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Refractive errors and ocular findings in children with intellectual disability: A controlled study

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Abstract

PURPOSE—To evaluate the ocular findings and refractive errors in children with intellectual disability and in controls of average intellectual development of similar socioeconomic backgrounds.

METHODS—The study was conducted at Diskapi Children's Hospital in Ankara, Turkey: 724 subjects with intellectual disability and 151 control subjects were evaluated. The subjects with intellectual disability were subdivided into mild (IQ 50–69, n = 490), moderate (IQ 35–49, n = 164), and severe (IQ <34, n = 70) groups, and syndromic (n = 138) versus nonsyndromic (n = 586) disability. All children underwent cycloplegic autorefraction or retinoscopy, slit-lamp biomicroscopy, and dilated fundus examination. Ocular alignment was assessed by Hirschberg, Krimsky, or prism cover test. The main outcome measure was the prevalence of refractive errors and ocular findings.

RESULTS—Seventy-seven percent of subjects with intellectual disability, and 42.4% of controls, had ocular findings. The children with intellectual disability had significantly more nystagmus, strabismus, astigmatism, and hypermetropia than controls. Children with syndromic intellectual disability had significantly more nystagmus, strabismus, astigmatism, and hypermetropia than subjects with nonsyndromic intellectual disability. Increasing severity of intellectual disability was related to higher prevalence of nystagmus, strabismus, astigmatism, hypermetropia, and anisometropia.

CONCLUSIONS—From a public health perspective, evaluation and treatment of ocular and refractive findings in children with moderate, severe, and syndromic intellectual disability categories is urgently needed and likely to be highly effective in alleviating future health and

social care costs, as well as improving the productive lives of individuals with intellectual disability.

Most previous studies evaluating ocular findings in individuals with intellectual disability have been conducted on subjects with known syndromes and, most importantly, in subjects with Down syndrome.¹⁻⁷ A number of recent studies conducted in adults with other syndromic causes of intellectual disability, including tuberous sclerosis, Fragile X, and Rett syndrome have indicated greater risks for ocular disorders.⁸ The subject's age, specific intellectual disability syndrome, and severity of intellectual disability have all been noted to be related to greater prevalence of ocular disorders.⁹⁻¹¹ The most frequently reported ocular findings in adult studies were optic atrophy, cataract, keratoconus, and strabismus; in addition, the most prevalent refractive error was hypermetropia.⁹⁻¹¹

The former studies were notable for a number of limitations. First, in many studies formal psychological testing and IQ scores were not available.^{4,5,9,12,13} Second, previous studies did not use controls,^{4,5,8-11,13,14} and, therefore, they compared their findings with previously available normative data. Some studies had relatively small sample sizes, making comparisons between the syndromic/nonsyndromic subgroups and intellectual disability severity subgroups difficult.^{4,5,13,14} The studies evaluating ocular findings in individuals with intellectual disability therefore have been descriptive,⁸ crudely grouping subjects into mild versus severe intellectual disability and with limited ability to detect meaningful subgroup differences.^{8,11} Finally, the studies have predominantly been on adults. From a public health perspective, this is a major constraint, since detection of ocular conditions including strabismus and refractive errors during early childhood is crucial to prevent amblyopia.

In the present study, we have attempted to address these methodological shortcomings by evaluating the etiology of intellectual disability in every child, testing every subject with standard age-appropriate formal IQ tests, and ascertaining a control group of similar age and socioeconomic background as the subjects with intellectual disability. Our study hypothesized that (1) children with intellectual disability would be at greater risk of ocular and refractive disorders, (2) the prevalence of ocular and refractive findings would be related to the severity of intellectual disability (mild, moderate, severe) as well as syndromic versus nonsyndromic distinctions, and (3) specific ocular and refractive findings would be related to severity and syndromic intellectual disability categories. This is the first large study in children and also the first study that allows one to look separately at nonsyndromic patients, for whom proper management of refractive errors may make a huge difference in daily functioning.

Materials and Methods

The study sample included consecutive children with intellectual disability applying to a Child Psychiatry Clinic of a Children's Hospital, in Ankara, Turkey, for an initial evaluation. The study was approved by the institutional ethics board, and all participating families gave their informed consent. The intellectual disability group comprised 724 subjects (405 boys, 319 girls; 9.3 ± 3.0 years [mean $\pm$ SD]; age range, 1-17 years). The

control subjects consisted of 151 children (109 males, 42 females; mean age $\pm$ SD 8.9 ± 2.4 years; age range, 3–15) of average intelligence consecutively recruited from the same Child Psychiatry outpatient clinic. The controls all had IQ scores greater than 80 and had no known neurological or medical disorders primarily related to ocular functioning. Therefore, the control group represented a “normal” population in terms of intellectual, but not ophthalmologic, functioning. Although the sex distribution was significantly different between the groups ($\chi^2 = 12.8$, $p < 0.001$), there was no significant difference for age ($F(1873) = 2.7$; $p = 0.10$).

All children underwent standardized formal IQ tests appropriate to the child’s developmental functioning. The subjects with intellectual disability were further divided into 3 groups according to the IQ levels obtained by these tests: mild (IQ of 50–69, $n = 490$), moderate (IQ of 35–49, $n = 164$), and severe (IQ < 34 , $n = 70$). The sex distribution was similar in each group (44.3%, 43.3%, and 44.3% girls, respectively; $\chi^2 = 0.51$, $p = 0.97$). Likewise, the mean age was also similar among the 3 groups (9.2 ± 2.8 , 9.7 ± 3.5 , and 9.1 ± 3.4 , respectively; $F(2721) = 1.64$; $p > 0.19$).

Full neurological examination was conducted for all subjects with intellectual disability and controls. Further investigation required to determine the possible cause of intellectual disability, such as cranial magnetic resonance imaging (MRI), electroencephalography, blood and urea amino acid levels, and chromosomal analysis, were performed whenever clinically necessary. The children with characteristic features of metabolic diseases were referred to the Department of Pediatric Metabolic Diseases, at the same hospital, for enzyme analysis. On the basis of these results, the subjects with intellectual disability were further categorized under syndromic and nonsyndromic groups. The definition of syndromic intellectual disability included those children with a defined predisposing cause of intellectual disability, eg, chromosomal disorders, including Fragile X Syndrome, Down syndrome, and Rett syndrome; known exposure to toxins or infections during pregnancy; prematurity complications; lead poisoning or other postnatal exposure to toxins; and evidence of metabolic disorders and head trauma. The subsample with syndromic intellectual disability included 138 children (see Table 1, e-Supplement 1, available at www.jaapos.org). The nonsyndromic group included 586 children with no defined predisposing cause of intellectual disability. Sex distributions were similar among syndromic and nonsyndromic intellectual disability subgroups (43.9% and 44.9%, respectively; $\chi^2 = 0.52$, $p = 0.82$); mean ages were different between the 2 groups (9.4 years ± 2.9 ; 8.8 years ± 3.4 , respectively; $F(1722) = 4.44$; $p = 0.034$).

All children underwent cycloplegic autorefraction (with cyclopentolate) and/or retinoscopy, slit-lamp biomicroscopy, and detailed dilated fundus examination. Ocular movements were checked and ocular alignment was assessed by Hirschberg, Krimsky, and/or prism cover test. Myopia is defined as the spherical equivalent refraction of at least -0.50 D, hyperopia as the spherical equivalent refraction of at least $+2.0$ D, and astigmatism as the cylinder of at least 1.0 D, and anisometropia as the spherical equivalent difference of at least 2.0 D between the two eyes of the same child.¹⁵ The prevalence of refractive errors and other ocular findings was compared between the intellectual disability and control groups and among all the intellectual disability subgroups.

The χ^2 test was used to compare categorical variables. For further analysis we used multivariate logistic regression analyses to further evaluate effects of age, severity of intellectual disability (mild, moderate, and severe), gender (male/female), and etiology of intellectual disability (syndromic vs nonsyndromic) on the prevalence of all evaluated parameters (refractive errors, hypermetropia, astigmatism, anisometropia, strabismus, nystagmus, and other ocular findings); $p < 0.05$ was regarded as statistically significant. SPSS version 13.0 used for all analysis (SPSS, Inc., www.spss.com).

Results

Between-Group Comparisons

Comparison of Subjects With Intellectual Disability Versus Controls—Seventy-seven percent of children with intellectual disability were noted to have ocular or refractive abnormalities compared with 42.4% for controls ($\chi^2 = 72.39$, $p < 0.0001$). Nystagmus, strabismus, astigmatism, hypermetropia, and other ocular findings (eg, including congenital cataract [1.5%], optic atrophy [0.27%], atypical retinitis pigmentosa [0.13%], microphthalmia [0.13%], microcornea [0.41%], enophthalmos [0.13%], corneal opacity [0.13%], aniridia [0.13%], macular hypoplasia [0.13%], and myelinated nerve fibers [0.13%]) were more prevalent in subjects with intellectual disability (Table 2). These results indicated that almost all of the investigated ocular problems were more common in the subjects with intellectual disability.

Comparison of the Intellectual Disability Severity Groups—The overall effect of severity on the prevalence of ocular findings was significant ($\chi^2 = 42.10$, $p < 0.0001$). The intellectual disability groups were treated as ordered groups to compare the prevalence of ocular findings in each severity group. The subjects with moderate or severe intellectual disability had significantly greater prevalence of astigmatism ($\chi^2 = 30.42$, $p < 0.0001$; and $\chi^2 = 20.34$, $p < 0.0001$), nystagmus ($\chi^2 = 13.36$, $p = 0.001$; and $\chi^2 = 11.92$, $p = 0.003$), and strabismus ($\chi^2 = 12.69$, $p = 0.001$; and $\chi^2 = 23.91$, $p < 0.0001$) compared with subjects with mild intellectual disability; there were no significant differences between moderate versus severe intellectual disability groups ($\chi^2 = 0.25$, $p = 0.88$; $\chi^2 = 0.14$, $p = 0.81$; and $\chi^2 = 2.69$, $p = 0.13$, respectively). There was a significant difference between severe versus mild intellectual disability groups in terms of the prevalence of anisometropia ($\chi^2 = 8.21$, $p = 0.008$) and other ocular findings ($\chi^2 = 5.75$, $p = 0.020$). The prevalence of hypermetropia was significantly different only between mild versus moderate intellectual disability groups ($\chi^2 = 21.08$, $p < 0.0001$; Table 3). These results showed that the prevalence of the ocular findings and refractive errors increased significantly with the severity of the intellectual disability.

Comparison of Syndromic Versus Nonsyndromic Intellectual Disability Groups—More children with syndromic intellectual disability (95.7%) had ocular or refractive findings than did children with nonsyndromic intellectual disability (78.7%; $\chi^2 = 33.6$, $p < 0.0001$). The subjects with syndromic intellectual disability ($n = 138$) had significantly more common nystagmus ($\chi^2 = 39.2$, $p < 0.0001$), strabismus ($\chi^2 = 8.62$, $p = 0.006$), astigmatism ($\chi^2 = 19.44$, $p < 0.0001$), and hypermetropia ($\chi^2 = 38.58$, $p < 0.0001$)

than subjects with nonsyndromic intellectual disability ($n = 586$). However, we noted that myopia was more common in the nonsyndromic intellectual disability group ($\chi^2 = 7.65$, $p = 0.022$; Table 4). These results indicated that the presence of syndromic intellectual disability was a significant risk factor for various ocular problems.

A total of 11.2% of the subjects with syndromic intellectual disability had mild, 32.9% had moderate, and 41.4% had severe intellectual disability, whereas of the patients with nonsyndromic intellectual disability 39.9% had mild, 39.1% moderate, and 21% had severe intellectual disability. The subjects with moderate or severe intellectual disability more often had syndromes than those with mild intellectual disability ($\chi^2 = 41.67$, $p < 0.0001$ and $\chi^2 = 43.87$, $p < 0.0001$, respectively).

Multivariate Regression Analyses

Multivariate regression analyses revealed that the risk of having any ocular findings or refractive errors was related to older age, syndromic intellectual disability, and severity of intellectual disability. The prevalence of hypermetropia was greater in children with syndromic intellectual disability of any severity. The prevalence of astigmatism was related only to severity of intellectual disability. Anisometropia was more common in older children with severe intellectual disability. Risk of having strabismus was higher in younger children with intellectual disability of any severity. Nystagmus was more prevalent in children with syndromic intellectual disability or with moderate and severe intellectual disability. Having any additional ocular finding was only related to the presence of severe intellectual disability. We noted that sex was not related to the prevalence of any evaluated parameter. Therefore, our results suggested that for most of the ocular findings and the refractive errors, with the exception of total prevalence of ocular findings and nystagmus, the severity of intellectual disability may be the more dominant risk factor than the presence of syndromic etiology. Age is also found to be an important factor affecting the prevalence of ocular problems. Multivariate regression analyses results, including odds ratios, with respective 95% CI for each parameter are summarized in e-Supplement 2 (available at jaapos.org).

Discussion

This is the first large-scale study in children with intellectual disability and also the first study that allows one to look separately at nonsyndromic patients. There were several important findings of the present study that call for further comment. First, the children with intellectual disability had a significantly greater incidence of nystagmus, strabismus, astigmatism, hypermetropia, and other ocular findings than controls. Second, children meeting the syndromic definition of intellectual disability had significantly more nystagmus, strabismus, astigmatism, and hypermetropia than subjects in the nonsyndromic group. Third, the increasing severity of intellectual disability was related to higher prevalence of nystagmus, strabismus, astigmatism, hypermetropia, and anisometropia. These findings appear to confirm our initial hypotheses.

The present study has a number of important methodological strengths compared with previous research. We used a control group of average intellectual development of similar background, recruited in similar setting and catchment area within a state-funded regional

pediatric center. The control group did not represent a “visually normal” population, which would artificially increase the significance of the findings in the intellectual disability group. Furthermore, all the case and control children in this present study were evaluated by standardized formal IQ tests. The underlying etiologies of intellectual disability were further investigated by pediatric neurologists for all subjects. All ophthalmologic evaluations were carried out by an attending ophthalmologist.

The first limitation of our study is that our subjects were recruited from a hospital outpatient psychiatry clinic population, so these results may not be representative of the general population as a whole. If the control group would have been recruited from the general population, the difference in the prevalence of refractive errors and other ocular findings would probably be even more marked. Another limitation of the present study was the different gender distribution between the intellectual disability and the control groups. However, our multivariate regression analyses demonstrated that there was no relation between gender and the prevalence of any ocular findings or refractive errors. The intellectual disability group included patients as young as 1 year of age, whereas the minimum age in the control group was 3 years. Many of the outcome variables are known to be changing quite drastically with age in normal children during the first few years of life, and such changes may therefore also play a role among the younger children included in this study. In fact, in the regression analyses, age was a significant factor in the prevalence of refractive errors, strabismus, myopia, anisometropia, and other ocular findings.

Van Splunder et al evaluated 1,539 adults with intellectual disability and reported that refractive errors were most prevalent (60.6%), followed by strabismus (44.1%), and lens opacities (18.1%). That study did not include a control group, and the investigators compared their results with known figures from the general populations and commented that the prevalence of ocular diagnoses in adults with intellectual disability was significantly higher.¹¹

Warburg investigated 837 adults with intellectual disability.⁹ The most widespread medical condition was cerebral visual impairment, and the most frequent eye disorders were optic atrophy, high myopia, cataract, and keratoconus. The most prevalent cause of visual impairment was uncorrected ametropia. Hypermetropia of $> +1.50$ was found in 151 of 710 subjects (21%); myopia < -1.0 was present in 213 individuals (30%). However, in that study neither IQ test results nor an average intelligence control group were available.

Van Istardael et al¹⁶ reported a retrospective medical record review of 6220 consecutive subjects examined ophthalmologically according to a standard protocol by one center that specialized in visual assessment and treatment of people with intellectual disability, between 1993 and 2003. The investigators concluded that in a large adult population the prevalence of severe and profound intellectual disability, visual impairment, visual disorders, or blindness decreased, and the proportion of mobile subjects increased from 1995 to 2003.

The present study shows the need for ophthalmologic evaluation of every child with intellectual disability, since more than three quarters of the subjects had an ocular or refractive finding. It has been shown that relative to persons with no visual impairment,

children with bilateral mild and unilateral or bilateral moderate/severe visual impairment report greater difficulties in performing daily activities, besides having poorer mental health.¹⁷ Protocols for efficient referral must be developed to improve the rate of evaluation, treatment, and aftercare of rates of ophthalmologic disorders. In conclusion, ocular examination of children with intellectual impairment, especially those with moderate, severe, and syndromic intellectual disability, is indicated and likely to be highly effective in alleviating future health and social care costs, as well as improving the productive lives of individuals with intellectual disability.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 2

The prevalence of ophthalmological disorders in the children with intellectual disability (ID) and controls

Variables	ID group (n = 724)	Controls (n = 151)	χ^2 ; <i>p</i> -values
Astigmatism	333 (46%)	38 (25.2%)	23.02; <0.0001
Unilateral	118 (6.3%)	17 (11.3%)	
Bilateral	215 (29.7%)	21 (13.9%)	
Hypermetropia	292 (40.3%)	24 (26.9%)	32.52; <0.0001
Unilateral	58 (8.0%)	6 (4.0%)	
Bilateral	234 (32.3%)	18 (11.9%)	
Myopia	149 (20.5%)	26 (17.2%)	1.49; 0.47
Unilateral	56 (7.7%)	12 (7.9%)	
Bilateral	93 (12.8%)	14 (9.3%)	
Anisometropia	51 (7.0%)	6 (4%)	1.93; 0.20
Nystagmus	38 (5.2%)	0 (0%)	8.28; 0.001
Horizontal	30 (4.1%)		
Rotatory	8 (1.1%)		
Strabismus	101 (14.0%)	2 (1.3%)	19.17; <0.0001
Exotropia-unilateral	6 (0.8%)	0	
-alternating	35 (4.8%)	0	
Esotropia-unilateral	6 (0.8%)	0	
-alternating	54 (7.5%)	2 (1.3%)	
Other ocular findings	33 (4.6%)	1 (0.7%)	5.08; 0.019

More than one finding can occur in a given subject.

Table 3

The prevalence of ophthalmological disorders in children with intellectual disability (ID) by levels of severity

Variables	ID group (n = 724)			χ^2 ; p-values
	Mild (n = 490)	Moderate (n = 164)	Severe (n = 70)	
Astigmatism	195 (39.8%)	95 (57.9%)	43 (61.4%)	40.9; <0.0001
Unilateral	86 (17.6%)	22 (13.4%)	10 (14.3%)	
Bilateral	109 (22.2%)	73 (44.5%)	33 (47.1%)	
Hypermetropia	173 (35.3%)	90 (54.9%)	29 (41.4%)	21.76; <0.0001
Unilateral	39 (8.0%)	15 (9.1%)	4 (5.7%)	
Bilateral	134 (27.3%)	75 (45.7%)	25 (35.7%)	
Myopia	97 (19.8%)	32 (19.5%)	20 (28.5%)	5.41; 0.25
Unilateral	37 (7.6%)	14 (8.5%)	5 (7.1%)	
Bilateral	60 (12.2%)	18 (11.0%)	15 (21.4%)	
Anisometropia	26 (5.3%)	15 (9.1%)	10 (14.3%)	8.97; 0.011
Nystagmus	14 (2.9%)	16 (9.8%)	8 (11.4%)	25.34; <0.0001
Horizontal	12 (2.4%)	11 (6.7%)	7 (10.0%)	
Rotatory	2 (0.5%)	5 (3.1%)	1 (1.4%)	
Strabismus	47 (9.6%)	33 (20.1%)	21 (30.0%)	43.38; <0.0001
Exotropia-unilateral	1 (0.2%)	4 (2.4%)	1 (1.4%)	
-alternating	21 (4.3%)	9 (5.5%)	5 (7.1%)	
Esotropia-unilateral	3 (0.6%)	3 (1.8%)	0	
-alternating	22 (4.5%)	17 (10.4%)	15 (21.4%)	
Other ocular findings	18 (3.7%)	8 (4.9%)	7 (10%)	5.69; 0.058

More than one finding can occur in a given subject.

Table 4

The prevalence of ophthalmological disorders in children with intellectual disability (ID) by syndromic vs nonsyndromic ID

Variables	ID group (n = 724)		χ^2 ; <i>p</i> -values
	Idiopathic (n = 586)	Syndromic (n = 138)	
Astigmatism	256 (43.7%)	77 (55.8%)	19.44; <0.0001
Unilateral	103 (17.6%)	15 (10.9%)	
Bilateral	153 (26.1%)	62 (44.9%)	
Hypermetropia	212 (36.2%)	80 (58.0%)	38.58; <0.0001
Unilateral	53 (9.0%)	5 (3.6%)	
Bilateral	159 (27.1%)	75 (54.3%)	
Myopia	129 (22.0%)	20 (14.5%)	7.65; 0.022
Unilateral	53 (9.0%)	3 (2.2%)	
Bilateral	76 (13.0%)	17 (12.3%)	
Anisometropia	39 (6.7%)	12 (8.7%)	0.7; 0.458
Nystagmus	16 (2.7%)	22 (15.9%)	39.20; <0.0001
Horizontal	13 (2.2%)	17 (12.3%)	
Rotatory	3 (0.5%)	5 (3.6%)	
Strabismus	71 (12.1%)	30 (21.7%)	8.62; 0.006
Exotropia-unilateral	6 (1.0%)	0	
-alternating	29 (4.9%)	6 (4.4%)	
Esotropia-unilateral	6 (1.0%)	0	
-alternating	30 (5.1%)	24 (17.4%)	
Other ocular findings	23 (3.9%)	10 (7.2%)	2.83; 0.110

More than one finding can occur in a given subject.