Factors Affecting Light-Adapted Pupil Size in Normal Human Subjects

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Purpose. To investigate the effect of age, gender, refractive error, and iris color on light-adapted pupil size in humans.

Methods. Pupil diameters of 91 subjects (age range, 17 to 83 years) with normal, healthy eyes were measured using an objective infrared-based continuous recording technique. Five photopic ocular illuminance levels were used (2.15 to 1050 lumens m^{-2}), and the accommodative status of each subject was precisely controlled at a constant level.

Results. Pupil size decreased linearly as a function of age at all illuminance levels. Even at the highest illuminance level, there was still a significant effect of age upon pupil size. The rate of change of pupil diameter with age decreased from 0.043 mm per year at the lowest illuminance level to 0.015 mm per year at the highest. In addition, the variability between pupil sizes of subjects of the same age decreased by a factor of approximately two as luminance was increased over the range investigated. Pupil size was found to be independent of gender, refractive error, or iris color ($P > 0.1$).

Conclusions. Of the factors investigated, only chronologic age had a significant effect on the size of the pupil. The phenomenon of senile miosis is present over a wide range of ocular illuminance levels. Invest Ophthalmol Vis Sci. 1994;35:1132–1137.

The size and responsiveness of the human pupil is governed by the antagonistic actions of the dilator and sphincter muscles in the iris that are controlled by sympathetic and parasympathetic nerves, respectively.[1,2] Several factors are known to affect pupil size, including the level of retinal illuminance,[3] the accommodative state[4,5] of the eye, and various sensory and emotional conditions.[6] In addition, the size of the pupil tends to change as a function of the individual's age,[7–11] with smaller pupils being predominant in the elderly population. Many explanations have been advanced to explain this age-related phenomenon, including a comparative atrophy of the dilator relative to the sphincter muscle, iridal rigidity, decrease in sympathetic tone, reduction in parasympathetic inhibition, and chronic fatigue.[11–16]

The majority of reports that have investigated pupil size as a function of age have done so with the eye in a dark-adapted state.[7–11] This does not reflect the status of the pupil in its normal working conditions in which it plays two important roles: controlling retinal illuminance and determining the quality of the retinal image.[17,18] Further, because individuals differ in their resting or tonic level of ocular accommodation in the dark, differences in this factor may manifest themselves as differences in pupil size. This is especially important because tonic accommodation is known to vary with age.[19]

Under photopic conditions, age-related differences in pupil size appear to be reduced. Several studies maintain that there is a significant reduction in pupil size in the elderly.[16,20,21] However, there is no systematic investigation of this effect as a function of luminance level. In addition to consideration of luminance level, it is essential that photopic experimental conditions be carefully controlled to eliminate accommodation and vergence effects. These also determine pupil size[4,5] and will have a preferential effect in

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Supported by the Visual Research Trust and NSERC (Canada)/Royal Society (UK) bilateral exchange program.
Submitted for publication February 11, 1993; revised June 29, 1993; accepted August 10, 1993.
Proprietary interest category: N.
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Investigative Ophthalmology & Visual Science, March 1994, Vol. 35, No. 3

younger observers, thereby potentially masking any age-related trend.

A further problem associated with pupil measurements is that the pupil is never entirely at rest but undergoes small, continuous oscillations known as hippus.[22] A single "snapshot" estimate of pupil size cannot, therefore, be accepted as a reliable predictor of its true mean size. Instead, the pupil should be monitored continuously for a suitable period to enable a confident estimate of mean size and standard deviation to be obtained.

The present study investigates the variation in pupil size over a large range of age and luminance levels using an objective, infrared, continuous recording technique. Further, our sample of subjects is subdivided to investigate other factors whose effects on light-adapted pupil size are matters of conjecture. These include the gender of the individual, refractive error, and color of the iris.

METHODS

A group of 91 white subjects (age range, 17 to 83 years) were recruited from the student, staff, and clinical population of Aston University. Exclusion criteria included systemic conditions with known ocular involvement, systemic medication with known central nervous system effects, use of topical eye treatment, and neurologic and psychiatric illness. Subjects younger than 50 years of age were visually normal, had acuity of at least 6/6 in the eye used for recording, and had no history of ocular abnormalities. Subjects older than 50 years of age had each undergone recent ocular examination within the University, had visual acuity of at least 6/7.5, and were free of ocular disease. Informed consent was obtained after an explanation of the experimental protocol. All procedures complied with the Declaration of Helsinki.

Continuous recording of pupil diameter was performed over a 10-second fixation period using a Hamamatsu (Hamamatsu, Japan) Perceptscope C3160 connected to the video camera of a Canon R1 infrared optometer (Canon Europe, Amsterdam, The Netherlands) providing an 8.2× magnified image of the eye. The output from the Perceptscope was fed into a digital storage oscilloscope (Gould [Hainault, UK] 1604) connected to an on-line computer (Epson PCe-XT) through an IEEE-488 interface to allow convenient acquisition and subsequent analysis of data. A sampling rate of 102.4 Hz was used during the acquisition period, with a frequency resolution of 0.1 Hz and an amplitude resolution of 0.04 mm.

The experimental protocol employed ensured that influences from accommodation and convergence were controlled and balanced for all age groups for all levels of luminance. When using a wide age range of observers, it is essential that all stimulus conditions are controlled to circumvent bias through differing levels of optical stimulation. Subjects viewed monocularly a fixation target in a Badal (+5 D) stimulus optometer positioned at a vergence of zero diopters to ensure accommodation was at a minimum level for all subjects. A Canon R1 infrared optometer was used in its static mode of operation to ensure that the accommodation was controlled for all subjects to negate the effect of accommodative drive to pupil that will clearly vary with age. The subject's refractive correction (spectacles or contact lenses) was used if required, and a correction factor was applied to the results to account for the effect of induced magnification or minification caused by the corrective lenses.

Subjects maintained steady fixation at the center of a 10° diameter, evenly illuminated circular field in Maxwellian view. Pupil diameter was measured at 5 luminance levels (9, 44, 220, 1100, and 4400 cd m^{-2}) that correspond to ocular illuminances of 2.15, 10.5, 52.5, 263, and 1050 lumens m^{-2}, respectively. One minute was allowed for adaptation to each of the luminance conditions. Measurement order always proceeded from the dimmest to the brightest condition. Mean and standard deviation were calculated for each of the three 10-second fixation periods at each level of luminance. This procedure allows the natural oscillation, or hippus, effects to be evaluated and taken into account during measurement. Continuous recordings of pupil size are shown for 3 luminance levels (9 cdm^{-2}, 220 cdm^{-2}, and 4400 cdm^{-2}) plotted against time (Fig. 1) for a typical young (25 years of age) and a typical older subject (67 years of age) showing the variation in response range and dynamics. Hippus is present except at the extreme values of pupil constriction or dilation, where the magnitude of responsiveness is attenuated by mechanical constraints.

Details of refractive error, gender, and iris color were noted for each subject. Iris color was classified on a 5-point scale that has been shown to provide valid and reliable results.[23] However, because all subjects participating in the present study were white, we needed to use only the first four categories. Subjects were classified into refractive groups on the basis of their mean spherical correction (sphere plus half cylinder power). Those with mean corrections between +0.50 and −0.50 diopters inclusive were classified as being emmetropic whereas all others were classified as either hyperopic or myopic. The number of subjects in each category (refractive error, gender, iris color) is shown in Table 1.

RESULTS

The mean pupil size of 91 subjects plotted as a function of age for five different levels of luminance is shown in Figure 2. The best-fitting linear regression line is shown, and the effect of age is highly significant

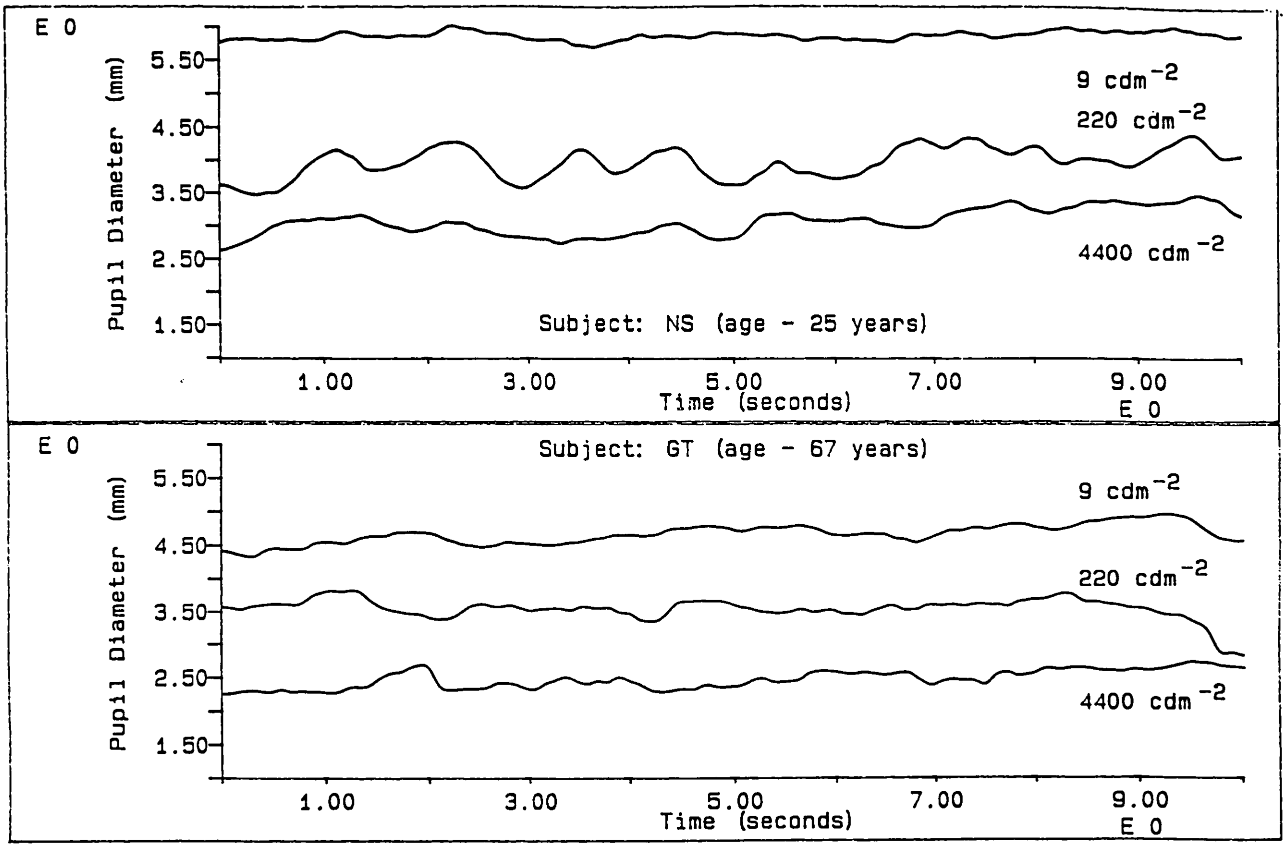


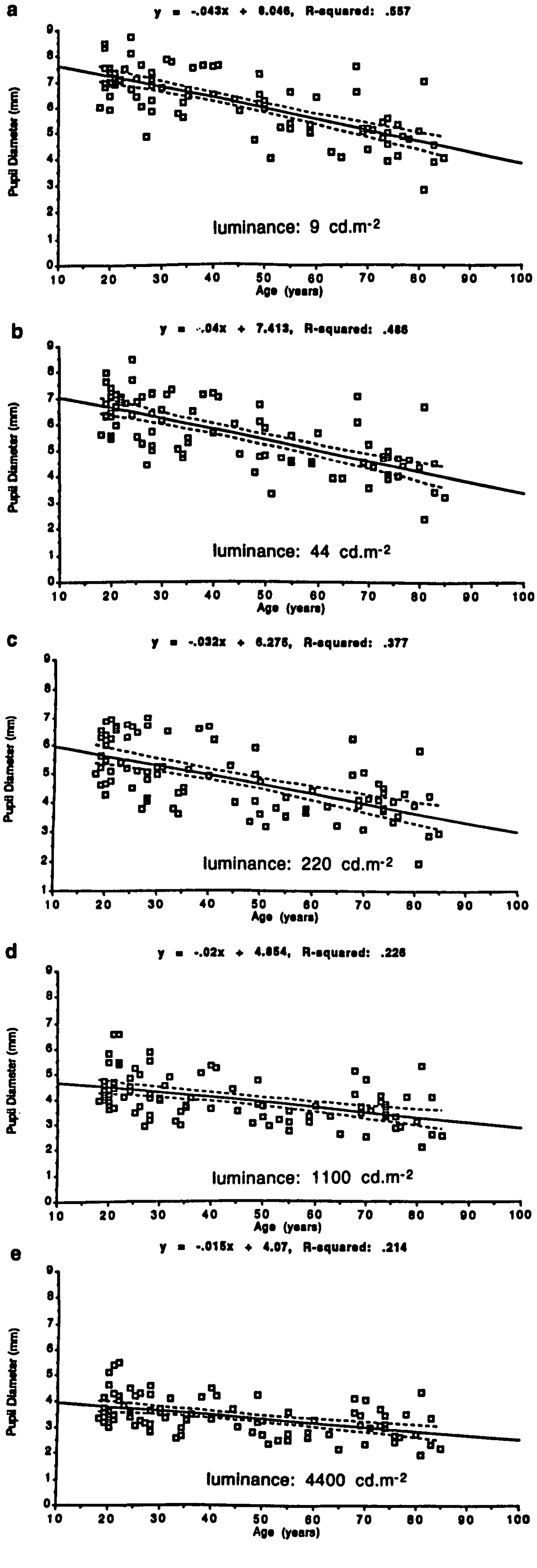
FIGURE 1. Typical pupil size data from a young subject (25 years of age) and an old subject (67 years of age) for three luminance levels (9, 220, and 4400 cdm^{-2}) for a 10-second recording period.

at each luminance level ($P < 0.001$). However, the gradient of the regression line does become smaller as luminance increases. At the lowest luminance level (9 cd m^{-2}), the gradient is 0.043 mm per year. This falls to just 0.015 mm per year at a luminance of 4400 cd m^{-2}. At all luminance levels, there appears to be a substantial amount of interindividual variation in pupil size for subjects of similar age. This variability decreases as luminance increases, and the residual sum-of-squares deviation about the regression line at the

TABLE 1. Number of Subjects and Mean Age of Each Subject Group Classified According to Gender, Refractive Error, and Iris Color

	N	*Mean Age (Yr)*	*df*	*F Value*	P *Values*
Gender					
Female	43	43.8			
Male	48	44.7			
			1, 89	0.078	0.780
Refraction					
Myopia	34	41.5			
Emmetropia	27	40.5			
Hyperopia	30	50.8			
			2, 88	0.413	0.663
Iris grade					
1	30	47.2			
2	26	47.4			
3	21	36.2			
4	14	44.4			
			3, 87	0.734	0.534

Also shown are the results of the analysis of variance examining the significance of each classification on the distribution of residuals around the linear regressions shown in Figure 2.



highest luminance level is approximately half that found at the low luminances.

Gender, refractive status, and iris color of each subject represented by the data points was noted. The residual deviations of the linear regression lines were then examined as a function of these three factors. Dealing with residual deviations removes the variance resulting from the age of the subject and allows us to look at the variance resulting from other factors alone. Repeated measures analyses of variance were performed on these residual deviations using either gender, refractive error, or iris classification as between-subject factors and the residuals from each luminance level regression as the within-subjects factor. The results are shown in Table 1. No significant effect of gender, refractive status, or iris color were observed ($P > 0.1$).

We examined the change in pupil size as a function of luminance for each subject. All but 2 of the 91 subjects demonstrated a significant linear relationship between pupil diameter and log luminance ($P < 0.05$). The gradient of the linear regression for each subject is shown in Figure 3. The gradient tends to decrease with increasing age, that is, a given change in luminance elicits a smaller pupil response in the elderly. However, as with pupil size itself, there is considerable variability in the gradient between subjects of the same age.

DISCUSSION

The results of this study are consistent with previous reports suggesting that pupil size becomes smaller in an almost linear manner with increasing age.[7–11,16,20] We found no significant relationship between gender, refractive error, or iris color with pupil size. This is in agreement with the most recent study investigating light-adapted pupil size at a single level of illumination.[24] The present results extend this conclusion to cover a large range of illumination.

Our results do not support the general clinical impression, also supported by some experimental evidence,[25] that women and myopes have larger pupils. In the present study, all subjects were required to wear their refractive correction during measurement, and accommodation was accurately controlled. It would not be surprising if uncorrected myopes had larger pupils than uncorrected hyperopes when viewing

FIGURE 2. Pupil diameter as a function of age for each luminance condition. Data are fitted by linear regression with the 95% confidence limits indicated by the dotted line. Note the reduction in slope with increasing luminance.

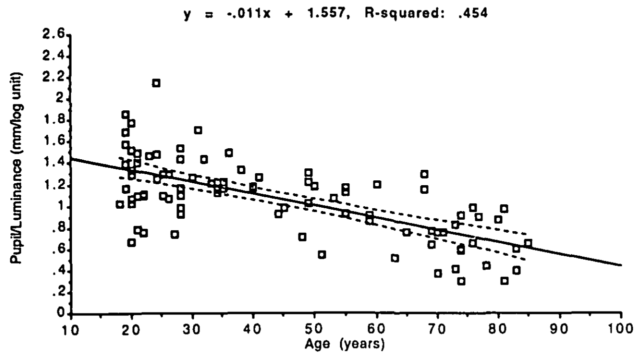


FIGURE 3. Change in pupil diameter per log unit change in stimulus luminance for each subject, plotted as a function of the individual's age. The data are fitted with a best-fitting linear regression.

under closed-loop conditions. The synkinesis between accommodation, vergence, and pupil size is well established, although recent reports[26,27] have questioned the potency and mechanism of the drive to pupil. We eliminated these effects by correcting any refractive error, opening the vergence loop, and controlling the accommodation response by selecting an appropriate closed-loop visual stimulus. If these significant parameters are not controlled, differences may be reported that are of little physiological significance but are simply artefacts of experimental design.

Our data confirm that pupil diameter varies linearly with age. This has previously led to the suggestion that pupil size may be a useful marker of biologic age[28,29] because its measurement is also noninvasive and simple to perform. It has been suggested that low luminance pupil measurements would be preferable as a marker of biologic age because the rate of change in pupil size with age is greater at these luminance levels.[30] Although our results confirm this, the usefulness of a biologic marker is also inversely dependent upon the variability of the measurement within a given chronologic age group.[28,30] Figure 2 shows that interobserver variability decreases with increasing luminance. However, the degree of scatter under all conditions reduces the usefulness of pupil diameter as a marker of biologic aging.

Senile miosis has the potential disadvantage of leading to lower retinal illuminance levels, thereby affecting visual performance under low levels of ambient illumination. However, several positive aspects of a smaller pupil size should not be overlooked. A smaller pupil has the advantage of approaching the optimum size for retinal image formation[17] and may serve to reduce the amount of light scatter produced by an ocular lens that invariably becomes less transparent with age. It has been proposed that this counteracts the expected decline in visual performance as a result of lower retinal illumination.[31,32,33] In addition, depth-of-focus is increased as pupil size is reduced. Finally, a smaller pupil may serve to protect the already vulnerable elderly retina from further phototoxic damage.

Normative pupil size data under various light levels may assist pupillary abnormalities associated with ocular or systemic disease to be identified. These abnormalities often become manifest at some, but not all, levels of adapting luminance. However, this is unlikely to be of much clinical value because variability in pupil size between subjects of the same age is considerable and the precise conditions of pupil measurement would need to be replicated. In addition, many pupillary abnormalities are unilateral, in which case the fellow eye acts as a control.

The data have important implications for design of bifocal contact lenses[34] and intraocular lenses[20] because they provide information across a range of luminances. The annular design of bifocal intraocular and contact lenses requires the central zone to be smaller than the pupil size under photopic conditions to allow both distance and near regions of the lens to produce an adequate retinal image. Differences in pupil size caused by increasing age would place more stringent conditions on the design of a lens for a 70-year-old than a lens ideal for a 50-year-old. A range of bifocal contact lenses or bifocal intraocular lenses designed for use with different pupil sizes would allow optical performance to be optimized and would help eliminate edge glare. Assessment of pupil size seems to be critical in selecting patients for bifocal contact lens fitting or implantation with a bifocal intraocular lens.

In conclusion, we have shown that when oculomotor responses are controlled adequately, pupil size decreases linearly with age over a wide range of photopic luminance levels. The rate of pupil change with age decreases at higher luminance levels, as does the variability between pupil sizes of subjects of the same age. Pupil size shows no dependence upon gender, refractive error, or iris color.

Key Words

pupil, age, refractive error, gender, human

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