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Research paper

Genetic and environmental-genetic interaction rules for the myopia based on a family exposed to risk from a myopic environment

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ABSTRACT

Objective: To quantitatively assess the role of heredity and environmental factors in myopia based on the family with enough exposed to risk from myopic environment for establishment of environmental and genetic index (EGI).

Methods: A pedigree analysis unit was defined as one child (university student), father, and mother. Information pertaining to visual acuity, experience in participating in the college entrance examination in mainland of China (regarded as a strong environmental risk for myopia), and occupation for pedigree analysis units were obtained. The difference between effect of both genetic and environmental factors (myopia prevalence in children with two myopic parents) and environmental factors (myopia prevalence in children of whom neither parent was myopic) was defined as the EGI. Multiple regression analysis was performed for 114 pedigree using diopters of father, mother, average diopters in parents, maximum and minimum diopters in father and mother as variables. A total of 353 farmers and 162 farmer families were used as a control group.

Results: A distinct difference in myopia rate (96.2% versus 57.7%) was observed for children from parents with myopia and parents without myopia (EGI = 0.385). The maximum diopter was included to regression equation which was statistically significant. The prevalence of myopia was 9.9% in the farmer. The prevalence in children is similar between the farmer and other families.

Conclusion: A new genetic rule that myopia in children was directly related with maximum diopters in father and mother may be suggested. Environmental factors may play a leading role in the formation of myopia.

1. Introduction

Myopia or nearsightedness is one of the most common human eye disorders, of which there is a high prevalence in Asian populations (30%–50%) (He et al., 2009; Sawada et al., 2008; Xiang et al., 2013). Over 80% of urban school children in China develop myopia (Sun et al., 2012; You et al., 2012). Although the cause of myopia is unknown, many studies have shown that environmental and genetic factors are jointly involved in myopia development (Shi et al., 2011). While environmental factors, such as the time spent indoors and visual close work, are capable of causing myopia (French et al., 2013; Lee et al., 2013; Pan et al., 2012), evidence for a genetic component to myopia is provided by population genetics or family studies (Yoshikawa et al., 2014; Li et al., 2015; Jiang et al., 2014). However, results regarding the extent of environmental and genetic factor involvement in the development of myopia differ due to inconsistent research methods and subjects. Most of such studies have confirmed the role of genetic factors in high myopia development through population observation (Yoshikawa et al., 2014; Li et al., 2015; Jiang et al., 2014), pedigree analysis (Jiang et al., 2014; Li et al., 2013; Tran-Viet et al., 2013), and twin methods (monozygotic and dizygotic twins) (Adenuga, 2014; Kim et al., 2013; Lee et al., 2012); however, the reliability of these results is questionable due to the lack of environmental factor control.

Environmental risk factors for myopia include close work; myopia prevalence is very low in occupations without prolonged close work, such as in farmers (Pärssinen, 1987). This means that a person is unlikely to develop myopia even if he/she has susceptibility genes for myopia if there are no environmental risk factors. Therefore, we can deduce that even using the twin method, only myopia resulting from environmental risk factors can be identified; this method is unable to determine whether a non-myopic person is affected as a result of the presence of anti-myopic genes or the lack of a myopia-inducing environment. Therefore, control of environmental factors is very important for studying any disease to which both environmental and genetic factors contribute.

For myopia, the evidence of genetic factors is substantial and

Abbreviation: EGI, environmental and genetic index

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environmental risk factors are generally clear and relatively simple and occurrence of myopia are not relative with aging; therefore, myopia is also an ideal model for studying diseases jointly involving environmental and genetic factors. In this study, adolescents participating in close work (students participating in the college entrance examination in the People's Republic of China) and their parents with participating in the college entrance examination in China were enrolled as subjects, so that we could simultaneously determine the contribution of genetic factors and environmental factors to provide basic data for in-depth research and strategies for the prevention of myopia and diseases with similar etiologies.

2. Materials and methods

2.1. Subjects and grouping

The farmer group was derived from 353 farmers; the control group comprised 237 non-farmer subjects, whose occupations included office worker, teacher, businessman, and civil servant. The number of subjects with myopia was compared between the two groups for observing a environmental role in myopia.

The farmer family group comprised 162 families in which both the father and mother were farmers and their child was a university student; 104 families in which neither the father nor the mother were farmers and their child was a university student were considered the control group. The percentage of children with myopia was compared between the two groups for observing a genetic role in myopia.

A total of 114 Chinese university students aged 18–22 years and their biological parents were enrolled as subjects for assessment of genetic rule. Each of these students and their parent pair were treated as a family, in which both the father and mother had experience participating in the college entrance examination in the People's Republic of China.

Three groups were divided for above 114 families for assessment of both environmental and genetic roles. The myopia family group comprised 62 families, in which both the father and mother suffered from myopia; the one-sided myopia family group comprised 26 families in which only the father or mother suffered from myopia; 26 families in which both the father and mother with normal visual acuity were considered the control group.

All students (children in the family) were unrelated ethnic Han Chinese individuals from urban or rural areas of the People's Republic of China and had participated in the college entrance examination in the People's Republic of China. None of the subjects had known ocular diseases or insults that could predispose them to myopia; nor did any of them have a known genetic disease associated with myopia, such as Stickler or Marfan syndrome.

The Institutional Ethics Committee of Dalian Medical University approved the study and waived the need for written informed consent from the participants due to the observational nature of the study.

2.2. Data collection

Data of the student and their parents were collected through self-reporting by each individual. Information included visual acuity, experience participating in the college entrance examination in the People's Republic of China, and occupation.

The diagnosis of myopia was determined by the refractive error. Myopia was defined with a refractive error less than − 0.50 diopters (D), and controls with + 0.50 to − 0.50 D. Myopia was further classified as physiologic (less than − 0.50 D to greater than − 6.00 D) and pathologic (equal or less than − 6.00 D). It was accepted for anisometropia of 3.00D or less; average refractive error of the two eyes was considered as the refractive error value for anisometropic individuals. Individuals with anisometropia over 3.00D should be excluded from study.

2.3. Assessment of genetic rule

In evaluating the genetic rule in myopia, the diopters in young adults (children) were applied as the dependent variable, while the father diopters, mother diopters, average diopters in father and mother, maximum diopters in father and mother, minimum diopters in father and mother were used as the independent variables. Subsequently, multiple regression analysis (Backward method) was performed on the collected data. When the multiple regression equation was statistically significant, the indicator was considered to be influenced by genetic factors, whose degree was measured with R^2.

2.4. Assessment of environmental and genetic roles

The myopia family group, in which both the father and mother suffered from myopia, represent the total effect of genetic susceptibility (G) and environmental factors (E); this total effect could be represented with children incidence in myopia family group (Pd) as following equation:

$$Pd = G + E$$

The non-myopia family group, in which both the father and mother had experience participating in the college entrance examination in the People's Republic of China (environmental factors) with normal visual acuity, represent the environmental factors (E); this total effect could be represented with incidence of children from non-myopia family group (Pn) as following equation:

$$Pn = E$$

The genetic predisposition (G) could be represented according to above two equation as follow:

$$Pd - Pn = (G + E) - E = G \quad Pd > Pn$$

Range of G was 0–1.0. Because sum of environmental and genetic roles in occurrence of disease was 1.0, the difference between Pd and Pn is was defined as the Environmental and Genetic Index (EGI).

$$EGI = Pd - Pn$$

where Pd represented percentage of individual with a disease in the disease family group; Pn represented percentage of individual with a disease in non-disease family group. Range of EGI was 0–1. A greater EGI indicates that the effect of genetic factors is more significant and the environmental effect is smaller.

2.5. Statistical analyses

Diopters of children with myopia were described in terms of quartile values because of their non-normal distribution. The Mann–Whitney *U* test was used to analyze differences among groups and the Chi-squared test was used to analyze differences in binary outcomes between the two groups.

Data were considered statistically significant when the probability of a type I error was 0.05 or less. Calculations were performed using the Windows version of SPSS (Statistical Package for Social Sciences) 13.0 software (SPSS Inc., Chicago, IL, USA).

3. Results

The prevalence of myopia in the farmer and control groups is shown in Table 1. The prevalence of myopia in the farmer group was significantly lower than that in the control group ($P < 0.05$).

The prevalence of myopia in children from farmer families and other families is shown in Table 2. Results indicate that the prevalence of myopia in children is similar between the two groups ($P > 0.05$).

We further assessed genetic rule in myopia with multiple regression equation; the variable of father diopters, mother diopters, average diopters in parents were removed from the equation; the maximum and