Refraction data survey: 2nd generation correlation of myopia

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Refraction data survey: 2nd generation correlation of myopia

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Abstract The objective herein is to provide refraction data, myopia progression rate, prevalence, and 1st and 2nd generation correlations, relevant to whether myopia is random or inherited. First- and second-generation ocular refraction data are assembled from $N = 34$ families, average of 2.8 children per family. From this group, data are available from $N = 165$ subjects. Inter-generation regressions are performed on all the data sets, including correlation coefficient r, and myopia prevalence [%]. Prevalence of myopia is $[M] = 38.5$ %. Prevalence of high myopes with $|R| > 6$ D is $[M-] = 20.5$ %. Average refraction is $\langle R \rangle = -1.84$ D $\pm$ 3.22 ($N = 165$). For the high myopes, $|R| > 6$ D, prevalence for the parents is $[M-] = 25$ %, for the 2nd generation $[M-] = 16.5$ %. Average myopia level for the high myopes, both generations, is $\langle S \rangle = -7.52$ D $\pm$ 1.31 D ($N = 33$). Regression parameters are calculated for all the data sets, yielding correlation coefficients in the range $r = 0.48$–0.72 for some groups of myopes and high myopes, fathers to daughters, and mothers to sons. Also of interest, some categories show essentially no correlation, $-0.20 < r < 0.20$, indicating that the refractive errors occur randomly. Time series results show myopia diopter rates $= -0.50$ D/year.

Keywords Emmetropia · Myopia · Progressive myopia · Refraction · Inter-generational correlation · Diopter rates

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Introduction

The cause of myopia is an intriguing mystery. Undoubtedly, part of the explanation is inherited factors, part is environmental factors. The prevalence of myopia in the United States is estimated at 25–42 % [1], as high as 50–60 % in some of the Asian countries [2, 3]. Although an optical impairment, myopia is fairly harmless with less than 6–7 diopters, but at higher levels, can result in staphyloma, detached retina, glaucoma, detached choroid or vitreous, macular problems. Theories are many and varied for possible causes of myopia, including inherited factors, premature birth, fever, intraocular pressure, excessive near work, poor lighting, etc. The purpose of this report is to quantify inter-generation correlation factors between the first generation (parents) and second generation (children). Using regression techniques, various indices can establish correlations between the fathers and their sons or daughters, and between the mother and their sons or daughters, for the

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four categories of myopia, high myopia, emmetropia, and hyperopia.

Saw et al. [2] ($N = 981$) report myopia incidence rates of 14 %/year for children, i.e., 14 new cases per year, per class of 100 students. Lin et al. [4], $N = 345$ report myopia prevalence of 94–96 % for medical school students at graduation [5–7]. Note that correlation of various parameters between generations is not the same as heritability. Mutti [8], $N = 232$, Zadnik et al. [9], $N = 716$, Kurtz et al. [10], $N = 232$, and Jones-Jordan [11], $N = 1854$, present data relevant to the heritability of myopia. Herein, some of the data sets have correlations between parents and children in the range $0.48 < r < 0.72$, suggesting possible inherited factors, father to daughters, and mother to sons. Equally likely, is the possibility of similar near-work interests, between the parents and children, for instance, a love of reading and academic studies, which could be the explanation. For some group comparisons, there is essentially no correlation between parents and children, with correlation coefficients in the range $r = -0.20$ to $+0.20$, as shown in Figs. 2, 3, 4, and 5.

Interest in this project developed as a result of the observations that [1] Identical twins, develop with virtually identical refractive errors within ± 1 D. Two sets of twins, from different families, report this phenomenon ($N = 4$, not reported here). This suggests an inherited component. [2] Certain professions, requiring long hours of study (engineering, medicine, etc.) can have remarkably high myopia prevalence rates >94 % [4, 12], possibly suggesting an environmental effect. An exponential or linear response function can describe the longitudinal development of myopia, when uncorrected or corrected, respectively [6, 7, 13, 14, 15–17].

Materials and methods

Data are reported from $N = 34$ college families surveyed in the northeast United States, including parents and children. This first- and second-generation demographic data allow calculation of average refraction $\langle R \rangle \pm \langle \text{std.dev} \rangle$ for 9 groups of subjects: the fathers, mothers, sons, daughters, parents, children, males, females, and total averages including all subjects. Basic data parameters, i.e., age and S.E.R. are collected from $N = 165$ subjects from these 34 college families, including age t [years.], refraction $R(t)$ [D], male or female, and number of siblings per family. Inter-generational correlations are calculated, for the categories of myopes [M], high myopes [$M-$] with $|R| > -6$ D, hyperopes, and emmetropes. Four inter-generation group correlations are investigated: father–son, father–daughter, mother–son, and mother–daughter. These various categories and groups are presented in Figs. 2, 3, 4, and 5. Data presented in these 4 figures include average <age> ± std. dev., average refraction $\langle R \rangle$ ±std.dev., regression correlation r between 1st and 2nd generation, and refraction diopter rates $\langle R' \rangle$ [D/year].

Regressions are performed on all the data sets, including correlation r, regression trend-line $\boldsymbol{R}(\boldsymbol{t}) = \langle \boldsymbol{R'} \rangle\, \boldsymbol{t} + \boldsymbol{Ro}$, and myopia prevalence. This allows quantifying the inter-generational correlation factors from father to sons and daughters, mother to sons and daughters, for four groups: [1] All subjects, [2] myopes, [3] high myopes, and [4] emmetropes and hyperopes.

Age and refraction data are collected from a group of families ($N = 34$), each of which has at least one or more college graduate. Average family size is 2.8 children per family. Nominal spherical equivalent refractions (S.E.R.) are provided by 165 subjects. A similar survey technique is employed by Fledelius [12], interviewing medical school students to determine their myopia prevalence, incidence rates, and diopter rates. When refractions are not directly available, the subject's spectacle refractive power was determined with a lens clock, or obtained from the written ophthalmic prescription. Data are stored as [t, $R(t)$] pairs for each individual. Tenets of the Helsinki declaration are adhered to. Subject confidentiality is maintained by deleting subject I.D. from the data set record.

Results

The mean ± SD age of the mothers and the fathers was 59.3 ± 8.6 and 59.6 ± 8.2 years, respectively, at the time refractive data were collected. Among the 68 parents who made up our sample, 41.2 % were myopic. Mothers had a lower frequency of myopia than did fathers, 35.3 versus 47.1 %, respectively. The mean refractive error was −1.38 D ± 3.13 in mothers and −2.41 D ± 3.52 in fathers. The frequency of "high" myopia (spherical equivalent refraction of −6.0 D or more minus) was similar in mothers and fathers with 17.6 % of the mothers and 32.4 % of fathers having at least this amount. Figure 1 shows a distribution diagram for the refraction values of all subjects ($N = 165$). Figure 2 presents refraction data for the 1st generation parent's data, 2nd generation children's data, age statistics for the various groups, inter-generational correlations, and refraction progression rate for the entire data set, $<R'> = -0.2$ D/year. ($8 < t < 27$ years.) Figure 3 presents myopia refraction data for the first generation (parents), second generation (children), myopia prevalence, correlations between generations, and diopter rate for all the myopes $<R'> = -0.50$ D/year ($17 < t < 27$ years). Figure 4 presents statistics for high myopia, including parents, their children, myopia prevalence, correlations, and myopia diopter rate $<R'> = -0.1$ D/year ($22 < t < 27$ years). Figure 5 has statistics for emmetropes and hyperopes, including prevalence for the 1st and 2nd generations, correlation statistics between generations, and refraction rate $<R'> = 0.08$ D/year. A total of 16 different correlations is calculated for 4 groups, Figs. 2, 3, 4, and 5. Of these 16 different regressions, only 6 show a significant correlation coefficient with $0.3 < r < 0.7$, as indicated in Figs. 2, 3, 4, and 5.

Statistics

Figure 2 presents the data summary for all subjects. The correlations $r = +0.27$ father to daughters and

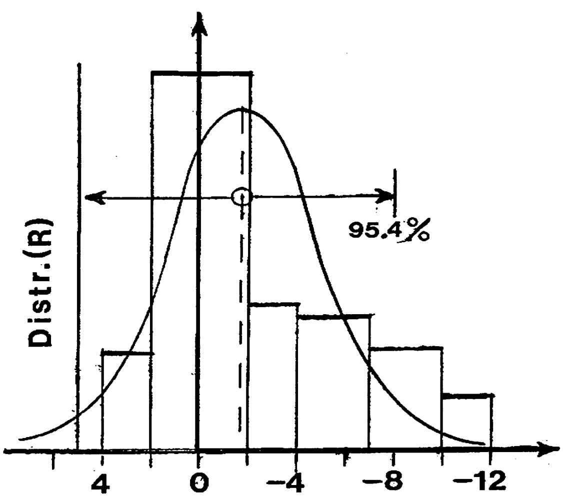

Fig. 1 Statistical distribution of refraction for $N = 165$ subjects, average refraction $<R> = -1.84$ D. ± 3.22, 95 % confidence interval as shown

Inter-generation Correlation of Refraction (N = 165)

	Fathers (N=34) <Age> = 59.6y <R> = -2.4D	Mothers (N=34) <Age> = 59.3y <R> = -1.4D
Sons (N=49) <Age> = 28.6y <R> = -1.8D	r = +0.21 (not signif.)	r = -0.08 (not signif.)
Daughters (N=48) <Age> = 28.5y <-1.8D>	r = +0.27 p < 0.05	r = +0.35 p < 0.05

Myopia rate : < R' >⊨ - 1.8 diopt./decade (-0.2 D/yr.)

Fig. 2 Parents to children refraction correlations, $N = 165$ myopes. The correlations $r = +0.27$ and $r = +0.36$ are significant at the $p < 0.05$ level

All Myopes, Inter-generation Correlations (N = 62)

	Fathers (N=16) <R> = -5.01 D	Mothers (N=12) <R> = -5.88 D
Sons (N=16) <R> = - 5.75D	r = -0.24 (not signif.)	**r = +0.48** p < 0.05
Daughters (N=18) <R> = - 5.06D	**r = +0.72** P < 0.001	r = +0.36 (not signif.)

Myopia rate: < R'> = - 4.9 diopters/decade (- 0.49 D/yr.)

Fig. 3 Parents to children refraction correlations, $N = 62$ myopes. The correlation values $r = +0.72$ and $+0.48$ are significant at the $p < 0.001$ and $p < 0.05$ level, respectively

$r = +0.36$ mother to daughters are significant at the $p < 0.05$ level, the values $r = +0.21$ and -0.08 (involving the sons) are not significant, $p > 0.1$. Figure 3 presents the data summary statistics for all myopic subjects; the correlation values $r = +0.72$ father to daughters and $r = +0.48$ mother to sons are significant at the $p < 0.001$ and $p < 0.05$ level, respectively, the other r values -0.24 and $+0.36$ are not significant, $p > 0.1$. Figure 4 displays data summary statistics for the high myopes. None of the r values, $r = -0.08$, $+0.25$, $+0.58$, or $+0.11$, are

Advanced Myopes, Inter-Generation Correlation (N = 33)

	Fathers (N=11) <R> = - 7.09 D	Mothers (N=6) <R> = - 6.67 D
Sons (N=9) <R> = - 7.33 D	r = -0.08 (not signif.)	r = +0.25 (not signif.)
Daughters (N=7) <R> = - 8.43 D	**r = +0.58** (not signif.)	r = +0.11 (not signif.)

Myopia rate: < R' > = -0.9 diopters/decade (-0.1 D/yr.)

Fig. 4 Parents to children refraction correlations, $N = 33$ high myopes. None of the r values are significant perhaps because of the small sample size, $p > 0.1$

Emmetropes & Hyperopes (N = 103)

	Fathers (N=18) <R> = 0.67 D	Mothers (N=22) <R> = 0.59 D
Sons (N=33) <R> = 0.09 D	r = +0.09 (not signif.)	r = +0.34 p < 0.05
Daughters (N=30) <R> = 0.20 D	r = +0.30 (not signif.)	r = +0.35 p < 0.05

Refraction rate: < R' > = 0.08 diopt./yr.

Fig. 5 Parents to children refraction correlations, $N = 103$ emmetropes and hyperopes. The correlation values $r = 0.34$ and $r = 0.35$ are significant at the $p < 0.05$ level. The values $r = 0.09$ and $r = 0.30$ are not significant, $p > 0.1$

significant ($p > 0.1$) because of the small sample size of the high myopes. Lastly, Fig. 5 shows the data summary statistics for the emmetropes and hyperopes. The correlation values $r = +\ 0.34$ mother to sons and $r = +\ 0.35$ mother to daughters are significant at the $p < 0.05$ level. The values $r = 0.09$ and r = 0.30 (involving the fathers) are not significant, $p > 0.1$. Lopes et al. [18] find heritability $\boldsymbol{h}^2 = 0.77$ for spherical equivalent refractive error between the 1st and 2nd generation using monozygotic and dizygotic twins ($N = 1152$ MZ, 1149 DZ subjects). n.b.- regression correlation $\boldsymbol{r}$ of a trait, such as spherical equivalent refractive error between generations as reported here, is not the same as the heritability $\boldsymbol{h}^2$, although both indices range from 0 to 1, and both involve regression correlation between the 1st and 2nd generation (Visscher et al. [19]). Correlation includes both hereditary and environmental factors, however, twin studies are required to deselect the environmental effects. Third-generation grandparent data are not required to calculate correlation r or heritability $\boldsymbol{h}^2$. Figure 6 displays confidence level isocons showing the trade-off between correlation r and the minimum number of subjects N required to achieve a significant confidence level $p < 0.05$.

Discussion

Myopia is often associated with academic students. At some colleges, for some professions, the prevalence can exceed 70–94 % [4, 12]. The debate continues, as to whether the myopes are intrinsically better students, or whether the studying causes the myopia. Whatever the situation, these parameters are correlated.

There are slight differences, in terms of prevalence and average refraction, between the parents and children, slight differences, between the males and females. In other words, according to our results, both generations, parents and children, males and females, all seem equally likely to acquire myopia, both in terms of prevalence, and the average refractive error. Some categories have significant inter-generation correlations, in the range $0.3 < r < 0.7$, suggesting a possible trend, fathers correlating with daughters, mothers with sons. This is an unexpected result, which cannot be detected from inspecting the original data lists. These inter-generational correlations are only revealed by computer analysis of these large groups of

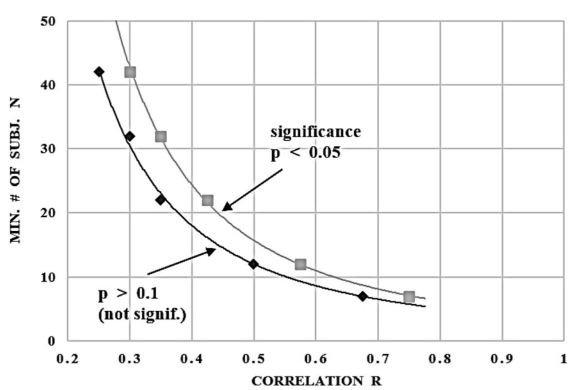

Fig. 6 Confidence level isocons show the trade-off between correlation r and the minimum number of subjects N required to achieve a significant confidence level $p < 0.05$

data. These correlation results suggest a possible sex-linked factor for myopia transmission, rarely reported, beyond the scope of this current report. Correlation ***r*** is not the complete result, the significance level ***p*** (e.g., $p < 0.05$) is also required, which depends strongly on the number of subjects N, Fig. 6.

Limitations of this study include the relatively small number of subjects, which is associated with somewhat wider confidence intervals. For instance, one can say the prevalence of myopia is 38.5 ± 2 % with a large survey, compared with 38.5 ± 5 % with a smaller survey, (see for instance Wu et al. [20] using similar statistical techniques).

Comparing our results with other similar reports, Wang et al. [21] report average myopia $\langle R \rangle = -4.93$ D ± 2.82 D ($N = 3709$), within 1/2 diopter of our value $\langle R \rangle = -5.44$ D ± 2.72 D ($N = 62$), Fig. 2. Similarly, in terms of high myopes, Wang et al. [21] report prevalence of $[M-] = 38.4$ % ($N = 1424$) compared with $[M-] = 20.5$ % ($N = 33$) as reported herein.

Average myopia for the high myopes is $\langle R \rangle = -7.52 \pm 1.31$ D, ($N = 33$). For these high myopes, $R < -6$ D, the prevalence is $[M-] = 20.5$ %, $N = 33$. A comparable report by Lin, Shih et al. [22], $N = 45{,}345$ find $[M-] = 15$ % for high myopes with $R < -7$ D in Taiwan (a slightly different definition of high myopia). Myopia prevalence overall in our study is $[M] = 38.5$ %, $N = 62$, remarkably close to the value $[M] = 41.6$ % reported by Vitale et al. [1] ($N = 9{,}609$) estimating the U.S. myopia prevalence. Lin et al. [4] report myopia prevalence greater than 94 % among medical students ($N = 345$). Our percentage of myopes with contact lenses (most use RGP lenses part-time) is 14.4 %. Four of the hyperopes use bifocals, 5 of the myopes use bifocals, 4 of the myopes use plus lenses, and 3 of the myopes use Progressive Add Lenses (PAL's). Thus, 19.4 % of our myopes use reading glasses of one type or another, all with a "(+) Add" of +1.5 to +2.5 D for reading.

It is well established that other anatomical parameters are correlated with parents and children, including height, weight, eye color, and body build. These well-known inherited traits are frequently observed among the $N = 34$ families (data not reported here). Thus, it is not surprising that refraction is also correlated, in many instances [23, 24, 25]. In terms of observed myopia progression rates after college, Bullimore et al. [26], $N = 104$ report that 36 % of myopes continue to progress at a rate of −0.75 D per 5-year interval (−1.5 D per decade) after college, consistent with our myopia rate results from Fig. 4, showing $R' = -0.9$ D per decade. The role of genetics in explaining inter-generational correlations in refractive error and axial length is very well documented in recent years [18, 23–25, 27, 28], and numerous susceptibility genes have been strongly implicated.

Conclusions

According to our results, if the mother is myopic, there is a 41.2 % chance that a son or daughter will be myopic ($N = 34$). If the father is myopic, there is a 39.5 % chance, if both parents are myopic, there is a 77.8 % chance. Five other studies report comparable myopia prevalence results, consistently showing that the likelihood of a child developing myopia is twice as great with two myopic parents as it is with one myopic parent, as reported by Zadnik et al. [9], Pacella et al. [28], Kurtz et al. [10], Jones-Jordan et al. [11], and Mutti [8].

Compliance with ethical standards

Conflict of interest The authors have no proprietary or financial conflicts of interest.

Appendix I: Regression statistics $N = 165$ subjects

Inter-generation refraction correlations:

(1) Father Rf to sons Rs:
$Rs = 0.20 * Rf - 1.39$ D. [$\sigma = \pm 2.97$ D, $r = 0.212$, $N = 49$]

(2) Father Rf to daughters Rd:
$Rd = 0.23 * Rf - 1.29$ D. [$\sigma = \pm 3.10$ D, $r = 0.267$, $N = 48$]

(3) Mother Rm to sons Rs:
$Rs = -0.08 * Rm - 1.92\ D$ [$\sigma = +/-3.02$ D, $r = -0.080$, $N = 49$]

(4) Mother Rm to daughters Rd:
$Rd = 0.35 * Rm - 1.45$ D. [$\sigma = \pm 2.94$ D, $r = 0.356$, $N = 48$]

$$t = |r|\ \mathrm{sqr}\left[df/\left(1 - r^2\right)\right] df = N{-}2, \tag{A1}$$

Figure 6.

$$r = t\ \mathrm{sqr}\left[1/\left(df + t^2\right)\right] r > 0 \tag{A2}$$

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