Eye Examinations at the National Institute for Longevity Sciences – Longitudinal Study of Aging: NILS-LSA

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The National Institute for Longevity Sciences-Longitudinal Study of Aging (the NILS-LSA) started in 1997, and involves many kinds of examination. The objective of this paper is to outline the eye examinations in the NILS-LSA. The eye examinations consist of checks on refractometry, visual acuity, intraocular pressure, contrast sensitivity, kinetic visual acuity, visual fields, fundus photography, and lens estimation. The subjects were 1,077 men and women aged 40-79 years who participated in the first year examination of the NILS-LSA. All subjective measurements (distant visual acuity, kinetic visual acuity, contrast sensitivity, and mean sensitivity of visual field) declined significantly from the 50s. Age-related structural changes in the lens or hypertensive and arteriosclerotic changes in retinal vessels began at least in the 40s. It is suspected that aging affects the subjective visual functions from the 50s. However, changes in the structure of eye may begin before the 40s. The data from the eye examinations of the NILS-LSA are useful to assess the aging effects on vision and to investigate the relationship between visual function and physical or psychosocial health problems among the elderly.


aging, visual function, epidemiological study, eye examination

INTRODUCTION

Recent population-based studies have shown a significant increase in the prevalence of impaired vision with advancing age 1-4. In addition, visual impairment is negatively associated with the independence and functional status of elderly people 5,6. Similarly, impaired vision may negatively affect cognitive functions and intelligence among the elderly 7-12. Thus, when age-related vision changes are assessed as part of human aging, eye examinations should accompany many kinds of testing in other areas, including physical and psychosocial measurements. However, there are few comprehensive studies on aging including eye examinations, despite a rapid increase in the elderly population in Japan.

The National Institute for Longevity Sciences – Longitudinal Study of Aging (NILS-LSA), a population-based longitudinal study in the middle-aged and elderly population, was designed to describe the physiological and psychological process of aging 13. The major objectives of NILA-LSA are to assess the effects of life style and disease on aging and to detect early markers of age-related disease and disabilities. The total number of participants will be around 2,400 men and women. They will be examined every two years. The NILS-LSA includes various tests of subjective visual function and objective eye measurements. The eye examinations measure refractometry, distant and near visual acuity, keratometry, intraocular pressure, kinetic visual acuity, contrast sensitivity, visual fields, color vision, stereo acuity, fundus photography, and lens estimation. These subjective visual functions may be associated with functional status of elderly people, and these objective measurements seem to show age-related changes in older Japanese. In this article, we outline the eye examinations in the first year of the NILS-LSA.

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METHODS

Data for this report came from the NILS-LSA, a population-based survey of aging conducted in Obu-shi and Higashiura-cho, Aichi prefecture. This survey includes information on clinical evaluation, blood chemical analysis, DNA analysis, sensory functions, body composition and anthropometry, physical functions, nutritional analysis, and psychological tests. All procedures for the study were reviewed by the Ethical Committee of the Chubu National Hospital, and written informed consent was obtained from all subjects. Eligible subjects aged from 40 to 79 were identified by random sampling from the municipal register, and stratified by age and gender. The participants underwent a physical and psychological examination at the research center for the NILS-LSA. From November, 1997 to March, 1999, 1130 subjects (574 men and 556 women) participated in the NILS-LSA in the first wave examination. The 53 subjects (26 men and 27 women) who had a history of cataract surgery in at least one eye were excluded in this study.

At the research center, interviewers administered a questionnaire to the participants. This questionnaire included demographic characteristics, medical and ophthalmologic history, and self-reported vision problems. Subsequently, all eye tests were performed for each eye, except the kinetic visual acuity and stereo acuity tests. For all the subjective tests, participants wore their optimal optical correction for the distance described in the manufacturers' manuals.

For visual acuity testing, distance visual acuity was measured with a Landolt broken ring at 5m. Visual acuity was assessed initially using current distance glasses, if worn. To evaluate best-corrected visual acuity, optimal refraction was obtained subjectively after objective autorefraction with an ARK700A (NIDEK, Gamagori, Japan). In this study, the logarithm value of visual acuity and the value of refractive errors, in a spherical equivalent, were calculated for each eye of the participants. The 333 participants for the first 7 months of the NILS-LSA did not complete the near corrected visual acuity assessment, so near visual acuity was not assessed in this article.

Kinetic vision, defined as the ability to see an object approaching from ahead, was measured by the AS-4C test (Kowa, Tokyo, Japan) with binocular vision, in which the target is a black Landolt broken ring printed on a round white board. Opening of the Landolt ring corresponds to 1 minute of a visual angle at 30 meters. The ring approaches the participant from 50 to 3 meters at 30 km per hour, becoming larger as it nears the participant. We measured the kinetic visual acuity five times for each participant after two sets of training. The mean value of the measurements was adopted as the kinetic visual acuity for the participant.

Contrast sensitivity was measured with a 6500 Vision Contrast Test System (Vistech, Dayton, U.S.A.) at 3 m.

The chart contained contrast gratings for five spatial frequencies: 1.5, 3, 6, 12, and 18 cycles per degree of visual angle. For each spatial frequency, the subject's contrast threshold was the grating of lowest contrast of which the orientation was identified correctly. Contrast sensitivity was the reciprocal of this threshold.

Visual fields were measured using an OCTOPUS 1-2-3 perimeter (Interzeag, Schlieren, Switzerland) : the G1X program with Dynamic strategy. A distant correction was used for the tested eye, and an eye patch was used to occlude the non-tested eye. The mean sensitivity, mean defect, loss variance, and central sensitivity of the second measurement were recorded for each eye. The first visual field measurement was not adopted because almost all participants had little experience of field testing.

Intraocular pressure was measured three times for each eye with a noncontact tonometer (NIDEK NT-3000, Gamagori, Japan) between 9 and 12 AM. The mean value of the three measurements of intraocular pressure was used for analysis.

Hypertensive and arteriosclerotic changes in retinal vessels and optic nerve heads were assessed on fundus photographs without pharmacological pupil dilatation. In each eye, a 45° color photograph centered on the macula area and a 20° color photograph on the disc were taken as digital images (Topcon TRC-NW5S non-mydriatic retinal camera, Japan). The changes in retinal vessels were assessed from a 45° photograph using a modified Keith-Wagener-Barker classification. Subsequently, the ratio of the vertical diameter of the cup to the diameter of the disc in the vertical axis (cup/disc ratio) was estimated on the 20° photographs. The cup/disc ratio is an indicator of glaucomatous optic neuropathy. The cup edge was identified by a kink in the blood vessels at the disc surface.

To evaluate the aging of the lens, Scheimpflug images were recorded and analyzed with an anterior eye segment analysis system (NIDEK EAS-1000, Gamagori, Japan) version 3.05. The images were taken using a 200 watt-second power source, a 10 mm high vertical slit and the temporal location of an illuminator in a dark room. The light scattering intensity, as an indicator of lens transparency, was densitometrically evaluated from the slit images by applying an equipped image analysis program. Light scattering intensity was measured at six points (anterior capsule, anterior cortex, anterior nucleus, central clear zone, posterior nucleus and posterior cortex) on the lens using the method of peak densitometry along the line of the optic axis. The intensity of the scattering light was evaluated in 256 steps and 'computer compatible tapes' were used as one unit.

Data were analyzed using the Statistical Analysis System (SAS) release 6.12. In the analysis, we used four age groups divided by decades ranging from 40-49 to 70-79 years. The differences in continuous variables among the age groups were analyzed using the Tukey multiple comparison method (SAS procedure PROC GLM, LSMEANS statement, ADJUST...
option) and the trends in age group differences were also tested (PROC GLM, CONTRAST option). The Cochran-Mantel-Haenszel tests was used to assess significant relationships among categorized variables (SAS procedure PROC FREQ, CMH option).

In this article, as for the examinations performed for each eye, only the data for the right eye was summarized. The participants’ information based on the questionnaire was not analyzed except for the history of cataract surgery which was used as an exclusion criterion.

RESULTS

Characteristics of the participants are shown in Table 1.

All of the subjective measurements (distant visual acuity, kinetic visual acuity, contrast sensitivity, and mean sensitivity of visual field) had the same specific pattern of results (Figure 1-3). All of these measurements declined with advancing age (p trend<0.001). However, the differences between the subjects in their 40s and 50s were not statistically significant. The subjective visual functions declined significantly from the 50s. Only at low spatial frequencies (1.5 and 3 cycles per degree) in the contrast sensitivity tests, was there no statistical difference between the 50-59 age group and the 60-69 age group.

The mean value of the spherical equivalent was -1.24±0.07 diopters (mean±standard error) in the 40s, -0.78±0.08 in the 50s, -0.13±0.08 in the 60s, +0.09±0.08 in the 70s, respectively (Figure 4). The mean spherical equivalent significantly increased with age (p trend < 0.001), especially from the 40s to 60s (Tukey multiple comparison, p<0.001). The 70-79 age group had more hyperopic refraction than the 60-69 age group, but the difference was not statistically significant.

Intraocular pressure decreased with age (Figure 5). The mean (±standard error) value of intraocular pressure was 14.2±0.16 mmHg in the 40s, 13.9±0.17 mmHg in the 50s, 13.7±0.17 mmHg in the 60s, 13.0±0.18 mmHg in the 70s. Intraocular pressure in the 70-79 age group was significantly lower than that in the other age groups, but the difference was not statistically significant.

Table 1. Characteristics of the participants.

<table>
<thead>
<tr>
<th>age (years)</th>
<th>number</th>
<th>height (cm) [mean±SD]</th>
<th>weight (kg) [mean±SD]</th>
<th>blood pressure (mmHg) systolic [mean±SD]</th>
<th>diastolic [mean±SD]</th>
</tr>
</thead>
<tbody>
<tr>
<td>40-49</td>
<td>298</td>
<td>161.9±9.1</td>
<td>60.3±10.7</td>
<td>118.0±18.1</td>
<td>73.5±11.2</td>
</tr>
<tr>
<td>50-59</td>
<td>279</td>
<td>159.7±8.2</td>
<td>58.3±9.0</td>
<td>121.2±20.5</td>
<td>75.2±11.5</td>
</tr>
<tr>
<td>60-69</td>
<td>266</td>
<td>156.5±8.4</td>
<td>56.3±9.1</td>
<td>127.5±19.7</td>
<td>78.3±11.5</td>
</tr>
<tr>
<td>70-79</td>
<td>234</td>
<td>154.5±8.9</td>
<td>53.6±9.6</td>
<td>126.2±19.5</td>
<td>75.1±10.7</td>
</tr>
<tr>
<td>total</td>
<td>1077</td>
<td>158.3±9.1</td>
<td>57.3±9.9</td>
<td>123.0±19.8</td>
<td>75.4±11.4</td>
</tr>
</tbody>
</table>

SD = standard deviation

Figure 6 shows the relationship between retinal findings classified according to the modified Keith-Wagener-Barker grading and age. The prevalence of hypertensive and arteriosclerotic changes increased with age (Cochran-Mantel-Haenszel tests, p<0.001). On the contrary, the prevalence without changes in retinal vessels decreased with advancing age. In the 40-49 age group, 72.1% of the participants were classified as no change, while the figure was only 21.4% in the 70-79 age group. Even in the 40s and 50s, there was a significant difference in the distribution of the hypertensive and arteriosclerotic changes (Chi-square test, p<0.001). On the other hand, there was no significant difference in the cup/disc ratio among all age groups. The mean values of the cup/disc ratio ranged from 0.40 (standard error: 0.007) in the youngest age group to 0.41 (standard error: 0.008) in the oldest age group.

The relationship between lens transparency and age is shown in Figure 7. The light scattering intensity at the anterior nucleus increased with age (p trend<0.001). There was a significant difference in the intensity in each combination of age groups (Tukey multiple comparison, p<0.001). There was a similar association between the intensity at the anterior cortex and age. These results showed that lens transparency decreased, at least from the 40s.

DISCUSSION

The decline in visual function with advancing age is well known, and visual impairments are associated with decreased physical and psychosocial functioning 5-9). In addition, visual impairment in the elderly is related to increased mortality 29). According to the Salisbury Eye Evaluation (SEE) study, subjective measurements of various visual functions including contrast sensitivity, glare sensitivity, stereopsis, and visual field, in addition to visual acuity, may correlate with mobility and activities of daily living 12). On the other hand, cataracts, one of the structural markers of aging, are the most common cause of age-related vision loss and limits the physical activity of the elderly 30-32). Some previous studies reported that it was also important to assess hypertensive and arteriosclerotic changes in retinal vessels and age-related macular degenera-
Figure 1. Best-corrected visual acuity and kinetic visual acuity according to age groups. The mean logarithm values of both acuities declined with advancing age ($p_{\text{trend}}<0.001$). A Tukey multiple comparison showed the differences were statistically significant among all age groups in both acuities, except for subjects between 40-49 years and 50-59 years. The vertical bars show the standard error of the mean.

Figure 2. The mean logarithm values of contrast sensitivity according to age groups. Contrast sensitivity declined with advancing age in each spatial frequency ($p_{\text{trend}}<0.001$). A Tukey multiple comparison showed the differences were statistically significant among all age groups, except for subjects between 40-49 years and 50-59 at all frequencies and the differences between those 50-59 years and 60-69 years in 1.5 and 3 cycles/degree.

c/d ; cycles per degree

Figure 3. The mean sensitivity of the visual field declined with advancing age ($p_{\text{trend}}<0.001$). Tukey multiple comparison showed the differences were statistical significant among all age groups except for between 40-49 years and 50-59 years. The vertical bars show the standard error of the mean.

Figure 4. The mean spherical equivalent significantly increased with age ($p_{\text{trend}}<0.001$). A Tukey multiple comparison showed the differences were statistically significant among all age groups, except for those between 60-69 years and 70-79 years. The vertical bars show the standard error of the mean.
Figure 5. Intraocular pressure decreased with age ($p_{\text{med}} < 0.001$). Intraocular pressure in the 70-79 years group was significantly lower than that in the other age groups (Tukey multiple comparison, $p < 0.05$). However, there was no significant difference in intraocular pressure among the other three age groups. The vertical bars show the standard error of the mean.

Figure 6. The relationship between hypertensive and arteriosclerotic changes in retinal vessels and age is shown. The changes were classified according to a modified Keith-Wagener-Barker grading (K-W)\textsuperscript{23}).

Figure 7. The relationship between the light scattering intensity at the anterior nucleus and age. A Tukey multiple comparison showed the mean intensity increased significantly with advancing age ($p_{\text{med}} < 0.001$). The vertical bars show the standard error of the mean.

cct; computer compatible tapes.

tion as causes of visual impairment in the elderly\textsuperscript{32,33}. Therefore, to design a comprehensive study of aging in the elderly, eye examinations, consisting of subjective tests on various visual functions and objective eye measurements such as estimation of the lens or fundus photography, are worthwhile including.

In this study, almost all the subjective visual functions were maintained until the 50s, although age-related structural changes in the lens or hypertensive and arteriosclerotic changes in the retinal vessels began at least in the 40s. It is suspected that the aging effects on subjective visual functions may be unclear until the 50s. However, changes in the structure of eye may begin before the 40s. One such problem is presbyopia, which appears as a blur in near vision by the middle 40s, though the human accommodative amplitude declines progressively, beginning in the second decade of life or perhaps earlier\textsuperscript{30}.

Structural changes in the lens begin at birth\textsuperscript{30}. The mass of lens cells is surrounded by an elastic acellular capsule and no
lens cells are shed; therefore the lens grows in size and weight throughout life. The older cells of the lens are displaced towards its center with aging. Consequently, there are a considerable number of post-translational molecular changes that take place in the lens throughout life. These changes are major causes for nucleus cataract development.

Hypertensive and arteriosclerotic changes in retinal vessels, which are associated with retinal hemorrhage, ischemia, and venous obstruction, may cause impairment in visual functions in the elderly. The Atherosclerosis Risk in Communities Study found that generalized narrowing of smaller arterioles and arteriovenous nicking were related to both current and previous blood pressure, and that age was associated weakly with the arterial/venous ratio only in men \(^{35}\). Therefore, the aging effect on retinal vessels should be assessed in further analysis, although our data showed a prevalence free from vessel changes decreased with advancing age.

We found that the mean value of refraction increased monotonically from -1.24 diopters in the 40-49 age group to +0.09 diopters in the 70-79 age group. It was suggested that this trend toward hyperopia was due to decreasing lens power with aging \(^{36}\) or an increasing optical density of the lens cortex making the lens more uniformly refractive \(^{37}\). Another possible explanation is that the relationship between age and refraction reflects a cohort phenomenon. Some surveys showed the prevalence of myopia has increased over the past several decades \(^{38,39}\). A possible reason for the increase in myopia rates in many countries is the increase in formal education, with more time being spent on close work in the past few decades \(^{40}\).

This cross-sectional analysis showed that intraocular pressure decreased with age, which was similar to the findings of other Japanese researchers \(^{41,42}\). We reviewed a large Japanese population retrospectively and found that a cross-section of the population showed a decrease in intraocular pressure with age. However, longitudinal analysis showed an increase in intraocular pressure with age \(^{43}\). It was suspected that birth cohort differences in ocular characteristics influenced intraocular pressure. It is expected that our findings will be confirmed prospectively by the progression of the NILS-LSA in the future.

Our data indicate the same pattern of age-related decline in all of the subjective measurements. It appears that the decline in kinetic visual acuity, contrast sensitivity, and visual field is due to the decline in visual acuity. However, the SEE study showed that, like visual acuity, contrast sensitivity, glare sensitivity, stereo acuity, and visual field declined with age as in our results, and the correlation among these vision tests was low-to-moderate, suggesting several different dimensions of vision were being assessed \(^{20}\). Therefore, our findings on subjective measurements may reflect not only the decline in visual acuity, but also various aspects of vision.

It is important to select noninvasive methods when conducting epidemiological surveys. Therefore, our eye examinations were performed without pupil dilatation which carries the risk of glaucoma attack \(^{46}\) and can influence other survey programs. Thus, we could not assess lens or macular degeneration in detail. The NILS-LSA is a population-based longitudinal study on aging, which contains information on clinical evaluation, blood chemical analysis, DNA analysis, sensory functions, body composition and anthropometry, physical functions, nutritional analysis, and psychological tests. Moreover, the eye examinations include subjective measurements of various visual functions and several objective measurements. Thus, the data from the eye examinations of the NILS-LSA may be useful not only to determine reference values in normal aging of the eye, but also to investigate the relationship between visual function and other physical or psychosocial variables.

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