993). If there are only subtle changes in the dynamics of accommodation with aging, studies using small sample sizes may not show significant results. A study involving a large sample size, multiple amplitudes and considering both accommodation and disaccommodation may shed light on some of the contradictory results reported in past studies. Measuring multiple response amplitudes allows comparison of the dynamics of a single low amplitude or a dynamic parameter based on multiple amplitudes. The dynamics, in terms of peak velocity or time constant, can be plotted against the response amplitude (the “Main Sequence”) to understand the overall dynamics of a system (Bahill, Clark, & Stark, 1975; Kasthurirangan et al., 2003; Mordi & Ciuffreda, 2004; Vilupuru & Glasser, 2002). Dynamic parameters, such as the peak velocity per diopter of accommodative response amplitude, can be calculated from the main sequence. The main sequence can be used as a tool to understand accommodative dynamics (Kasthurirangan et al., 2003; Vilupuru & Glasser, 2002) and the age related changes in accommodative dynamics.

In this study, the dynamics of accommodation and disaccommodation are reported for a range of response amplitudes in 66 subjects aged 14–45 years. Age related changes in dynamics in terms of latency, time constant and peak velocity are reported.

2. Methods

2.1. Subjects

Eighty six (86) subjects were recruited for the study. Twenty 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 to 45 years, are reported. The age of the subjects was calculated in years including month [age = year + (month/12)]. The subjects were either emmetropes ($n = 32$) or myopes corrected with soft contact lenses ($n = 33$) or LASIK procedure ($n = 1$). Subjects were not excluded based on refractive error because previous studies using similar methods did not reveal any significant differences in the accommodative dynamics between myopes and emmetropes (Kasthurirangan & Glasser, 2005c; Kasthurirangan et al., 2003). The distribution of subject age and refractive error is provided in Table 1. The subjects underwent a short optometric exam to ensure 20/20 Snellen visual acuity at distance and residual refractive error within ± 0.50 D. The research was performed according to institutionally approved human subjects protocols with full informed consent and followed the tenets of the Declaration of Helsinki.

The preliminary screening was followed by dynamic measurement of accommodation and disaccommodation between a far stimulus and a near stimulus placed successively at various near distances (see Section 2.2. Dynamic experiment). At the end of the dynamic experiment, the maximum accommodative amplitudes of the subjects were measured subjectively and objectively during a push up task, monocularly in the right eye. In the subjective push up test, a near reading card was slowly brought close to the right eye and the subjects were asked to report the first noticeable blur of the 1 M letters. The reciprocal of the distance from the point of first blur to the corneal plane of the subject was measured as the subjective maximum amplitude of accommodation. In the objective test, a near card was slowly brought close to the right eye of the subjects until

Table 1
Distribution of age and refractive errors of the subjects

Age group (years)	Number of subjects	Number of myopes	Number of emmetropes
14–16	2	1	1
17–19	1	1	0
20–22	11	9	2
23–25	20	8	12
26–28	11	10	1
29–31	5	1	4
32–33	5	0	5
34–36	3	1	2
37–39	1	1	0
40–42	5	1	4
43–45	2	1	1

The refractive errors ranged from -12.5 D to $+0.50$ D. Subjects with refractive errors < -0.50 D were classified as myopes and between -0.50 D and $+0.50$ D as emmetropes. The age range of myopes (15.9–45.5 years) and that of emmetropes (14.67–45 years) are comparable.

the subject's reported sustained blurring of the letters. The refractive state of the subjects was continuously monitored with a Hartinger coincidence refractometer during the push up task. The difference between the maximum accommodated refraction and the baseline, distance refraction was recorded as the objectively measured maximum amplitude of accommodation.

2.2. Dynamic experiment

The experimental set up is the same as that described previously (Kasthurirangan & Glasser, 2005a, 2005b; Kasthurirangan et al., 2003) and only a short description is provided here. 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 D to 6 D in 1 D steps. The far target at 6 m subtended 0.86° at the eye and the near target at 1 m subtended 1.66° . A 2 D fast fourier transform (Matlab, Mathworks) indicated that the target was spatially broadband consisting of multiple spatial frequencies from 1 to 30 cpd, with predominantly less than 9 cpd, at 6 m. The angular size of the target increased approximately 1.5 times with each diopter increase in accommodative demand. Data was collected for one stimulus amplitude at a time, following which the stimulus amplitude was increased and data collected again.

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. 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^2 on the white background. The level of luminance of the targets was well beyond the threshold luminance ($\sim 5 \text{ cd/m}^2$) required to produce robust accommodative responses (Johnson, 1976) and was similar to luminance levels used in previous studies of dynamic accommodation (Charman & Heron, 1988; Gray, Winn, & Gilmartin, 1993; Kasthurirangan & Glasser, 2005b, 2005c; Kasthurirangan et al., 2003; Schor & Kotulak, 1986). The target luminance was measured with a light meter (LS 100, Konica Minolta, New Jersey, USA) through the apparatus from the subjects' view and the intensity of the LEDs was adjusted with rheostats. The left eye of the subject was covered with an eye patch and the subjects' 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). For 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.

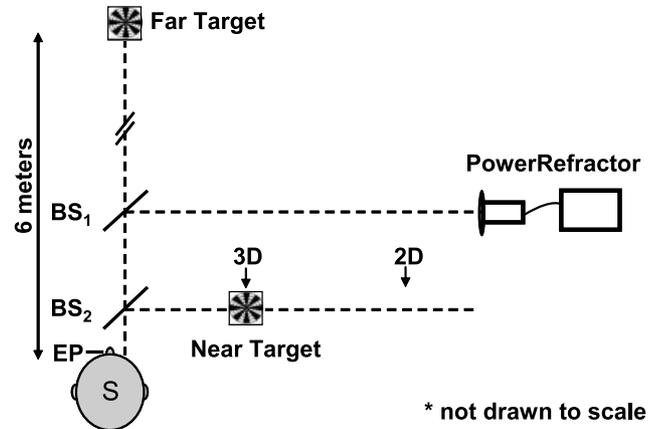


Fig. 1. The right eye of the subject (S) was aligned with the far target at 6 m. The near target was presented at stimulus demands from 1 D (1 m) to 6 D (16.7 cm). The far target, near target and the PowerRefractor camera were aligned with the subject's right eye with two beam splitters (BS₁ and BS₂). 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.

2.3. Measurement of accommodation

Refraction was 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, 2005b; Kasthurirangan et al., 2003; Schaeffel, 2002; Schaeffel et al., 1993; Wolfsohn, 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. The right eye was covered with a visible block infrared pass filter (Kodak Wratten filter # 89b, high pass at 700 nm) to block the vision of this eye. 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. Only linear calibration functions with r^2 values greater than 0.95 were considered for further analysis.

2.4. Data analysis

The refraction measurements during accommodation are inherently noisy. Therefore, to extract meaningful dynamic metrics, the responses were fit with first order exponential functions (Beers & Van Der Heijde, 1994; Kasthurirangan et al., 2003). No averaging was done and each response was analyzed individually. The latency of each accommodative and disaccommodative response was first determined as described previously (Kasthurirangan et al., 2003). Exponential functions were fit to the entire response from the start of the response, following the latency period, till the end of the stimulus period. Accommodative and disaccommodative responses were fit with individual exponential equations (Eqs. (1) and (2), respectively).

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

$$\text{Disaccommodation : } y = y_0 - a \times (1 - e^{-t/\tau}), \quad (2)$$

where "y" represents the response, " y_0 " the response starting point, "a" the response amplitude, "t" time in seconds and " τ " the time constant.

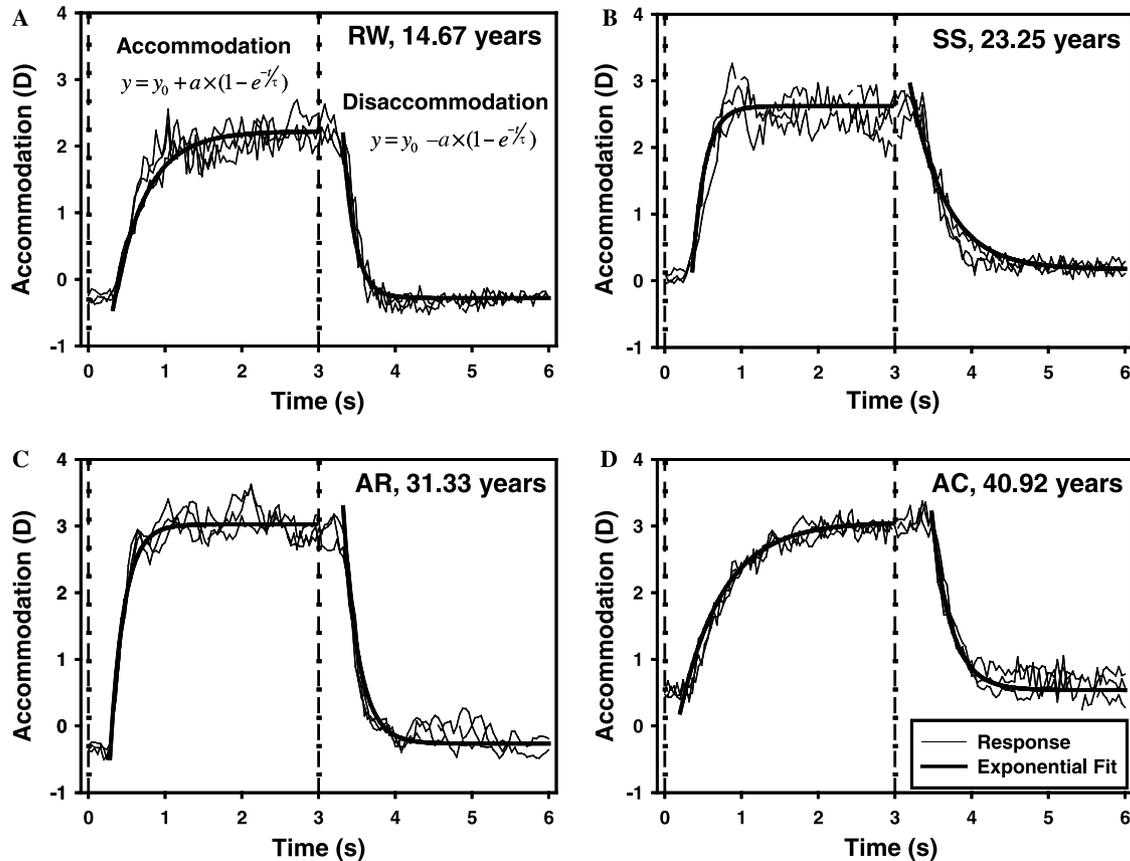


Fig. 2. Three representative accommodative and disaccommodative responses (thin lines) to a 4 D stimulus are shown for four subjects (separate panels) of various ages. Because stimulus durations varied, only three seconds of the response is shown in each case. The vertical dashed line represents the onset of the near stimulus at 0 s and the onset of the far stimulus at 3 s. Exponential functions (thick lines) are fit to one of the accommodative and disaccommodative responses in each case. The equations used to fit accommodative and disaccommodative responses are shown in (A).

Exponential functions were fit using the Levenburg–Marquadt algorithm based on χ^2 reduction (Press, Teukolsky, Vetterling, & Flannery, 2002). In general, the exponential functions provided excellent fits to the data (Fig. 2). Each fit was evaluated based on the residuals, i.e., the difference between the fit and the response at each time point of the response. Only those responses for which the exponential fits resulted in no residual greater than 1.0 D were considered for further analyses. The exponential fits provided response amplitude in diopters and time constant in seconds. The maximum value of the derivative of the exponential fits provided the peak velocity in diopters/second.

Although 10–15 cycles of far and near targets were presented at each stimulus amplitude, not all responses were included for further data analyses because of blinks, lack of a clear response at low stimulus amplitudes or poor exponential fits to individual responses. Therefore, the number of responses included for further data analyses at each stimulus demand is different in a subject and between subjects.

3. Results

Out of the 86 subjects, 20 were rejected for 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 (~ 3 D) stimulus amplitudes ($n = 10$, aged 21 to 31 years) affecting the reliability of PowerRefractor measurements, inability to follow the dynamic far and near targets ($n = 5$, aged 21–36 years) and non-linear PowerRefractor calibration functions

($n = 2$, aged 24 and 27 years). Although 20 subjects were excluded, considerable data from subjects in the same age range as those excluded is reported.

The maximum objective and subjective accommodative amplitudes of the subjects decreased linearly with age (Fig. 3). The calculated age at which accommodation is completely lost is 50 years, as measured from the linear regression fit to the objective accommodative amplitude data. The smallest accommodative amplitude measured objectively was 0.50 D and subjectively was 1.67 D for a 45-year-old subject. The distribution of the maximum accommodative amplitudes was tested statistically with the Kolmogorov–Smirnov normality test. The maximum subjective accommodative amplitude ($p = 0.08$) and maximum objective accommodative amplitude ($p = 0.15$) were normally distributed. The subjectively measured accommodative amplitudes were greater than the objectively measured accommodative amplitudes (paired t test, $df = 65$, $p < 0.01$). The difference between subjective and objective accommodative amplitude decreased with age (p value for linear regression = 0.02; $r = -0.28$; slope = -0.09 D/year).

In 20 young subjects of similar age (20–25 years), the effect of stimulus amplitude on the latency of accommodation and disaccommodation was tested. Stimulus, rather

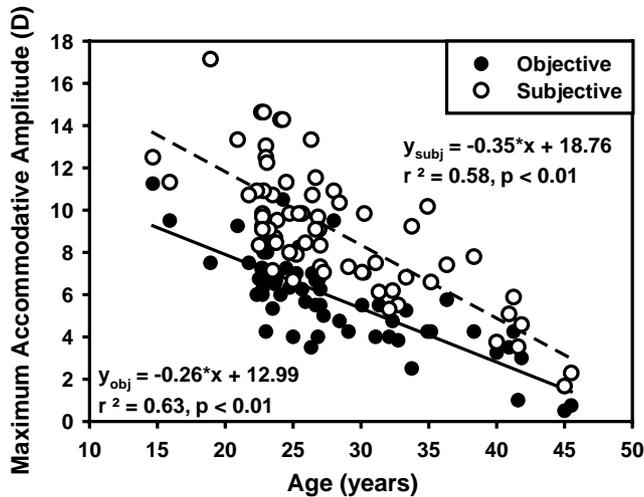


Fig. 3. The maximum accommodative amplitudes measured objectively (filled circles) and subjectively (open circles) are shown as a function of age. The objective maximum accommodative amplitude was lower than the subjective maximum accommodative amplitude in all subjects.

than response, amplitude was chosen for this analysis for two reasons; (a) the response amplitude may be influenced by feedback factors that follow the latency period and (b) a mean and standard deviation of the latency for each stimulus can be calculated. A one-way ANOVA procedure showed that the latency was significantly different as a function of stimulus amplitude for accommodation and disaccommodation. A post hoc analysis with Tukey correction showed that only the 1 D stimulus produced longer latencies (mean \pm SD: 0.38 ± 0.12 s for accommodation and 0.34 ± 0.14 s for disaccommodation) as compared to the other stimulus amplitudes from 2 D to 6 D for accommodation (mean \pm SD latency: 0.29 ± 0.07 s) and disaccommodation (mean \pm SD latency: 0.26 ± 0.07 s). To understand age related changes, the latency of accommodation and disaccommodation were compared as a function of age for a 2 D and a 4 D stimulus amplitude (Fig. 4). The latency of accommodative responses did not change with age for the 2 D ($p = 0.27$ for linear regression; mean \pm SD: 0.32 ± 0.08 s) or the 4 D ($p = 0.08$ for linear regression; mean \pm SD: 0.28 ± 0.07 s) stimulus amplitudes (Fig. 4A). The latency of disaccommodative responses showed a slight yet significant linear increase with age for both the 2 D ($p = 0.02$) and 4 D ($p < 0.01$) stimulus amplitudes (Fig. 4B).

In 86% of the subjects, considering each subjects' data individually, there was a significant linear increase in time constants with the response amplitude of accommodation, as has been reported previously (Kasthurirangan et al., 2003). Fig. 5 shows the time constant vs response amplitude relationships of the same four subjects as in Fig. 2, encompassing the age range in the study. Time constants were not related to response amplitude in the two youngest subjects aged 14.67 years (Fig. 5A) and aged 15.9 years (not shown). In 57 out of the remaining 64 older subjects, time constant increased linearly with response amplitude (Figs.

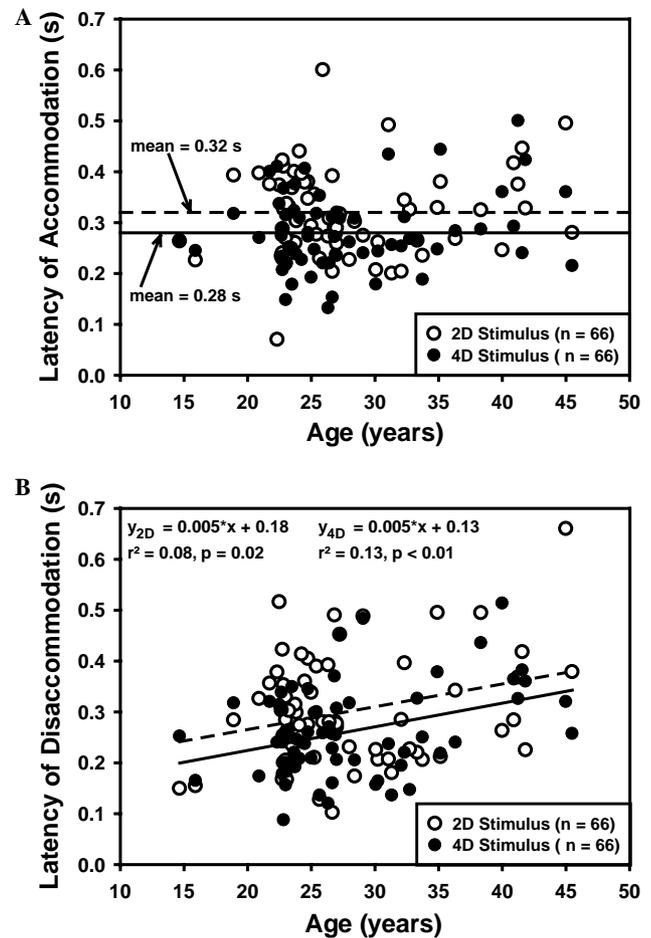


Fig. 4. The latency of accommodation (A) and disaccommodation (B) for a 2 D (open circles) and a 4 D (filled circles) stimulus amplitude are plotted as a function of age. Accommodative latency did not change with age ($p = 0.27$ for 2 D and $p = 0.08$ for 4 D stimuli) and disaccommodative latency increased significantly with age ($p = 0.02$ for 2 D and $p < 0.01$ for 4 D stimuli).

5B–D), with no evidence of any specific non-linear trends in the relationship with increasing age. To explore age related changes in accommodative dynamics, the slopes of the statistically significant linear relationships between time constant and accommodative response amplitude (time constant per diopter of accommodation) were plotted against age (Fig. 6A). For these 86% (57 out of 66) of the subjects, a significant age related increase in the time constant per diopter of accommodation was found (slope = 0.01 s/D/year, $p < 0.01$). In 97% of the subjects, peak velocity of disaccommodation increased linearly with response amplitude, as described previously (Kasthurirangan et al., 2003). No systematic trend between time constants and response amplitude of disaccommodation was found. The slope of peak velocity vs disaccommodative response amplitude relationship provides the peak velocity per diopter of disaccommodation. This did not change with age (p value for linear regression = 0.18, mean \pm SD: 3.93 ± 1.45 s⁻¹, Fig. 6B). Accommodative dynamics slow down with age but not disaccommodative dynamics.

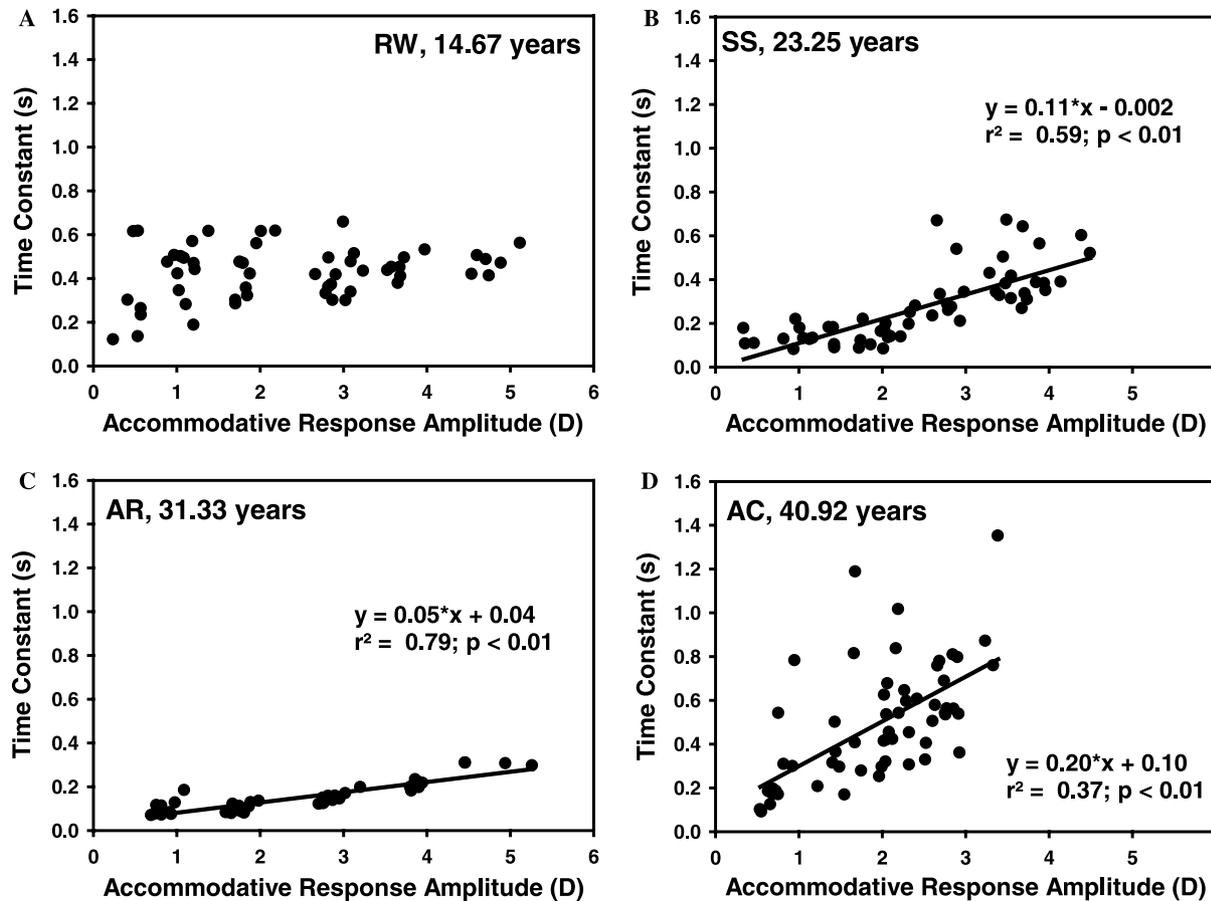


Fig. 5. Time constant vs response amplitude of accommodation plots are shown for the same four subjects as in Fig. 2. In the youngest subject, no clear relationship between time constant and amplitude of accommodation was seen. In the other three subjects, a significant linear increase in time constant with accommodative response amplitude was found ($p < 0.01$).

The age related analyses reported above were also performed as a function of the maximum objective accommodative amplitude. The results are no different whether analyzed as a function of the maximum accommodative amplitude in each subject or as a function of age. For simplicity and to be able to compare with previous studies, the results are reported as a function of age and not the maximum accommodative amplitude of the subjects.

In only 56% of the subjects a significant linear relationship between peak velocity and response amplitude of accommodation was found over the full range of response amplitudes tested. Significant linear relationships were obtained only in subjects between the ages of 14 and 38 years (mean \pm 1SD: 25.65 ± 5.2 years). The shape of the peak velocity vs accommodative response amplitude relationship changed with age. Fig. 7 shows the peak velocity vs response amplitude relationships of the same four subjects as in Fig. 2, encompassing the age range in the study. The relationship is linear in the youngest subject (slope = 2.01 s^{-1} , $p < 0.01$, Fig. 7A). In the next two older subjects, peak velocity saturates at higher response amplitudes (Figs. 7B and C). In the oldest subject, peak velocity is constant over 3.5 D of accommodative response amplitudes (Fig. 7D). The saturation of peak velocity occurs at lower response amplitudes with increasing age.

To further explore the effects of aging on amplitude dependent dynamics, a sub-group comparison of a group of young and old subjects was undertaken. The objective of this analysis was to compare the accommodative dynamics of a group of young and old subjects. An a priori decision was made to include five subjects in each of the young and old groups with a small range of ages within each group and a wide age range between the two groups. Five subjects between 22.33 and 22.75 years (mean \pm SD: 22.6 ± 0.18 years) in the younger age range and five subjects between 38.33 and 41.25 years (mean \pm SD: 40.46 ± 1.37 years) in the older age range satisfied these conditions and were considered. The data from all the subjects in each group were pooled without prior knowledge of any resultant trends. The dynamics for response amplitudes < 3.5 D are shown for these subjects in Fig. 8. Only response amplitudes up to 3.5 D were used for this comparison as this is the upper limit of the accommodative response amplitudes available in the older group.

To statistically test if time constant and peak velocity changed with accommodative response amplitude in each age group, the accommodative responses up to 3.5 D were divided into 0.5 D bins. A one-way ANOVA analysis was performed for the time constant and peak velocity measured for these accommodative response amplitude bins

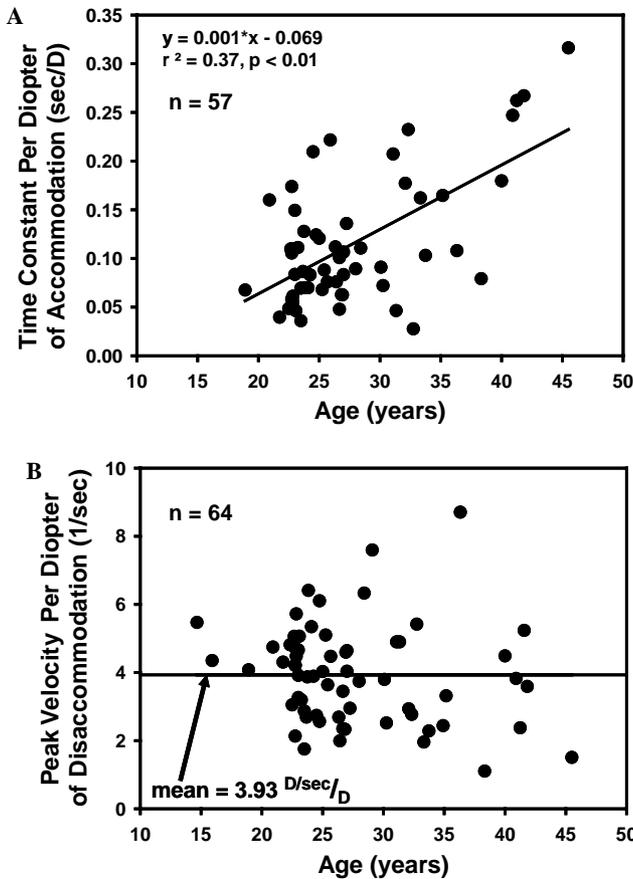


Fig. 6. The slope of significant linear fits to time constant vs response amplitude of accommodation from 86% of the subjects increased linearly with age ($p < 0.01$) (A). The slope of significant linear fits to peak velocity vs response amplitude of disaccommodation relationship did not change with age ($p = 0.18$) (B).

in young and old subjects. In the older group of subjects, time constant increased significantly with amplitude ($F_{6,159} = 16.12$, $p < 0.01$), but peak velocity did not change significantly with accommodative response amplitude ($F_{6,159} = 2.03$, $p = 0.064$). In the younger group, both time constant ($F_{6,203} = 5.07$, $p < 0.01$) and peak velocity ($F_{6,203} = 5.00$, $p < 0.01$) increased with amplitude. The one-way ANOVA analysis revealed that peak velocity is invariant with accommodative response amplitude in the older subjects and increases with response amplitude in the younger subjects, reiterating the trends observed in Fig. 7.

Significant differences between young and old were found for accommodation in the time constant vs response amplitudes (Fig. 8A, F test for comparison of linear fits, $F_{2,372} = 58.27$, $p < 0.01$). Time constants as a function of response amplitude increased at a greater rate for the older subjects than the younger subjects (t test for comparison of slopes: $t = 4.67$, $p < 0.01$, Fig. 8A). Lower peak velocities as a function of response amplitude were recorded in the older subjects than in the younger subjects (Fig. 8B). The peak velocity vs accommodative response amplitude data were fit with a modeled function as described previously

(Kasthurirangan et al., 2003). For this non-linear model, the linear relationship between time constant and accommodative response amplitude for the young group data and the older group data from Fig. 8A was used to calculate the peak velocities for various accommodative response amplitudes up to 3.5 D in each group using Eq. (3). This equation was printed incorrectly in the previous publication (Equation 5 in Kasthurirangan et al., 2003) and is given in the correct form here

$$V_{\max} = a/\tau, \quad (3)$$

where “ V_{\max} ” represents the peak velocity, “ a ” the response amplitude and “ τ ” the time constant.

The modeled peak velocity vs response amplitude curves provide an accurate representation of the peak velocities because of the interrelationship between time constant and peak velocity (Kasthurirangan et al., 2003). This model does not provide parameters that can be statistically compared between young and old subjects. Therefore, the 95% confidence interval of the model fit (grey area) to the young group data is provided for comparison between young and old. The 95% confidence interval of the model was calculated using the 95% confidence interval of the parameters of the linear fits to time constant vs accommodative response amplitude data shown in Fig. 8A. It was mathematically determined that the model fit to the old group (dashed line) crossed the lower 95% confidence interval of the model fit to the young group at an accommodative amplitude of 0.46 D. Therefore, above this accommodative amplitude, peak velocities predicted for the old group are significantly smaller than the peak velocities predicted for the young group. The difference between the peak velocities predicted for the young and old groups above 0.46 D increase progressively with increasing accommodative response amplitude.

For disaccommodation, no significant differences were found between young and old subjects in the time constant vs response amplitude (Fig. 8C, t test for comparison of mean time constant: $t = 0.20$, $p = 0.84$) or peak velocity vs response amplitude relationship (Fig. 8D, F test for comparison of linear fits, $F_{2,341} = 2.79$, $p = 0.063$). These results show that aging affects the speed of accommodation and not that of disaccommodation. When the data plotted in Figs. 8A and B were compared for response amplitudes only up to 2D, the same general relationships were seen and there was still a difference between young and old in the accommodative dynamics for these lower response amplitudes.

Clear differences in dynamics between young and old subjects can be seen for response amplitudes between 2 D and 3 D of accommodation (Figs. 8A and B). To compare the peak velocity of accommodation and disaccommodation as a function of age, a mean peak velocity, for response amplitudes between 2 D and 3 D, was calculated for accommodation and disaccommodation in each subject. The mean peak velocities are plotted against age in Fig. 9. Although there is considerable variability in this

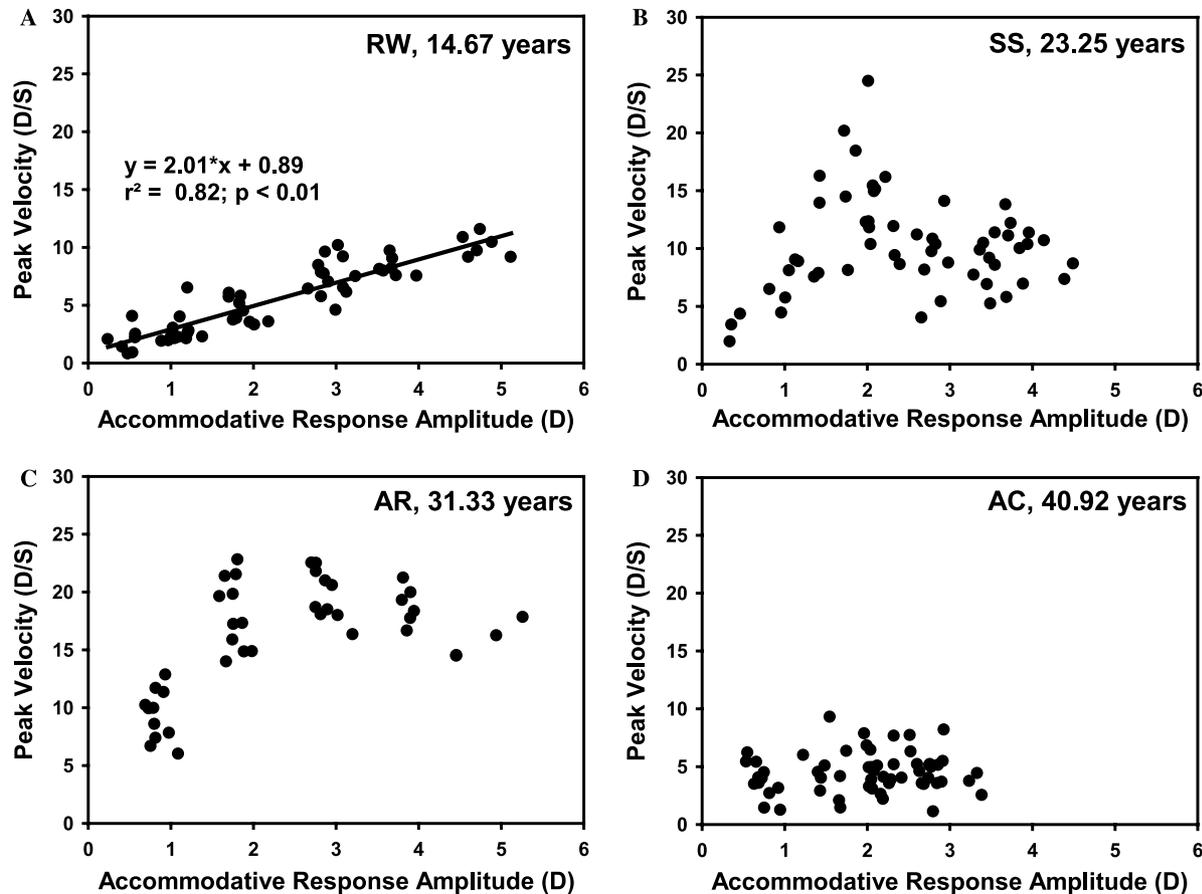


Fig. 7. Peak velocity vs response amplitude of accommodation plots (main sequence) are shown for the same four subjects as in Fig. 2. The form of the relationship changes with age, from linear in the youngest subject to flat in the oldest subject. The saturation of peak velocity occurs at lower response amplitudes with increasing age.

data, it was found that the mean peak velocity for 2–3 D of accommodation decreased linearly with age ($n = 62$, p value for linear regression = 0.04, solid line) and the linear regression fit to the peak velocity for 2–3 D of disaccommodation with age failed to achieve statistical significance ($n = 63$, p value for linear regression = 0.06) so a mean \pm SD = 11.07 ± 2.81 D/S was calculated (Fig. 9). The p values of 0.04 and 0.06 for the linear fits are very similar and so the differences between accommodative and disaccommodative dynamics as a function of age are small. However, the peak velocity of accommodation was progressively lower than the peak velocity of disaccommodation for similar response amplitudes with increasing age.

4. Discussion

Targets in this study were presented at real distances, as opposed to optically, to provide adequate cues for accommodation and to elicit robust accommodative responses. Subjects were also given practice sessions to become familiar with the experimental procedures. Nevertheless, five subjects had trouble following the dynamic accommodative stimuli. All these five subjects had normal amplitudes of accommodation and did not complain of any near vision

problems. It has been reported that normal subjects may have difficulty in accommodative tasks with real targets or with optical targets (Stark & Atchison, 1994). Due to the alignment procedure at the beginning of each trial, the subjects were aware of the far and near target positions prior to data collection. There was no randomization of target positions, although the duration of presentation was randomized. While accommodative dynamics per se may be influenced by the order of target presentation, non-randomization of the target positions is not expected to affect the comparison of dynamics as a function of age, as the experimental procedure was the same for all subjects. The experiment involved repeated accommodative testing for stimulus amplitudes from 1 D to 6 D. Repeated accommodative responses can be elicited with no evidence of fatiguing for up to 30 min to a demanding task with a large stimulus amplitude (6 D) (Vilupuru, Kasthurirangan, & Glasser, 2005). Therefore, the repeated accommodative testing, with frequent breaks, as in the present study is not expected to induce fatiguing or influence the results.

Even with real targets, practice and encouragement, considerable variability was observed in the accommodative responses. The within and between subject variability

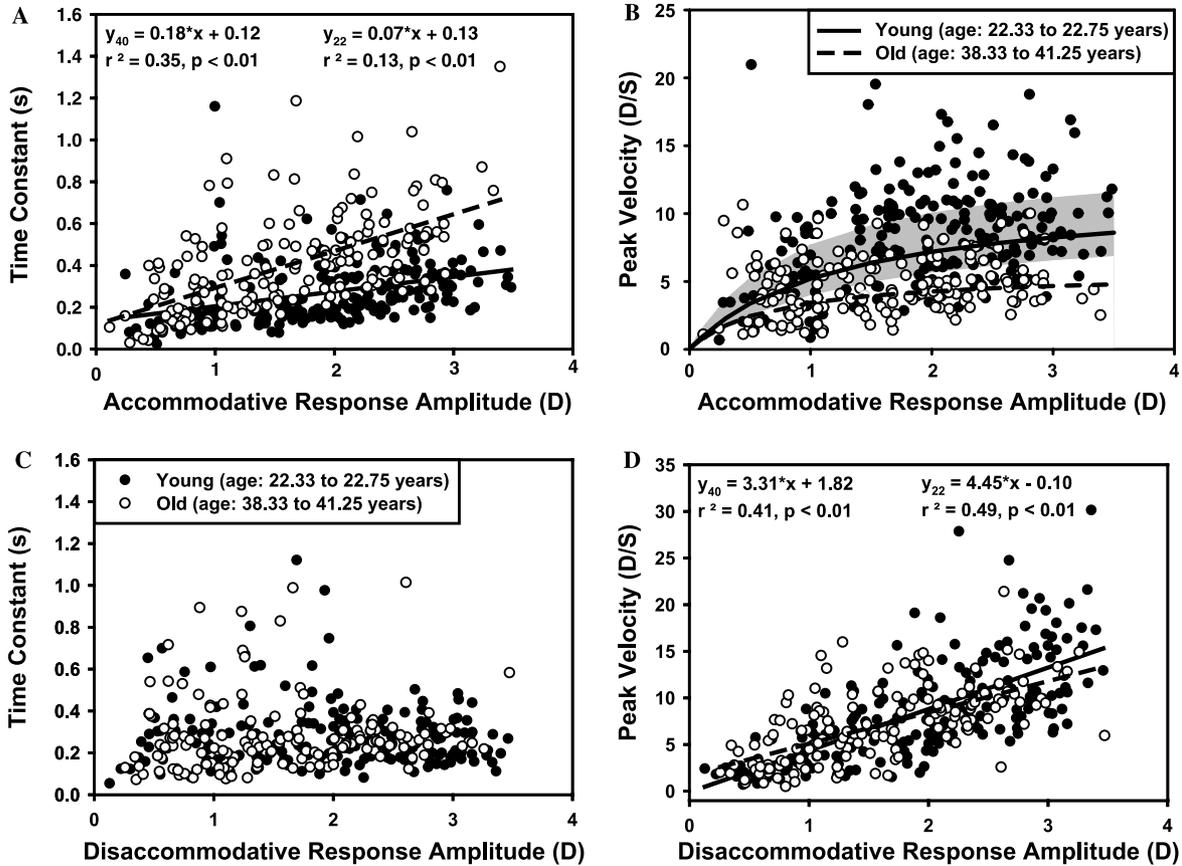


Fig. 8. The dynamics, in terms of time constant (A and C) and peak velocity (B and D), are plotted against the response amplitude of accommodation (A and B) and disaccommodation (C and D) for a young (closed circles) and an old (open circles) group of subjects for response amplitudes less than 3.5 D. The young group consists of five subjects aged 22.33–22.75 years (mean: 22.6 years). The old group consists of five subjects aged 38.33–41.25 years (mean: 40.46 years). Statistically significant linear regression fits are shown as solid black lines for young subjects and dashed lines for older subjects in A and D. In (B) the non-linear model fits are shown as a dashed line for older subjects and as a solid black line with corresponding 95% confidence interval (grey area) for young subjects. For accommodation, the older subjects had larger time constants and smaller peak velocities than the younger subjects. For disaccommodation, there was no difference in the time constants or the peak velocities between young and old.

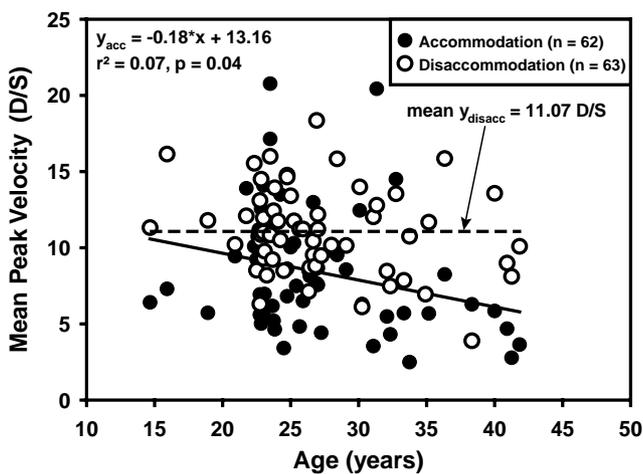


Fig. 9. Mean peak velocity for response amplitudes between 2 D and 3 D of accommodation (filled circles) and disaccommodation (open circles) are plotted as a function of age. The peak velocity of accommodation decreased significantly with age ($p = 0.04$, solid line) and the peak velocity of disaccommodation did not change with age ($p = 0.06$, horizontal dashed line shows mean peak velocity). Consequently, older subjects had lower peak velocities for accommodation than for disaccommodation for corresponding response amplitudes.

is a recognized feature of accommodation (Heron et al., 1999; Kasthurirangan et al., 2003; Schaeffel et al., 1993; Stark & Atchison, 1994). The PowerRefractor measurement frequency is 25 Hz and has noise of approximately ± 0.50 D. To obtain dynamic metrics, first order exponential functions were fit to the responses, as has been done previously (Beers & Van Der Heijde, 1994; Kasthurirangan et al., 2003; Yamada & Ukai, 1997). Recently, second order characteristics of accommodative responses have been described (Bharadwaj & Schor, 2005a; Schor & Bharadwaj, 2005). The first order approximation of the responses ignores any second order characteristics. This study only reports the changes in the first order characteristics of accommodative and disaccommodative responses with age. Additional information on age changes in dynamics may be available from analysis of second order characteristics.

In this study, the speed of accommodation declines with age but not the speed of disaccommodation. This is evident from three different analyses (Figs. 6, 8, and 9). Interestingly, the latency of accommodation did not change with age but the latency of disaccommodation increased with age

(Fig. 4). In the age range over which maximum accommodative amplitude declines by a factor of 10, only subtle changes in the dynamics of accommodation or disaccommodation were observed. Contradictory results in prior studies on accommodative dynamics might have resulted from the relatively small changes in the accommodative dynamics being missed due to using relatively few subjects.

Prior studies of the change in the speed of accommodation with age have reported contradictory results. This may largely be due to a comparison of different response amplitudes in young and old subjects or due to using a small number of subjects. Past studies have used a single large amplitude such as a 5 D stimulus resulting in different response amplitudes in young and old (Schaeffel et al., 1993; Sun et al., 1988; Temme & Morris, 1989), different stimulus amplitudes depending on the subject's maximum accommodative amplitude, consequently resulting in different response amplitudes (Mordi & Ciuffreda, 2004) or a single low response amplitude within the accommodative reserve of each subject (Beers & Van Der Heijde, 1996; Heron et al., 1999). Accommodative dynamics are dependent on the amplitude of the response (Bharadwaj & Schor, 2005a; Ciuffreda & Kruger, 1988; Kasthurirangan et al., 2003). Different response amplitudes are associated with different response dynamics and may involve different amounts of effort. Therefore, comparing responses of different amplitudes in young and old subjects may not be justified. A single low response amplitude may represent a different proportion of the accommodative reserve in young and old subjects. Past studies suggest that only small, if any, changes in accommodative dynamics are expected. In the present study the speed of accommodation declined with age when considering a cumulative index based on various response amplitudes (86% subjects, $n = 57$, Fig. 6A) or a restricted range of response amplitudes (94% subjects, $n = 62$, Fig. 9). The results add to evidence from studies that show a decline in the speed of accommodation with age (Beers & Van Der Heijde, 1996; Schaeffel et al., 1993; Sun et al., 1988; Temme & Morris, 1989).

The speed of disaccommodation with age has been considered in only a few studies (Beers & Van Der Heijde, 1996; Heron et al., 1999; Heron et al., 2002; Heron et al., 2001; Schaeffel et al., 1993; Temme & Morris, 1989). Two of these studies show a reduction in the speed of disaccommodation with age (Beers & Van Der Heijde, 1996; Schaeffel et al., 1993). In one study using continuous A-scan ultrasonography, it was found that the time constants of disaccommodation increase with age for a 1 D stimulus amplitude presented to subjects in a supine position (Beers & Van Der Heijde, 1996). It is not clear why the results are contrary to the results from the present study. The differences could possibly be due to the subjects being supine (Beers & Van Der Heijde, 1996) vs sitting upright and facing forward (present study) or due to differences between biometry vs optical refractive change as a function of age (Dubbelman, Van Der Heijde, & Weeber, 2005), resulting

from age related changes in the lens structure (al-Ghoul et al., 2001; Koretz, Cook, & Kuszak, 1994), density (Heys et al., 2004; Weeber et al., 2005) or refractive index (Moffat, Atchison, & Pope, 2002). In the study by Schaeffel et al. for a 4D stimulus amplitude, peak velocity of disaccommodation decreased with age (Schaeffel et al., 1993). Peak velocity of disaccommodative responses directed towards a common far point has been shown to be related to the response amplitude (Bharadwaj & Schor, 2005b; Kasthurirangan & Glasser, 2005c; Kasthurirangan et al., 2003; Vilupuru & Glasser, 2002). Therefore, if the older subjects had lower response amplitudes for a 4 D stimulus, then lower peak velocities are expected. It is not clear if the age related changes reported by Schaeffel et al. (1993) are true age related changes in the dynamics or a mere consequence of the reduced response amplitudes in the older subjects. The present study agrees with other studies that suggest that the speed of disaccommodation does not change with age (Heron et al., 1999, 2001, 2002; Temme & Morris, 1989).

Recently, it was shown that time constant and peak velocity of accommodation do not change with age (Mordi & Ciuffreda, 2004). That study used optical as opposed to real stimuli and used different stimulus amplitudes depending on the maximum accommodative amplitude of the subjects. The mean time constants of accommodation and disaccommodation for five year age groups from 21 to 45 years were compared and no change was reported. It has been shown previously that time constants increase linearly with accommodative response amplitude (Kasthurirangan et al., 2003). Therefore, the similar time constants for large response amplitudes in young subjects and small response amplitudes in older subjects, reported by Mordi and Ciuffreda (2004), might actually be an indicator of decrease in speed of accommodation with age. Mordi and Ciuffreda (2004) also report on the peak velocity of accommodation as a function of age. Peak velocity was calculated as the "maximum gradient (or slope) of the tangent to the initial response trajectory" (Mordi & Ciuffreda, 2004). This velocity was shown to increase with response amplitude and was independent of age. They provide linear regression fits to peak velocity vs response amplitude relationship for each 5 year age group, but the response amplitudes from each age group are not available from the data provided. Evidently, the linear regression fits were to a range of response amplitudes that were obtained for only a single stimulus amplitude in each age group. Consideration of response amplitudes between 2 D and 3 D, in the present study, showed a linear decrease in peak velocity as a function of age. It is not clear why the results of the present study are different from those presented by Mordi and Ciuffreda (2004).

In the present study, time constant increased and peak velocity decreased with age for similar response amplitudes of accommodation (Figs. 6, 8, and 9). Interestingly, the shape of the peak velocity vs response amplitude (main sequence) relationship for accommodation also changed

with age (Figs. 7 and 8). Within the available amplitude of accommodation, the saturation of peak velocity at lower amplitudes in older individuals (Figs. 7 and 8) suggests that the peak velocity for similar amplitudes is lower in older individuals. In other words, for accommodative amplitudes where the peak velocity is still increasing in young individuals, the peak velocity had saturated and is therefore smaller in older individuals.

Recently, a new ‘pulse-step’ model of accommodation was proposed which suggests that the saturation of peak velocities at high response amplitudes of accommodation reported previously (Kasthurirangan et al., 2003) is due to the firing pattern of the neurons in the Edinger–Westphal nucleus (Bharadwaj & Schor, 2005a; Schor & Bharadwaj, 2005). The model predicted that the peak velocity vs accommodative response amplitude relationship will change with age, with the peak velocity saturating at earlier response amplitudes with increasing age (Schor & Bharadwaj, 2005). The present study empirically demonstrates this change in the shape of the peak velocity vs accommodative response amplitude relationship with age. In their model, Schor and Bharadwaj (2005) also suggested that peak velocity of low accommodative response amplitudes, within the linear range of the peak velocity vs amplitude relationship, does not change with age. They modeled this age invariant trend based on previous studies using smaller number of subjects that did not show any changes in accommodative dynamics with age (Heron et al., 1999, 2001, 2002; Mordi & Ciuffreda, 2004). The present study shows that the peak velocity for similar low amplitude responses is reduced with age (Figs. 8B and 9), in agreement with other studies that show a change in accommodative dynamics with age (Beers & Van Der Heijde, 1996; Sun et al., 1988; Temme & Morris, 1989). The empirical data reported in the present study may be useful in developing or refining the models of accommodation and presbyopia.

It has been shown previously that disaccommodation is progressively faster than accommodation with increasing response amplitudes in anesthetized monkeys and conscious humans (Kasthurirangan et al., 2003; Vilupuru & Glasser, 2002). This difference in dynamics has been attributed to the differences in the biomechanics of accommodation and disaccommodation (Beers & Van Der Heijde, 1994; Kasthurirangan et al., 2003; Vilupuru & Glasser, 2002). It is suggested that the dynamics of accommodation is dominated by the biomechanics of the lens capsule and lens substance and that the dynamics of disaccommodation reflect the elastic properties of the lens, zonules and choroid (Beers & Van Der Heijde, 1996; Beers & Van Der Heijde, 1994). Based on a simple biomechanical model, Beers et al suggest that, of the structures influencing the dynamics of accommodation, the elasticity of the lens/capsule changes with age but that of the zonules and choroid do not (Beers & Van Der Heijde, 1996). The present study suggests that the intraocular structures that dominate dynamics of accommodation undergo age related changes but the structures that dominate disaccommodative dynamics do not

undergo appreciable age related changes in the age range from 15 to 45 years. However, of the structures that dominate disaccommodation, it has been suggested that the choroid undergoes age related changes in the age group used in the present study (van Alphen & Graebel, 1991; Wyatt, 1993) and that the zonular fibers either do not undergo age related changes (Fisher, 1986; van Alphen & Graebel, 1991) or do so after about 70 years of age (Assia, Apple, Morgan, Legler, & Brown, 1991).

Recently, it was reported that the latency of accommodation increases with age and the latency of disaccommodation does not change with age (Mordi & Ciuffreda, 2004). Other studies have shown that the latency of accommodation does not change with age (Heron et al., 1999, 2001, 2002; Sun et al., 1988). The present study adds to the evidence that the latency of accommodation does not change with age. Several studies have addressed the latency of disaccommodation (Heron et al., 1999, 2001, 2002; Mordi & Ciuffreda, 2004). Two of these studies report that the latency of disaccommodation does not change with age (Heron et al., 2001; Mordi & Ciuffreda, 2004). The other two studies report a significant linear increase in the latency of disaccommodation with age (Heron et al., 1999; Heron et al., 2002). Similar to the latter two studies, the present study found that the latency of disaccommodation increases with age.

Once disaccommodation begins, the disaccommodative response occurs with the same speed in young and old subjects. It is possible that an effort to accommodate to a particular stimulus amplitude, produces the same amount of ciliary muscle contraction in young and old, but that less accommodative optical change occurs in the lens of older individuals, due to a reduced accommodative capacity of the older lens (Glasser & Campbell, 1998). At the peak of the accommodative response, zonular tension would then be lower in the older compared to the younger eye. This would be consistent with reduced accommodative movements of the lens/capsular complex in conjunction with configurational changes in the ciliary body (Strenk et al., 1999; Tamm, Tamm, & Rohen, 1992). As the ciliary muscle relaxes during disaccommodation, the initial relaxation in the saturation range would then not impact the lens in the older eye, but would in the young eye (Strenk et al., 1999, 2005). Only once the zonular tension is again restored sufficiently to change the lens shape, would the lens begin to return to an unaccommodated state, and it then would do so with the same speed in old and young individuals. The loss of accommodative amplitude, alterations in accommodative dynamics but without a change in disaccommodative dynamics and increased disaccommodative latency are consistent with prior studies suggesting alterations in the lens and capsule as causative factors in the progression of presbyopia in humans (Fisher, 1973; Glasser & Campbell, 1999; Glasser & Campbell, 1998; Heys et al., 2004; Koretz & Handelman, 1986; Koretz & Handelman, 1988; van Alphen & Graebel, 1991; Weeber et al., 2005; Wyatt, 1993).

It is possible that an inadequate accommodative response to stimulus amplitudes greater than approximately 2 D in older subjects might result in a blurred retinal image. The disaccommodative responses in the older subjects might start from a lag of accommodation with a blurred retinal image, potentially affecting the latency of disaccommodation. Except for one 45-year-old subject (subject JW), all other subjects had subjective accommodative amplitudes greater than 2D. Therefore, for all the subjects except for subject JW, the target at 2D stimulus would have been subjectively clear. The increase in disaccommodative latency with age even for a 2D stimulus suggests that the age related increase in the disaccommodative latency may not be merely due to the influence of blurred retinal image on the latency of disaccommodation.

In conclusion, it was found that aging results in decreased speed of accommodation and increased latency of disaccommodation in the age group 15–45 years. The shape of the peak velocity vs accommodative response amplitude relationship changes with age, with peak velocity saturating at lower response amplitudes in older individuals. The age related decline in the speed of accommodation and not disaccommodation suggests that age related changes leading to presbyopia mostly occur in the crystalline lens and capsule rather than in the ciliary muscle and ciliary body.

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