Amplitude of Accommodation in Type 1 Diabetes

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PURPOSE. People with diabetes have accelerated age-related biometric ocular changes compared with people without diabetes. We determined the effect of type 1 diabetes on amplitude of accommodation.

METHODS. There were 43 participants (33 ± 8 years) with type 1 diabetes and 32 (34 ± 8 years) age-balanced controls. There was no significant difference in mean equivalent refractive error and visual acuity between the groups. Amplitude of accommodation was measured using two techniques: objective by determining the accommodative response to a stimulus in a COAS-HD wavefront aberrometer and subjective with a Badal hand optometer. Influences of age and diabetes duration on amplitude of accommodation were analyzed using multiple regression analysis.

RESULTS. People with diabetes had lower objective (2.7 ± 1.6 diopters [D]) and subjective (4.0 ± 1.7 D) amplitudes than controls (objective 4.1 ± 2.1 D, subjective 5.6 ± 2.1 D). Across both groups, objective amplitude was less than subjective amplitude by 1.4 ± 1.2 D. For subjective amplitude, the duration of diabetes contributed 57% variation to the loss of amplitude relative to that provided by age. For the objective amplitude and only objective amplitude and the whole group, the duration of diabetes contributed 57% variation to the loss of amplitude relative to that provided by age. For the objective amplitude and only the diabetes group, this was 78%. For subjective amplitude, the corresponding proportions were 68% and 103%.

CONCLUSIONS. Lowered amplitude of accommodation exists in individuals with type 1 diabetes when compared with age-matched controls. The loss correlated strongly with duration of diabetes. The results suggest that individuals with diabetes will experience presbyopia earlier in life than people without diabetes, mainly due to changes in the lens.

Keywords: amplitude of accommodation, diabetes type 1, presbyopia

Diabetes mellitus is a group of metabolic diseases characterized by chronic hyperglycemia. Its main classifications are type 1 diabetes mellitus (DM1), which is characterized by autoimmune destruction of pancreatic beta-cells that leads to loss of insulin secretion, and type 2 diabetes mellitus, which is characterized by insufficient insulin production; the latter is the most common form. Diabetes affects all parts of the human eye, with diabetic retinopathy being the most clinically obvious complication. The optics and biometry of the eye are also altered in people with diabetes.

In many respects, from an optical perspective, diabetic eyes act like older normal eyes. With increasing age, there are several biometric changes1 that seem to be exacerbated in diabetes: anterior chamber depth decreases, lens thickness increases, lens surface curvatures increase, and lens equivalent refractive index decreases.2-8 As an example, DM1 is associated with nearly twice the rate of change in equivalent refractive index (0.0007/y) compared with people without diabetes.8

Studies have reported lower amplitudes of accommodation in people with diabetes than in healthy age-matched controls,9-12 with two of them using wide age ranges.9,12 Moss et al.,9 Pawelski and Gliem,13 and Braun et al.14 found that duration of diabetes explained approximately 60%, 46%, and 40% as much variation of amplitude, respectively, as did age.

Leffler et al.15 found that the preferred reading addition in a 43- to 71-year-old population was significantly related to the duration of diabetes, although not the presence of diabetes, such that the addition was predicted to increase by 0.06 diopters (D) per year of diabetes duration.

With the exception of Yamamoto et al.,16 who used an indirect method based on pattern-reversal visually evoked cortical potentials, the above studies were subjective techniques and were thus affected by depth of focus, which overestimates amplitude. In this study we obtained direct objective as well as subjective estimates in order to better understand loss of accommodation accompanying DM1.

METHODS

Participants

This investigation comprised participants under 47 years of age. There were 43 participants (33 ± 8 years) with DM1 and 32 (34 ± 8 years) age-matched control participants. Details of participants are given in the Table. There were no significant differences in the mean equivalent refractive error and visual acuity between the two groups.
Typed 1 Diabetes and Amplitude of Accommodation

Table. Characteristics of Participants For Amplitude of Accommodation Testing

<table>
<thead>
<tr>
<th></th>
<th>DM1</th>
<th>Controls</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of participants</td>
<td>43</td>
<td>32</td>
<td>0.43</td>
</tr>
<tr>
<td>Age (mean ± SD) and age range, y</td>
<td>(33 ± 8), 19–46</td>
<td>(34 ± 8), 20–46</td>
<td>0.04*†</td>
</tr>
<tr>
<td>Number of eyes, R/L</td>
<td>30/13</td>
<td>29/3</td>
<td></td>
</tr>
<tr>
<td>Sex, F/M</td>
<td>17/26</td>
<td>19/13</td>
<td>0.09†</td>
</tr>
<tr>
<td>Visual acuity, logMAR</td>
<td>−0.05 ± 0.07</td>
<td>−0.01 ± 0.27</td>
<td>0.41</td>
</tr>
<tr>
<td>Log contrast sensitivity</td>
<td>1.83 ± 0.14</td>
<td>1.91 ± 0.08</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Spherical equivalent refraction, D</td>
<td>−0.83 ± 1.04</td>
<td>−0.62 ± 0.83</td>
<td>0.35</td>
</tr>
<tr>
<td>Anterior chamber depth, mm</td>
<td>2.94 ± 0.29</td>
<td>3.05 ± 0.28</td>
<td>0.18</td>
</tr>
<tr>
<td>Lens thickness, mm</td>
<td>3.97 ± 0.31</td>
<td>3.86 ± 0.25</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Axial length, mm</td>
<td>23.52 ± 0.90</td>
<td>23.79 ± 0.86</td>
<td>0.19</td>
</tr>
<tr>
<td>Objective amplitude of accommodation, D</td>
<td>2.7 ± 1.6</td>
<td>4.1 ± 2.1</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Subjective amplitude of accommodation, D</td>
<td>4.0 ± 1.7</td>
<td>5.6 ± 2.1</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>HbA1c, mM</td>
<td>8.0 ± 1.2</td>
<td>5.0 ± 0.4</td>
<td>&lt;0.01*</td>
</tr>
<tr>
<td>Diabetes duration, y</td>
<td>16 ± 8</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

R/L, right/left; F/M, female/male.
* Significant difference between groups with unpaired t-test.
† χ² test.

Visual functions testing and ocular health assessment included case history, slit lamp biomicroscopy, fundus examination, intraocular pressure (I-Care, Tiolat Oy, Helsinki, Finland), and color vision assessment (Lanthony desaturated D15). Blood was collected from participants and analyzed for HbA1c levels.

Participants with corrected visual acuities ≥0.1 logMAR, Pelli-Robson contrast sensitivity scores ≥ 1.65, equivalent spherical refraction ≤ ±3.5 D, and normal color vision were included. Participants with mild diabetic retinopathy were also included, for example, microaneurysms, hard exudates, cotton-wool spots, and/or mild retinal hemorrhages. Some participants were recruited through the Longitudinal Assessment of Neuropathy in Diabetes using novel ophthalmic Markers (LANDMark) study at the Institute of Health and Biomedical Innovation. Participants were screened for other conditions that could affect accommodation, including, for example, microaneurysms, hard exudates, cotton-wool spots, and/or mild retinal hemorrhages. Some participants were recruited through the Longitudinal Assessment of Neuropathy in Diabetes using novel ophthalmic Markers (LANDMark) study at the Institute of Health and Biomedical Innovation. Participants were excluded if they had conditions that could affect accommodation, such as glaucoma, retinal disease, hemorrhage, or severe visual impairment.

Objective amplitude of accommodation was measured using a Complete Ophthalmic Assessment System high-definition wavefront aberrometer (COAS-HD, Wavefront Sciences, Albuquerque, NM, USA). Usually, the high-contrast internal target of the aberrometer is fogged automatically in the “auto-acquire mode” by approximately 1.5 D, but the position of the internal target can be controlled manually in “acquire (single) mode” to provide a variable accommodative stimulus. A calibration procedure for this has been described.19 Accommodative response was determined as the difference in mean spherical equivalent refractions between the two modes, where the refraction was determined from the average of three aberration measurements using second- and fourth-order Zernike aberration terms for a 4-mm pupil. The aberrations were referenced to the anterior corneal plane. The target was adjusted in 1-D stimulus steps until it was clear that a maximum accommodation response had been achieved. Pilot work established the optimum luminance of the target. Figure 1 presents an example to determine objective amplitude of accommodation.

Analysis

To determine the relationship between accommodative amplitude and diabetes, multiple regression analysis was performed, with age and diabetes duration as predictor variables. Bland-Altman plots and paired t-tests were used to compare objective and subjective measures of amplitude of accommodation.

Results

Figure 2 is a Bland-Altman plot of agreement between objective and subjective methods for combined data of both DM1 and controls. Objective amplitudes were smaller than subjective amplitudes by 1.4 ± 1.2 D (P < 0.001, paired t-test). People...
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FIGURE 1. Accommodative response/stimulus curves of a young control participant. Error bars indicate the standard deviations from three measurements.

FIGURE 2. Bland-Altman plot comparing objective and subjective amplitudes of accommodation. Different symbols are used for the DM1 and control groups. The regression fit (central curve), its 95% confidence intervals (intermediate curves), and the 95% prediction limits (outer curves) are shown.

DISCUSSION

In support of a previous study,9 we have found lowered amplitude of accommodation in participants with DM1 when compared with age-matched controls. We have estimated the importance of duration of diabetes relative to that of age to be 0.6 to 1.0, which overall indicates greater importance of age than of diabetes duration. These estimates are a little higher than previous estimates using subjective amplitudes of 0.4 to 0.6.9,13,14

Figure 4 shows predictions of objective amplitude in people with DM1 as a function of age based on the age fit shown in Figure 3A and on the multivariate Equation 1 corresponding to diabetic durations of 5, 10, and 20 years. The age-only equation matches the 10- and 20-year duration plots at 15 and 50 years of age, respectively.

With diabetes had lower objective (2.7 ± 1.6 D) and subjective (4.0 ± 1.7 D) amplitudes of accommodation than controls (objective 4.1 ± 2.1 D, subjective 5.6 ± 2.1 D).

Figure 3 shows the relationship between age and the two measures of amplitude of accommodation for the two groups. The rates of change of both objective and subjective amplitude loss with age were greater in controls than in DM1.

Multiple regression analysis was performed with age and diabetes duration as predictors using the whole subject group (duration of diabetes = 0 for controls). The independent effects of both of these factors on objective amplitude of accommodation were significant, and both contributed significantly to the fit:

\[ y = 8.9(\pm 0.7) - 0.145(\pm 0.018) \text{Age} - 0.083(\pm 0.015) \text{DiabDur} \]

\[ = 0.59, \tag{1} \]

where the numbers in parentheses are standard errors. When the multiple regression analysis was restricted to the DM1 group, again both factors contributed significantly to the fit:

\[ y = 7.1(\pm 0.7) - 0.097(\pm 0.022) \text{Age} - 0.076(\pm 0.025) \text{DiabDur} \]

\[ = 0.51. \tag{2} \]

Similarly, the independent effects of diabetes duration and age on subjective amplitude of accommodation were both significant, and both factors contributed significantly to the fit:

\[ y = 10.7(\pm 0.6) - 0.154(\pm 0.017) \text{Age} - 0.105(\pm 0.014) \text{DiabDur} \]

\[ = 0.68. \tag{3} \]

When the multiple regression analysis was restricted to the DM1 group, again, both factors contributed significantly to the fit:

\[ y = 9.1(\pm 0.7) - 0.103(\pm 0.021) \text{Age} - 0.106(\pm 0.022) \text{DiabDur} \]

\[ = 0.63. \tag{4} \]

From the ratios of the coefficients in Equations 1 to 4, estimates of the contribution of diabetes duration to loss of accommodation amplitude, relative to that provided by age, are, in order, 0.57, 0.78, 0.68, and 1.03.
Although our results show clearly that amplitude of accommodation is reduced in DM1 compared with in controls, and that this difference is exacerbated as the duration of diabetes increases (Fig. 5), the rate of loss with age is smaller in the DM1 group. Taking presbyopia as occurring at 45 years in people without diabetes, Figures 3 and 5 suggest that people with DM1 become presbyopic 3 to 5 years earlier than people without diabetes. The DM1 group in our study may not have been representative of a wider DM1 group. The LANDMark study17, from which the majority of people with DM1 (30/43) were recruited, included participants with DM1 with no or mild diabetic neuropathy in order to facilitate a longitudinal evaluation of the progression of severity of neuropathy. Thus, effects of age on amplitude in diabetes may have been underestimated in this relatively healthy and well-controlled group with diabetes.

Two of the people with diabetes had zero objective accommodation response. This biased the results as it was not known at what age they would have ceased to have a response, but we believed it was appropriate to include them rather than bias the results even more by excluding them.

There are considerable differences in the biometry and optics of lenses between people with and without diabetes,2,4,6–8 indicating that it is mainly the lens that is responsible for loss of amplitude in diabetes. However, there are other possible contributors, including loss of ciliary muscle tone, a deficit in neural input to the ciliary muscle, adverse changes to the zonules, or changing geometrical relationships between the lens and surrounding accommodative structures.

CONCLUSIONS

Objective and subjective techniques showed lowered amplitude of accommodation in participants with type 1 diabetes when compared with age-matched controls, and the loss was affected strongly by duration of diabetes. The results indicate that individuals with diabetes will experience presbyopia earlier in life than people without diabetes and probably earlier in the wider diabetes group than in the well-controlled diabetes group in this study.

Figure 3. Amplitude of accommodation as a function of age in DM1 and controls. (A) Objective amplitude: linear fits are $y = 6.6(\pm 0.8) - 0.117(\pm 0.025)\text{Age}$, $R^2 = 0.38$, $P < 0.01$ with DM1, and $y = 11.9(\pm 1.0) - 0.226(\pm 0.027)\text{Age}$, $R^2 = 0.70$, $P < 0.01$ for controls. The numbers in parentheses are standard errors. (B) Subjective amplitude: linear fits are $y = 8.4(\pm 0.9) - 0.131(\pm 0.025)\text{Age}$, $R^2 = 0.41$, $P < 0.01$ with DM1, and $y = 13.7(\pm 0.9) - 0.252(\pm 0.026)\text{Age}$, $R^2 = 0.73$, $P < 0.01$ for controls.

Figure 4. Objective amplitude of accommodation fits as a function of age for DM1. Plots are the age fit from Figure 3B and the multivariate equation (2) corresponding to diabetes durations of 5 years, 10 years, and 20 years.

Figure 5. Subjective amplitudes of accommodation from the studies of Moss et al.,9 Braun et al.,14 and Pawelski and Gliem,13 as well as from the present study. For Moss et al., mean results have been shown in 5-year intervals from 10 to 15 years; for Braun et al., mean results have been shown in 5-year intervals from 22 to 42 years; and for Pawelski and Gliem, their regression fit is shown. The fits for the present study are those from Figure 3B.
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References