Original Article

Do static and dynamic pupillary parameters differ according to childhood, adulthood, and old age? A quantitative study in healthy volunteers

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Purpose: We aimed to evaluate the normative pupillometry values and mean pupil dilatation speed in healthy individuals in different age groups in our study. **Methods:** The study group included 180 eyes of 90 healthy volunteers in different age groups. Group 1 consisted of 30 participants between the ages of 6 and 18, group 2 consisted of 30 participants aged 19–40, and group 3 consisted of 30 participants aged 41–75. Scotopic, mesopic, photopic, and dynamic measurements were taken with automatic pupillometry of Sirius Topographer (CSO, Firenze, Italy). The mean pupil dilation speed at the 18th second was calculated according to dynamic measurements. **Results:** Group 1 had a significantly larger pupil diameter than groups 2 and 3 in all static and dynamic parameters, and the mean pupil dilation speed was the highest among the groups ($P < 0.001$ for all static and dynamic parameters). In addition, group 2 had a significantly larger pupil diameter than group 3 ($P < 0.001$ for all static and dynamic parameters) and the mean pupil dilation speed was faster than group 3 ($P = 0.027$). **Conclusion:** We have presented the static and dynamic parameters and the mean speed of pupil dilatation at the 18th second with automatic pupillometry in healthy individuals in childhood, adulthood, and old age. More studies with higher participants and younger age children are needed.

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Pupillary functions and pupil width are controlled by the autonomic nervous system. Mydriasis occurs when the sympathetic nervous system innervates the iris dilatator muscle; on the other hand, miosis occurs with the innervation of the iris sphincter muscle by the parasympathetic nervous system.[1] Evaluations such as pupillary reflexes, pupil symmetry, and pupil size and shape provide significant information about the diagnosis of neuroophthalmological diseases and intracranial pathologies.[2] Hence, objective and highly reliable examination methods are required in the evaluation of pupillary functions. Pupillary functions are examined subjectively by clinicians; therefore, interobserver reliability may be limited. Today, automatic pupillometries can provide more reliable information about pupillary reflexes by giving reproducible and objective measurements.[3] As a matter of fact, recently, automatic pupillometries have taken their place in the literature and their usability has been investigated in diseases such as coronavirus disease 2019 (COVID-19), diabetes mellitus, and oculomotor nerve palsies.[3-5]

It has been reported that factors such as light stimulus intensity, aging, gender, and smoking may affect pupillary light reflex parameters.[6] Aging is an important factor affecting pupillary characteristics. As a result of atrophy in the iris dilatator muscle with aging, a reduction in the basic pupil diameter occurs.[2,7] However, the effect of age on pupillary light reflexes is still controversial. While there are studies reporting that pupillary reflexes change with age, there are studies showing they are independent of age.[7-9] Studies examining the effect of age in healthy individuals with automatic pupillometry and presenting normative data are very limited.[1,2,10-12] In our study, we investigated the effects of age on static and dynamic pupillometry parameters and mean pupil dilation speed. Moreover, we aimed to determine the normative pupillometry values and mean pupil dilatation speed in healthy individuals in different age groups.

Methods

This cross-sectional study was approved by the local ethical review committee, and written consent was obtained from each patient before the eye examination. Our study was conducted in accordance with the Declaration of Helsinki.

The study group was formed from the patients who came to our hospital's ophthalmology outpatient clinic for examination. Participants consisted of volunteers who did not have any eye

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pathology other than refractive error and whose visual acuity in both eyes was at full level according to the Snellen chart. In all three groups, those with systemic disease and were using ocular and systemic drug, pregnant and breastfeeding women, those with spherical errors greater than 3 D and cylindrical errors greater than 2 D, and those who underwent ocular surgery were excluded from the study. Patients who smoked and used alcohol were also not included in the study. Caffeine was banned 24 h before examination.

Participants were divided into three groups. Group 1 consisted of 30 individuals aged 6–18, group 2 consisted of 30 individuals aged 19–40, and group 3 consisted of 30 individuals aged 41–75. Both eyes of all volunteers were included in the study. Age, gender, and detailed medical history of all cases were recorded. All individuals underwent a full ophthalmoscopic examination including corrected visual acuity, eye movements, color vision, direct and indirect light reflexes, relative afferent pupillary defect (RAPD), biomicroscopic examination, pachymeter-corrected eye pressure with pneumotonometry, and dilated fundus examination. All patients had eye pressure below 21 mmHg. Humphrey visual field examination (with HFA II-i, Carl Zeiss) and retinal nerve fiber layer (with Cirrus HD-OCT; Carl Zeiss Meditec Inc., Dublin, CA, USA) measurements were used to exclude glaucoma in patients.

Measurements were taken by the same clinician at the same time of the day (09.00–12:00). Pupillary parameters were measured by automatic pupillometry of Sirius Topographer (CSO, Firenze, Italy). During the measurement, the patients were asked to look at a target 3 m away with their other eyes to prevent the accommodative reflex. After a 5-min dark adaptation was achieved, scotopic measurements were performed at 0.4 lx illumination, mesopic measurements at 4 lx illumination, and photopic measurements at 40 lx illumination. Following these measurements, dynamic measurements were performed at 500 lx illumination. In dynamic lighting condition, after the 500 lx lighting is turned off, it is possible to monitor pupil dilation in conditions from illumination to absence of light and analyze the pupil size. In the analysis output of the dynamic measurements, the time intervals are determined as 2 second and the first measurement is made at the 0th second. Then, the mean pupil dilation speed can be found by calculating the pupil widths and time differences in the desired time interval. We used the data measured at the 18th second, the longest time we were able to include the largest number of participants in the study. We calculated the mean pupillary dilation speed by dividing the difference in pupil widths at the 0th and 18th seconds by 18 (mm/s). Measurements were performed monocularly, first in the right eye and then in the left eye. Scotopic, mesopic, photopic measurements and dynamic pupillometry measurements at the 0th second and mean pupil dilation speed at the 18th second were compared between groups.

Statistical analysis

G*Power 3.1 was used to calculate the power analysis of the study. Results showed that a minimum of 180 participants were required to achieve a power of 0.85.

Statistical analyses were performed in the Statistical Package for Social Sciences (SPSS) version 22.0 for Windows package program. Descriptive statistics are presented as mean ± standard deviations, frequency distributions, and percentages. Chi-square test was used in the analysis of categorical variables. Equality of variances was tested with the Levene test, and the data distribution was tested using the Kolmogorov–Smirnov test. One-way analysis of variance (ANOVA) test was used for finding differences between groups. Significance level was accepted as <0.05.

Results

Group 1 consisted of 30 participants between the ages of 6 and 18; group 2 consisted of 30 participants aged 19–40, and group 3 consisted of 30 participants aged 41–75. One hundred and eighty eyes of 90 patients were included in the study. There was no difference between the three groups in terms of gender (P = 0.315). The mean age of group 1 was 12.55 ± 3.22 years and there were 16 females and 14 males in the group. The mean age of group 2 was 33.02 ± 6.13 years and there were 13 females and 17 males in the group. The mean age of group 3 was 59.1 ± 9.12 years and there were 17 females and 13 males in the group [Table 1].

Table 2 shows the comparison of scotopic, mesopic, photopic, and dynamic pupil diameters at the 0th second and the mean pupil dilatation speed at the 18th second between the three groups. There were significant differences between the groups in all parameters. Group 1 had a significantly larger pupil diameter than groups 2 and 3 in all static and dynamic parameters, and the mean pupil dilation speed was the highest among the groups. In addition, group 2 had a significantly larger pupil diameter than group 3, and the mean pupil dilation speed of group 2 was faster than that of group 3.

Discussion

Pupillometry gives significant information about the balance between the sympathetic and parasympathetic nervous systems by providing the noninvasive measurement of the pupil diameter. Recent studies have reported that pupillometry may have a place in the diagnosis and treatment follow-up of many diseases.[13-16] Due to the increasing use of pupillometry recently, it is essential to know the normative pupillometry values in healthy individuals in different age groups. In our study, which consisted of groups with the age ranges 7–18, 19–40, and 41–75, mean static and dynamic pupillary parameter values for the three groups were found and differences between the age groups were evaluated. In our study, in which we also evaluated the mean pupil dilation speed, the three groups were found to be significantly different from each other in terms of all parameters. Furthermore, it has been determined that these parameters (scotopic, mesopic, photopic, dynamic and mean pupil dilation speed) decrease with age.

Age is an important factor affecting pupil diameter. Many studies have stated that pupillary diameter decreases with age.[2,17,18] In our study, the largest pupil diameters in scotopic, mesopic, photopic, and dynamic measurements were in the 6–18 years age group and the smallest pupil diameters were in the 41–75 years age group. While Netto *et al*.[17] reported a decrease in pupil width with age in individuals over 20 years of age, they did not find any effect of gender and refraction error on pupil width. In their study of healthy individuals aged 50–79 years, Sharma *et al*.[18] reported that pupillary light

Table 1: Demographic characteristics of the groups

	Group 1 (*n*=60)	Group 2 (*n*=60)	Group 3 (*n*=60)	*P*
Age, mean±SD (range) (years)	12.55±3.22 (6-18)	33.02±6.13 (19-40)	59.1±9.12 (41-75)	
Female/male (*n*/*n*) (number of eyes)	32/28	26/34	34/26	0.315

SD=standard deviation

Table 2: Comparison of the static and dynamic pupillometry measurements and the mean pupil dilation speed in the groups

	Group 1 (*n*=60)	Group 2 (*n*=60)	Group 3 (*n*=60)	*P*
Scotopic pupil diameter, mean±SD (mm)	6.43±0.638	5.63±0.459	4.95±0.874	<0.001[a], <0.001[b], <0.001[c]
Mesopic pupil diameter, mean±SD (mm)	5.00±0.734	4.47±0.574	3.79±0.795	<0.001[a], <0.001[b], <0.001[c]
Photopic pupil diameter, mean±SD (mm)	3.88±0.665	3.47±0.519	3.09±0.565	<0.001[a], <0.001[b], <0.001[c]
Dynamic pupil diameter at the 0th second, mean±SD (mm)	4.09±0.650	3.68±0.661	3.17±0.601	0.001[a], <0.001[b], <0.001[c]
Speed of pupil dilatation at the 18th second, mean±SD (mm/s)	0.145±0.040	0.128±0.029	0.115±0.028	0.004[a], <0.001[b], 0.027[c]

SD=standard deviation. [a]Comparison of groups 1 and 2. [b]Comparison of groups 1 and 3. [c]Comparison of groups 2 and 3

contraction amplitude decreased with increasing age and iris thickness. Rickmann *et al*.,[10] in their study of individuals aged 6–87 years, reported that the pupil diameter decreased with increasing age. Tekin *et al*.[2] enunciated an inverse relationship between age and pupil diameter after the 20s in their study of seven groups, which they formed by dividing the 0–70 years age group into 10 years. Brown *et al*.,[12] on the other hand, found a positive correlation between increasing age and pupil diameter in their study between the ages of 1 and 18. Considering the studies in the literature, it is clear that there are different pupil sizes in different age groups. In general, it has been stated that after the pupil diameter reaches its widest level in adolescence, the pupil diameter decreases due to the increasing parasympathetic effect with age.[2] The results of our study are compatible with the literature.

The mean pupil dilatation speed, which we obtained using dynamic measurements of automatic pupillometry, was evaluated among the three groups, and it was found that the first group was the fastest and the third group was the slowest. Pupillary dynamics has been examined in diseases such as diabetes, Parkinson's, and obstructive sleep apnea, and its use in diagnosis and treatment has been evaluated.[19-21] Marques *et al*.[22] found a decrease in pupillary contraction and dilatation speed due to iris changes in patients with endocular hereditary transthyretin amyloidosis. Additionally, they reported that the light reflex in these patients may not be reliable in evaluating neurological diseases. Therefore, it is important to present normative pupillary values for the healthy population and reveal the affecting factors. Bitsios *et al*.[23] conducted a study with infrared television pupillometry and stated that the speed of pupil constriction and dilation decreases with aging. Ishikawa *et al*.[6] reported that age, gender, light intensity, smoking, and eye symmetry affect the pupillary light reflex, and these variables should be taken into account if light reflexes are to be used as a diagnostic tool. According to Fotiou *et al*.,[24] age negatively affects the maximum contraction speed and acceleration from pupillary parameters. On the other hand, Tekin *et al*.[2] also reported that age affects pupil contraction and dilatation speed in the opposite direction. Despite these existing studies, Kankipati *et al*.[9] reported that age had no effect on the pupillary reflex after illumination after correcting the basic pupil diameter, which decreases with age.

Although the normative data on pupillary parameter values are not plentiful, they increase over time. Tekin *et al*.,[2] Shah *et al*.,[11] Brown *et al*.,[12] Crippa *et al*.,[25] Hsu *et al*.,[26] and Winston *et al*.[1] presented normative values in a healthy pediatric population. Tekin *et al*.,[2] Venkata Sivakumar *et al*.,[27] Sharma *et al*.,[18] and Rickmann *et al*.[10] also reported pupillometric parameter values in the adult population.

Our results provide information on pupil size and pupil dilation speed under static and dynamic conditions for normal subjects in different age groups by using automatic pupillometry. We believe that we achieved results which have high reliability and reproducibility by obtaining objective data with automatic pupillometry in a constant illumination in our study. Our study has some limitations. Measurements of the participants were carried out between 09:00 and 12:00 hours. Due to the effects of circadian rhythm on pupillary function, we think that it may not be correct to use these results for measurements performed outside the hours of our study. In addition, although there are studies reporting that refraction errors have no effect on pupillary functions, we limited the refraction errors in our study group due to reasons such as amblyopia and degenerative myopia.[2] We did not examine whether there was a difference in refractive values among the three groups. Another important inadequacy of our study was that we did not perform an examination by correcting for the decreasing pupil diameter with age. Due to the low compatibility with the device, we could not perform measurements in children under the age of 6 years. Another limitation of our study was that it could not evaluate the mean contraction speed. The reason was that our pupillometry device did not have this facility. The device did not show the amount of miosis according to the time.

Conclusion

In conclusion, in our study, quantitative data are presented for static and dynamic parameters, the pupil dilation speed is measured with automatic pupillometry in healthy individua ls in childhood, adulthood, and old age, and the relationship

between age and pupillary functions is demonstrated. In order to confirm our findings, there is a need for high-participation studies with individuals with higher refraction values by measuring at different times of the day.

Ethics committee approval

Ethics committee approval number: 2022/49

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patients have given their consent for their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published, and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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