Adult-Onset Myopia: The Genes in Myopia (GEM) Twin Study

Mohamed Dirani,1,2 Sri N. Sbekar,3 and Paul N. Baird1,2

PURPOSE. To report the frequency of adult-onset myopia in a large cohort of Caucasian twins that were assessed as part of the Genes in Myopia (GEM) twin study and to quantify the genetic contribution in adult-onset myopia using the classic twin model.

METHODS. All twins aged 18 years or older were invited to participate in the GEM twin study through the Australian Twin Registry (ATR). Each twin completed a standard questionnaire and underwent a comprehensive eye assessment, including cycloplegic objective examination. Adult-onset myopia was defined as having the first spectacle/contact lens correction at adulthood. To the authors' knowledge, the GEM twin study is the first study of its kind to provide evidence to support a genetic component in adult-onset myopia. (Invest Ophthalmol Vis Sci. 2008;49:3524–3527) DOI:10.1167/iovs.07-1498

Myopia is a common eye condition that affects approximately one in four individuals in Western populations.1 However, the prevalence of myopia is markedly higher (over 80%) in urbanized regions of Southeast Asia, such as Singapore.2 It is estimated that by 2020 approximately one third of the world's population will be affected by myopia.3 As a consequence, the global initiative for the elimination of avoidable blindness (VISION 2020—The Right to Sight) has grouped refractive error as one of five leading causes of blindness and visual impairment in the world.4

Myopia can be categorized by severity and age of onset. Severity is often categorized as low myopia (between −0.50 and −2.99 D), moderate myopia (between −3.00 and −5.99 D), and high myopia as worse than or equal to −6.00 D.4,5 On the one hand, a large proportion of myopia, known as child-

From the 1Centre for Eye Research Australia, University of Melbourne, Melbourne, Australia; the 2Vision Cooperative Research Centre, Sydney, Australia; and 3Genetic Epidemiology, Queensland Institute of Medical Research, Brisbane, Australia. Submitted for publication November 21, 2007; revised January 29, 2008; accepted May 27, 2008.

Disclosure: M. Dirani, None; S.N. Sbekar, None; P.N. Baird, None.

The publication costs of this article were defrayed in part by charge payment. This article must therefore be marked "advertisement" in accordance with 18 U.S.C. §1734 solely to indicate this fact.

Corresponding author: Mohamed Dirani, Centre for Eye Research Australia, The University of Melbourne, 32 Gisborne Street, East Melbourne, 3002, Australia; m.dirani@pgrad.unimelb.edu.au.

Adult-Onset Myopia: The Genes in Myopia (GEM) Twin Study

In the other hand, a large proportion of myopia, known as child-

1,2

Copyright © Association for Research in Vision and Ophthalmology

August 2008, Vol. 49, No. 8

Investigative Ophthalmology & Visual Science
**METHODS**

**Recruitment**

All twins in Victoria, Australia, aged 18 years or older were invited to participate in the GEM twin study through the Australian Twin Registry (ATR). Ethical approval for the GEM study was obtained through the Royal Victorian Eye and Ear Hospital (RVEEH) Human Research and Ethics Committee and the ATR. Written informed consent was obtained from each twin before any testing. The protocol adhered to the tenets of the Declaration of Helsinki and all privacy requirements were met.

**Study Protocol**

Each twin completed a standard questionnaire, and a comprehensive eye examination was administered that included a cycloplegic objective refraction. As part of the questionnaire, the age of onset of myopia was determined based on maximum-likelihood (ML) and likelihood between the sub and the full models (the best-fitting model). Statistical analyses.19 In the GEM twin study, the sex-limitation ADE model was applied, as MZ intrapair correlations were more than double that in DZ twin pairs (rMZ intrapair correlation, 0.50 ± 2.17 D) and DZ twin pairs (−0.015 ± 2.12 D; P = 0.60). There was no statistically significant difference in mean SE between MZ twin pairs (0.50 ± 2.17 D) and DZ twin pairs (−0.015 ± 2.12 D; P = 0.60). There was no statistically significant difference in mean SE between the right eyes (0.025 D; range, +6.75 to −14.50 D) and left eyes (0.104 D; range, +7.5 to −14.00 D; P > 0.05); therefore, statistical analysis in the GEM twin study was undertaken only for the right eye.

**Frequency of Myopia**

Out of the 1224 twins examined, 54 (33 MZ twins and 21 DZ twins) had no objective refraction measurements, because they left the examination before the completion of all tests. In some cases the autorefractor was not available to the primary investigator. A total of 1170 twins were included in this analysis, to estimate the frequency of myopia in the GEM twin study. Myopia (worse than or equal to −0.50 D) was found in 347 (29.66%) of the 1170 twins, with low myopia (between −0.50 and −2.99 D) accounting for 70.03% (243/347), followed by moderate myopia (between −3.00 and −5.99 D; 80/347, 23.05%), and the remaining (24/347, 6.92%) having high myopia (worse than or equal to −6.00 to −14.50 D). All adult-onset myopes (96 twins) had low/moderate myopia (range, −0.50 to −4.00 D) and approximately 70% (68/96 twins) of these had bilateral myopia.

**Table 1. Baseline Characteristics of Twin Pairs in the GEM Study, Defined by Zygosity**

<table>
<thead>
<tr>
<th></th>
<th>MZ Twins</th>
<th>DZ Twins</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Twin pairs, n (%)</td>
<td>345 (56%)</td>
<td>267 (44%)</td>
<td>—</td>
</tr>
<tr>
<td>Age (y)</td>
<td>52.11 ± 15.85</td>
<td>52.63 ± 14.96</td>
<td>0.56</td>
</tr>
<tr>
<td>Sex (male/total)</td>
<td>223/690 (32.3%)</td>
<td>178/534 (33.3%)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>SE (D)</td>
<td>0.051 ± 2.17</td>
<td>−0.015 ± 2.12</td>
<td>0.60</td>
</tr>
</tbody>
</table>

**RESULTS**

**Baseline Measures**

A total of 1224 twins (690 MZ twins and 534 DZ twins) between 18 and 86 years of age (mean, 52.36 ± 15.42 SD) were recruited into the GEM study. Of the twins recruited, approximately two thirds were females (n = 823; Table 1). Most of the twins were of a Caucasian background, and therefore no ethnic comparisons could be undertaken. There was no significant difference in mean SE between MZ twin pairs (0.50 ± 2.17 D) and DZ twin pairs (−0.015 ± 2.12 D; P = 0.60). There was no statistically significant difference in mean SE between the right eyes (0.025 D; range, +6.75 to −14.50 D) and left eyes (0.104 D; range, +7.5 to −14.00 D; P > 0.05); therefore, statistical analysis in the GEM twin study was undertaken only for the right eye.

**Frequency of Adult-Onset Myopia**

Of the twins that had myopia (n = 347 twins), a total of 96, 50 MZ and 46 DZ (96/347; 27.7%) were first prescribed optical correction for myopia (mean SE = −1.47 D) at the age of 18 years or older. Of the 96 twins with adult-onset myopia, 58 (60.4%) were females and 38 (39.6%) were males. In more than 90% of these twins (87/96), myopia developed between the ages of 18 to 30 years (mean SE = −1.54 D) with the remaining (9/96, 9.4%) reporting development of myopia between 31 and 45 years (mean SE = −1.42 D). In the whole GEM twin cohort (twins with refraction measurements), less than 10% of the twins (96/1170, 8.2%) had myopia defined as adult-onset.

**Intrapair Twin Correlations for Adult-Onset Myopia**

Intrapair correlations for SE in all twin pairs (n = 612 twin pairs) were significantly higher in MZ twin pairs (r = 0.82) than in DZ twin pairs (r = 0.36, P < 0.01). In data from only twins with myopia (worse than or equal to −0.50 D), the MZ intrapair correlation (r = 0.77) was significantly higher than that in DZ twin pairs (r = 0.28, P < 0.01). Moreover, a major genetic component of SE was found in twins with adult-onset myopia (MZ intrapair correlation, r = 0.61; DZ, r = 0.16; P < 0.01).

We excluded individuals with adult-onset myopia from the main analysis to determine whether this would have any effect on the overall heritability estimates. After excluding these...
be the best-fit genetic model to explain the variance in SE and the females, the sex limitation ADE model was found to explain 26% of the variance in the females. For both the males and the females, the sex limitation ADE model was found to be the best-fit genetic model to explain the variance in SE (Tables 2, 3).

**DISCUSSION**

The GEM twin study is novel, in that it has provided the frequency of adult-onset myopia in a twin cohort that is more representative of the general population, compared with studies that included selected participants. We found that adult-onset myopia accounted for approximately one third of all myopia and was also present in 8.2% of all twins in our cohort. Our findings demonstrate that onset of myopia during adulthood is common and should be taken into account in the study of myopia, particularly in research investigating its genetic and environmental determinants. For instance, it has been postulated that perhaps some aspect of the workload or how eyes respond to various tasks in adult life accounts for myopia, to assess whether the heritability estimates would differ when compared to the analysis including all twins reported in the GEM twin study. We found that the exclusion of individuals with adult-onset myopia had no significant effect on the heritability estimates reported in the GEM twin study. Moreover, the MZ intrapair correlation was significantly different compared to that in DZ twin pairs, which provided further evidence to support a genetic component in adult-onset myopia. Therefore, it is likely that myopia has a major genetic component, irrespective of the age of onset (childhood/youth onset versus adult-onset).

A limitation in the GEM twin study is the lack of ocular history data that would have confirmed or disproved the self-reported age of myopia onset ascertained through a questionnaire. It may be argued that an individual had myopia for several years before being aware of its existence or being informed of its presence, and this may have inflated the number of twins with adult-onset myopia reported in the GEM twin study. Nonetheless, it is common for studies to determine the age of onset through questionnaires, with the question of age at which one was first prescribed glasses for refractive error being the most commonly asked question. Furthermore, a study by Fleck et al. determined the age of onset of myopia in 151 individuals aged 26 to 64 years by self-report (the age when first prescribed glasses to correct distance vision were prescribed). They found that this method of defining age at onset was reliable and described the experience of obtaining one’s first pair of glasses as a “strong emotional experience.”

In conclusion, we have found that adult-onset myopia is common, with approximately one-third of myopia being acquired in adulthood years in a Caucasian twin population. In addition, all adult-onset myopia reported in the GEM twin study was low to moderate, with no cases of high myopia. Therefore, more research is needed into the biological and developmental processes involved in adult-onset myopia. To our knowledge, the GEM twin study is the first study of its kind

**Table 2. Correlations for SE by Sex for Each Twin Zygosity Group without Adult-Onset Twins**

<table>
<thead>
<tr>
<th>Zygosity</th>
<th>Sex</th>
<th>SE (D)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monozygotic</td>
<td>M/M</td>
<td>0.88 (0.83–0.92)</td>
</tr>
<tr>
<td></td>
<td>F/F</td>
<td>0.76 (0.69–0.81)</td>
</tr>
<tr>
<td>Dizygotic</td>
<td>M/M</td>
<td>0.31 (−0.02–0.58)</td>
</tr>
<tr>
<td></td>
<td>F/F</td>
<td>0.27 (−0.04–0.53)</td>
</tr>
<tr>
<td></td>
<td>M/F</td>
<td>0.39 (0.11–0.61)</td>
</tr>
</tbody>
</table>

**Table 3. Results of Sex Limitation ADE Model Fitting without Adult-Onset Twins**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Model</th>
<th>Log-likelihood</th>
<th>df</th>
<th>χ² fit</th>
<th>cd.df</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>SE</td>
<td>Sex lim. ADE</td>
<td>4190.94</td>
<td>1052</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ADE</td>
<td>4205.26</td>
<td>1055</td>
<td>14.33</td>
<td>3</td>
<td>&lt;0.002</td>
</tr>
<tr>
<td></td>
<td>AE</td>
<td>4210.15</td>
<td>1056</td>
<td>4.89</td>
<td>1</td>
<td>0.03</td>
</tr>
<tr>
<td></td>
<td>E</td>
<td>4531.75</td>
<td>1057</td>
<td>321.597</td>
<td>1</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
to provide evidence to support a genetic component in adult-onset myopia. From our findings, we may postulate that both youth/childhood and adult-onset myopias are influenced similarly by genetics, with the ADE model being the most parsimonious model to explain the variance in myopia, thus indicating that myopia is most likely a spectrum with variable age of penetrance—a finding that has important implications in genetic modeling.

References