

PEDIATRICS®

OFFICIAL JOURNAL OF THE AMERICAN ACADEMY OF PEDIATRICS

Mental Illness in Young Adults Who Had Strabismus as Children

Brian G. Mohny, Jeff A. McKenzie, Jason A. Capo, Kevin J. Nusz, David Mrazek
and Nancy N. Diehl

Pediatrics 2008;122;1033

DOI: 10.1542/peds.2007-3484

The online version of this article, along with updated information and services, is
located on the World Wide Web at:

<http://pediatrics.aappublications.org/content/122/5/1033.full.html>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2008 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™



Mental Illness in Young Adults Who Had Strabismus as Children

Brian G. Mohnney, MD^a, Jeff A. McKenzie, BA^b, Jason A. Capó, MD^b, Kevin J. Nusz, MD^a, David Mrazek, MD^c, Nancy N. Diehl, BS^d

^aDepartment of Ophthalmology, ^bCollege of Medicine, ^cDepartment of Pediatric and Adolescent Psychiatry and Psychology, and ^dDivision of Biostatistics, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

The authors have indicated they have no financial relationships relevant to this article to disclose.

What's Known on This Subject

There is a single report of a genetic association of schizophrenia and "constant exotropia," but there are no other data on this association.

What This Study Adds

A strong link between childhood exotropia and the subsequent development of various forms of mental illness is demonstrated.

ABSTRACT

OBJECTIVE. We investigated the prevalence and types of psychiatric disorders diagnosed by early adulthood among patients who had common forms of strabismus as children.

METHODS. The medical records of children (<19 years) who were diagnosed as having esotropia ($N = 266$) or exotropia ($N = 141$) while residents of Olmsted County, Minnesota, between January 1, 1985, and December 31, 1994, were reviewed retrospectively for psychiatric disease diagnoses. Each case subject was compared with a randomly selected, individually birth- and gender-matched, control subject from the same population.

RESULTS. A mental health disorder was diagnosed for 168 (41.3%) of the 407 patients with a history of childhood strabismus, who were monitored to a mean age of 17.4 years, compared with 125 control subjects (30.7%). Children with exotropia were 3.1 times more likely to develop a psychiatric disorder than were control subjects when monitored to a mean age of 20.3 years. Children with esotropia were no more likely to develop mental illness than were control subjects when monitored for similar periods. Patients with intermittent exotropia also were significantly more likely to have greater numbers of mental health disorders, mental health emergency department visits, and mental health hospitalizations and to have suicidal or homicidal ideation.

CONCLUSIONS. Children diagnosed as having strabismus in this population, especially those with exotropia, were at increased risk for developing mental illness by early adulthood. Patients with intermittent exotropia seemed to be particularly prone to developing significant psychiatric diseases by the third decade of life. *Pediatrics* 2008;122:1033–1038

www.pediatrics.org/cgi/doi/10.1542/peds.2007-3484

doi:10.1542/peds.2007-3484

Key Words

strabismus, esotropia, exotropia, mental illness, psychiatric disease

Abbreviation

ADHD—attention-deficit/hyperactivity disorder

Accepted for publication Feb 25, 2008

Address correspondence to Brian G. Mohnney, MD, Department of Ophthalmology, Mayo Clinic, 200 First St Southwest, Rochester, MN 55905. E-mail: mohnney@mayo.edu

PEDIATRICS (ISSN Numbers: Print, 0031-4005; Online, 1098-4275). Copyright © 2008 by the American Academy of Pediatrics

STRABISMUS IS A disorder of ocular alignment that afflicts 3% to 5% of children.^{1–6} Esotropia (an inward deviation of the eyes) is more common than exotropia (an outward deviation) in Western populations, although exotropia predominates among Asian individuals.⁷ Two reports, one genetic⁸ and the other clinical,⁹ suggested a link between strabismus and adult schizophrenia. However, this association was found either with a rare form of childhood strabismus (constant exotropia)⁸ or among patients with a family history of schizophrenia.⁹ Moreover, adult schizophrenia was the only disorder of mental health found to be associated with strabismus. The purpose of this study was to evaluate the prevalence and types of psychiatric disorders diagnosed by early adulthood among patients who had common forms of strabismus as children.

METHODS

The medical records of all patients <19 years of age who were residing in Olmsted County, Minnesota, and were diagnosed by an ophthalmologist as having the more-prevalent forms of esotropia (including the accommodative, acquired nonaccommodative, and congenital forms) or exotropia (intermittent exotropia or convergence insufficiency), between January 1, 1985, and December 31, 1994, were reviewed retrospectively.^{4–6} Institutional review board approval was obtained for this study. Patients with strabismus with an underlying or associated developmental, neurologic, or ocular sensory disorder were excluded. Potential cases were identified by using the resources of the Rochester Epidemiology Project, a medical records linkage system designed to capture data on any patient-physician

TABLE 1 Historical and Clinical Characteristics of Patients With Strabismus (*N* = 407) and Control Subjects (*N* = 407)

| Characteristic | Esotropia (<i>N</i> = 266) | | | Exotropia (<i>N</i> = 141) | | |
|--|-----------------------------|------------------|----------|-----------------------------|------------------|----------|
| | Case | Control | <i>P</i> | Case | Control | <i>P</i> |
| Male, <i>n</i> (%) | 146 (55) | 146 (55) | 1.00 | 59 (41.8) | 59 (41.8) | 1.00 |
| Prematurity, <i>n/N</i> (%) ^a | 12/78 (15.4) | 16/226 (7.1) | .04 | 4/83 (4.8) | 8/118 (6.8) | .76 |
| Birth weight, median (range), g | 3500 (1030–4850) | 3460 (1230–5160) | .99 | 3330 (955–4540) | 3430 (1210–4650) | .34 |
| White, <i>n/N</i> (%) | 243/249 (97.6) | 240/243 (98.8) | .50 | 118/127 (92.9) | 132/137 (96.4) | .28 |
| Difficulty with pregnancy, <i>n/N</i> (%) ^b | 80/122 (65.6) | 137/265 (51.7) | .01 | 78/131 (59.5) | 70/138 (50.7) | .18 |
| Family history of psychiatric disease, <i>n/N</i> (%) | 45/169 (26.6) | 46/178 (25.8) | .90 | 33/104 (31.7) | 24/102 (23.5) | .21 |
| Maternal history of chemical abuse, <i>n/N</i> (%) | 23/144 (16) | 22/177 (12.4) | .42 | 18/101 (17.8) | 7/99 (7.1) | .03 |
| Family history of chemical abuse, <i>n/N</i> (%) | 30/157 (19.1) | 30/178 (16.9) | .67 | 27/101 (26.7) | 19/101 (18.8) | .24 |
| Age at psychiatric diagnosis, median (range), y | 10.6 (1.1–26.6) | 12.7 (2–25) | .13 | 13.6 (3–28.3) | 15.9 (4–32.3) | .01 |

For categorical variables, *P* values were obtained by using Fisher's exact test; for continuous variables, *P* values were obtained by using the Wilcoxon rank sum test.

^a Born at gestational age of <37 weeks.

^b Including cesarean section birth, nuchal chords, and forceps delivery.

encounter in Olmsted County, Minnesota.¹⁰ The racial distribution of Olmsted County residents in 1990 was 95.7% white, 3.0% Asian American, 0.7% black, and 0.3% each for Native American and other. The population of this county (106 470 residents in 1990) is relatively isolated from other urban areas, and virtually all medical care is provided to residents by a largely unified medical care system (Mayo Clinic, Olmsted Medical Group, and affiliated hospitals) that has accumulated comprehensive clinical records for nearly 100 years.

A total of 627 children with strabismus were diagnosed during the study years; however, 407 (64.9%) met the inclusion criteria of the study and demonstrated the 5 most-common forms of strabismus. For each case subject with strabismus, we identified 1 control subject, from the same population-based cohort of children living in Olmsted County, who did not have a diagnosis of strabismus. Control subjects were chosen by selecting Olmsted County residents who were of the same gender and whose year of birth and registration (within our 2 medical institutions) matched for each of the index case subjects. Residence status, which was verified by trained residency checkers, was assessed for case and control subjects at the time of birth and at diagnosis by using information from city and county directories. Patients not residing in Olmsted County, Minnesota, at the time of diagnosis were excluded from the study.

The medical records of the patients with strabismus and the matched control subjects were reviewed for a diagnosis of mental illness (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition* codes), use of psychotropic medication, mental health emergency department visits or hospitalizations, suicide attempts, and suicidal or homicidal ideation. Information was obtained from cumulative paper and electronic records that included inpatient and outpatient psychiatric, psychological, and primary care and emergency department records. A history of mental illness diagnosed elsewhere was included when the diagnosis was confirmed by a mental health care provider within Olmsted County. The use of psychiatric medications included the type, concurrent use, and total duration. A history of suicide attempts or ideation was elicited from the mental health care record, whereas data on family history of psychiatric disease, substance abuse, and mater-

nal substance abuse during pregnancy among case and control subjects were collected from mental health and self-reporting primary care records. The historical data were collected by 4 of the authors in 2006, 1 (Mr McKenzie) of whom reviewed and confirmed the information for all 814 study subjects.

Continuous data are presented as medians and ranges. Categorical data are presented as counts and proportions. Comparisons between case and control subjects for continuous variables were completed by using Wilcoxon rank-sum tests, and Fisher's exact test was used in comparisons between case and control subjects for categorical data. All statistical tests were 2-sided, and the threshold of significance was set at $\alpha = .05$.

RESULTS

A total of 266 children with esotropia and 141 with exotropia were identified during the 10-year study period. Girls represented 120 (45%) of the 266 children with esotropia and 82 (58.2%) of the 141 children with exotropia. The 266 children with esotropia, who were diagnosed at a mean age of 3.9 years, were monitored to a mean age of 15.8 years (range: 6 months to 29.4 years), compared with 17.2 years for control subjects. Children with exotropia were diagnosed at a mean age of 7.8 years and were monitored to a mean age of 20.3 years (range: 4–37.7 years), compared with control subjects, who were monitored to a mean age of 20.9 years.

Table 1 presents historical and clinical characteristics of the 407 children with strabismus, according to the type of strabismus, and the control subjects. Children with esotropia were more likely than control subjects to have been born prematurely and to have had a complicated pregnancy. Children with exotropia had a younger age at psychiatric illness and were more likely to have mothers with a history of chemical abuse while pregnant, compared with control subjects. None of the study children was diagnosed as having fetal alcohol syndrome or other disorders known to be associated with maternal chemical abuse during pregnancy. The diagnosis of strabismus predated the mental illness for 153 (91.1%) of the 168 patients who suffered from both disorders.

Table 2 presents the prevalence of specifically queried factors of mental illness among patients with strabismus

TABLE 2 Mental Health Characteristics of Young Adults Who Had Esotropia or Exotropia as Children and Control Subjects

| Characteristic | No. (%) | | | | | | | | |
|--|----------------------|------------|--------------------|---------------------|-----------|-----|---------------------|-----------|--------------------|
| | Strabismus (N = 407) | | | Esotropia (N = 266) | | | Exotropia (N = 141) | | |
| | Case | Control | P | Case | Control | P | Case | Control | P |
| No. of patients with mental illness | 168 (41.3) | 125 (30.7) | .002 ^a | 93 (35) | 87 (32.7) | .65 | 75 (53.2) | 38 (27) | <.001 ^a |
| Total no. of disorders | 406 | 283 | .003 ^a | 220 | 195 | .43 | 186 | 88 | <.001 ^a |
| No. of patients using psychiatric medications | 92 (31.6) | 74 (21.4) | .004 | 51 (27.1) | 49 (20.9) | .17 | 41 (38.3) | 25 (22.3) | .01 |
| No. of patients with psychiatric emergency department visits | 35 (9.9) | 24 (6.3) | .08 | 14 (6.2) | 13 (5.3) | .70 | 21 (16.4) | 11 (8.0) | .04 |
| No. of patients with psychiatric inpatient admissions | 27 (7.6) | 15 (3.9) | .04 | 13 (5.8) | 8 (3.2) | .26 | 14 (10.9) | 7 (5.1) | .11 |
| No. of patients with suicide attempts | 12 (3.4) | 8 (2.1) | .36 | 5 (2.2) | 4 (1.6) | .74 | 7 (5.5) | 4 (2.9) | .36 |
| No. of patients with suicidal ideation | 40 (11.4) | 16 (4.2) | <.001 ^a | 19 (8.5) | 10 (4.1) | .05 | 21 (16.4) | 6 (4.4) | .002 ^a |

P values were obtained by using Fisher's exact test.

^a P values remained significant even after adjustment for family history variables in logistic regression analyses.

(exotropia and esotropia combined) and control subjects. A mental health disorder was diagnosed for 168 (41.3%) of the 407 patients with a history of childhood strabismus, compared with 125 (30.7%) of control subjects ($P = .002$). Children with strabismus were also significantly more likely to have a greater number of psychiatric disorders, to use psychotropic medications, to require psychiatric hospitalizations, and to have suicidal or homicidal ideation.

There was a significant difference, however, in the 2 forms of strabismus, as shown in Table 2. During the follow-up period of this study, children with exotropia or an outward deviation of the eyes (intermittent exotropia and convergence insufficiency) were 3.1 times (95% confidence interval: 1.9–5.1 times) more likely to develop a psychiatric disorder than were control subjects. Patients with exotropia were also more likely than control subjects to develop a greater number of psychiatric disorders, to use psychotropic medications or outpatient psychiatric services, and to have suicidal ideation. Children with esotropia were no more likely to develop mental illness than were control subjects, although levels of suicidal ideation seemed to be marginally higher among patients with esotropia ($P = .05$) when they were monitored for a similar period. There was no significant difference in the rates of mental illness between genders, and the rate of psychiatric illness among control subjects with esotropia (32.7%) was not different from that among control subjects with exotropia (27%; $P = .26$).

Table 3 presents the types and total numbers of psychiatric disorders diagnosed among case and control subjects, separated according to the type of strabismus. A mental illness predated the diagnosis of strabismus for 5 of the children with esotropia (5.4%); all 5 cases involved either a learning disability or attention-deficit/hyperactivity disorder (ADHD). Ten of the patients diagnosed as having exotropia (13.3%) already had 1 of the same 2 disorders. Depression not otherwise specified, ADHD, adjustment disorder, illicit drug use, and alcoholism were the 5 most common types of disorders. Although depression was similarly prevalent among case and control subjects, dysthymia and major depression were more common among subjects with strabismus than among control subjects. ADHD, adjustment disorder,

TABLE 3 Type and Prevalence of All Mental Illnesses Diagnosed Among Patients Who Had Strabismus as Children and Control Subjects

| Type of Diagnosis Reported | n | | | | | |
|---------------------------------------|---------------------|---------|------|---------------------|---------|------|
| | Exotropia (N = 141) | | | Esotropia (N = 266) | | |
| | Case | Control | P | Case | Control | P |
| Depression, not otherwise specified | 29 | 29 | 1.00 | 35 | 48 | .15 |
| ADHD | 25 | 7 | .001 | 42 | 40 | .90 |
| Adjustment disorder | 20 | 6 | .007 | 32 | 20 | .11 |
| Drug use | 14 | 5 | .06 | 17 | 18 | 1.00 |
| Alcoholism | 14 | 8 | .27 | 12 | 11 | 1.00 |
| Generalized anxiety | 7 | 6 | 1.00 | 13 | 17 | .57 |
| Major depression | 14 | 5 | .06 | 10 | 5 | .29 |
| Learning disabilities | 12 | 2 | .01 | 14 | 8 | .28 |
| Dysthymia | 11 | 5 | .19 | 11 | 4 | .11 |
| Personality disorder | 7 | 4 | .54 | 7 | 3 | .34 |
| Anxiety/panic disorder | 5 | 4 | 1.00 | 4 | 5 | 1.00 |
| Anxiety/obsessive-compulsive disorder | 3 | 3 | 1.00 | 2 | 4 | .69 |
| Eating disorder | 3 | 2 | 1.00 | 8 | 1 | .04 |
| Anxiety/phobia | 4 | 1 | .37 | 3 | 3 | 1.00 |
| Bipolar disorder | 3 | 1 | .62 | 2 | 2 | 1.00 |
| Somatoform/conversion | 5 | 0 | .06 | 0 | 3 | .25 |
| Psychoses | 2 | 0 | .50 | 2 | 0 | .50 |
| Aggression disorder | 2 | 0 | .50 | 0 | 0 | NA |
| Schizophrenia | 1 | 0 | 1.00 | 0 | 0 | NA |
| Other | 5 | 0 | .06 | 6 | 3 | .50 |
| Total | 186 | 88 | | 220 | 195 | |

NA indicates not applicable.

der, drug use, major depression, and learning disorders were all more prevalent among children with exotropia, compared with control subjects, whereas eating disorders were the only significantly increased group of disorders among children with esotropia.

Table 4 presents the prevalence of mental health characteristics among children with exotropia, according to the type of exotropia, compared with control subjects. Patients with intermittent exotropia were significantly more likely than control subjects to develop mental illness, to have a greater number of mental health disorders, to have a greater number of mental health emergency department visits or hospitalizations, and to have suicidal or homicidal ideation. They were also more

TABLE 4 Prevalence of Psychiatric Factors Among Patients With Specific Forms of Exotropia (*N* = 141) and Control Subjects (*N* = 141)

| Factor | No. (%) | | | | | |
|--|---|-----------|--------------------|---|-----------|-------------------|
| | Intermittent Exotropia ^a (<i>N</i> = 101) | | | Convergence Insufficiency ^b (<i>N</i> = 40) | | |
| | Case | Control | <i>P</i> | Case | Control | <i>P</i> |
| No. of patients with mental illness | 49 (48.5) | 25 (24.8) | <.001 | 26 (65) | 13 (33) | .007 ^c |
| Total no. of disorders | 127 | 50 | <.001 ^c | 59 | 38 | .16 |
| No. of patients using psychiatric medications | 25 (36.8) | 18 (24.3) | .14 | 16 (41) | 7 (18.4) | .05 |
| No. of patients with psychiatric emergency department visits | 13 (14.8) | 5 (5.2) | .04 | 8 (20) | 6 (15) | .77 |
| No. of patients with psychiatric inpatient admissions | 9 (10.1) | 1 (1.0) | .007 ^c | 5 (12.5) | 6 (15) | 1.00 |
| No. of patients with suicide attempts | 3 (3.5) | 0 (0) | .10 | 4 (10) | 4 (10) | 1.00 |
| No. of patients with suicidal/homicidal ideation | 13 (14.8) | 2 (2.1) | .002 ^c | 8 (20) | 4 (10) | .35 |
| No. of patients with family history of chemical abuse | 16 (25) | 13 (18.8) | .41 | 11 (29.7) | 6 (18.8) | .40 |
| No. of patients with family history of mental illness | 23 (34.3) | 14 (20) | .08 | 10 (27) | 10 (31.3) | .79 |
| No. of patients with maternal history of chemical abuse | 17 (26.2) | 7 (10.1) | .02 | 1 (2.8) | 0 (0) | 1.00 |

P values were obtained by using Fisher's exact test.

^a Intermittent exotropia, the most common form of exotropia,^{4,7,24} is characterized by intermittent outward deviation of one or both eyes and is managed with observation, eye exercises, or surgery.

^b Convergence insufficiency is characterized by the tendency for the eyes to drift outward while viewing near, often accompanied by symptoms of headaches, difficulty with reading, or double vision. This disorder is managed with prism glasses or eye exercises.

^c *P* values remained significant even after adjustment for family history variables in logistic regression analyses.

likely than control subjects to have a maternal history of chemical abuse. Convergence insufficiency was associated only with increased incidence of mental health disorders and use of psychotropic medications.

Table 5 presents the prevalence of psychiatric illness among children with esotropia, according to the type of esotropia, compared with control subjects. Although patients with a history of congenital esotropia tended to have more psychiatric illnesses (*P* = .06) and to require the use of psychiatric medications (*P* = .06), these 3 common forms of childhood esotropia were not significantly associated with the later development of mental illness.

DISCUSSION

Children with exotropia from Olmsted County, Minnesota, were 3 times more likely than control subjects to develop a mental illness by early adulthood. Conversely, children with esotropia were no more likely than control subjects to develop a mental illness. Patients with inter-

mittent exotropia, the most common form of exotropia, were also significantly more likely to have greater numbers of mental health disorders, mental health emergency department visits, and mental health hospitalizations and to have suicidal or homicidal ideation.

Strabismus is a common disorder that affects 3% to 5% of children, with ~126 400 new cases occurring each year in the United States.⁴⁻⁶ The intermittent form of exotropia, which constitutes one half of all exodeviations in the West, is more common than all other types of strabismus in Asia and may be the most common form of strabismus worldwide. Although intermittent exotropia seems to be significantly associated with the development of mental illness among white individuals in the United States, it is not known whether Asian individuals or other populations with intermittent exotropia are similarly at risk for developing significant psychiatric illness by early adulthood.

Why exotropia and not esotropia would be associated

TABLE 5 Prevalence of Psychiatric Factors Among Patients With Specific Forms of Esotropia (*N* = 266) and Control Subjects (*N* = 266)

| Factor | No. (%) | | | | | | | | |
|--|--|----------|----------|---|-----------|----------|--|-----------|----------|
| | Congenital (<i>N</i> = 29) ^a | | | Acquired Nonaccommodative (<i>N</i> = 64) ^b | | | Accommodative (<i>N</i> = 173) ^c | | |
| | Case | Control | <i>P</i> | Case | Control | <i>P</i> | Case | Control | <i>P</i> |
| No. of patients with mental illness | 10 (34.5) | 4 (13.8) | .12 | 23 (35.9) | 25 (39.1) | .86 | 60 (34.7) | 58 (33.5) | .91 |
| Total no. of disorders | 30 | 9 | .06 | 58 | 57 | .95 | 132 | 129 | .90 |
| No. of patients using psychiatric medications | 7 (35) | 2 (8) | .06 | 13 (29.6) | 13 (23.2) | .50 | 31 (25.6) | 34 (22.2) | .57 |
| No. of patients with psychiatric emergency department visits | 1 (4.4) | 0 (0) | .45 | 6 (11.5) | 6 (10.5) | 1.00 | 7 (4.6) | 7 (4.3) | 1.00 |
| No. of patients with psychiatric inpatient admissions | 1 (4.4) | 0 (0) | .45 | 5 (9.6) | 4 (7) | .73 | 7 (4.6) | 4 (2.5) | .37 |
| No. of patients with suicide attempts | 0 (0) | 0 (0) | NA | 3 (5.9) | 3 (5.3) | 1.00 | 2 (1.3) | 1 (0.6) | .61 |
| No. of patients with suicidal/homicidal ideation | 1 (4.4) | 1 (3.6) | 1.00 | 8 (15.4) | 3 (5.3) | .11 | 10 (6.7) | 6 (3.7) | .31 |
| No. of patients with family history of chemical abuse | 1 (6.3) | 3 (20) | .33 | 10 (27.8) | 11 (25) | .80 | 19 (18.1) | 16 (13.5) | .36 |
| No. of patients with family history of mental illness | 4 (25) | 5 (33.3) | .70 | 11 (30.6) | 11 (25) | .62 | 30 (25.6) | 30 (25.2) | 1.00 |
| No. of patients with maternal history of chemical abuse | 3 (21.4) | 3 (18.8) | 1.00 | 8 (25.8) | 7 (16.7) | .39 | 12 (12.1) | 12 (10.1) | .67 |

P values were obtained by using Fisher's exact test. NA indicates not applicable.

^a Congenital esotropia is a constant inward deviation of the eyes that develops before 6 months of age and is corrected with surgery.

^b Acquired nonaccommodative esotropia is an inward deviation of the eyes with onset after 6 months of age and is corrected with surgery.

^c Accommodative esotropia, the most common form of childhood esotropia,^{9,24} is associated with far-sightedness and is corrected with glasses or glasses and surgery.

with the development of mental illness by early adulthood is unclear. Ocular misalignment would seem to have similar effects on individuals with strabismus regardless of whether it is esotropic or exotropic. Studies on the psychosocial impact of strabismus have reported no differences between subjects with exotropia and those with esotropia with respect to adverse effects on self-esteem, academic performance, interpersonal relationships, athletic achievement, and gainful employment.^{11–14} Although some investigators have concluded that, at smaller angles of deviation, exotropia is more readily apparent than esotropia,^{15,16} there are no known studies to suggest that exotropia is associated with greater psychosocial stress. In fact, reports using digitally altered photographs of children¹⁷ and adults¹⁸ have demonstrated that individuals with esotropia are viewed more negatively than patients with exotropia. Moreover, exotropia is more likely than esotropia to be intermittent in nature. Regardless of the psychosocial stress of strabismus, there is no direct evidence to support the notion that these stresses, by themselves, can evolve into frank mental illness.

Hereditry is a more likely basis for any association between exotropia and mental illness. The more-prevalent forms of strabismus¹⁹ and most childhood mental illnesses are thought to be the result of interactions between a number of susceptibility genes. Such interactions make it unlikely for any single gene to have a large effect on the onset of either strabismus or childhood mental disorders. However, this provides a potential hypothesis for how an individual gene may be associated with 2 distinct oligogenetic illnesses. The only known example involved an adult with a specific but rare form of strabismus (constant exotropia) and schizophrenia.⁸ A polyalanine-length variant of a single gene, *PMX2B*, was demonstrated to be associated with both conditions. The future identification of other gene variants may provide additional links between the various forms of strabismus and mental illness.

Other potential explanations for the association between childhood exotropia and the later development of mental illness may involve factors not captured by this study. For example, the finding of a significantly higher incidence of maternal chemical abuse during pregnancy among children with exotropia ($P = .02$) may explain a direct or indirect environmental effect on the development of strabismus or mental illness, although it is unclear whether the abused substances are associated with the development of strabismus. Various types of prenatal exposures and not the exotropic alignment may be, at least in part, the basis for the subsequent development of psychiatric disease.

Unlike patients with exotropia, children with esotropia were no more likely than control subjects to develop mental illness by early adulthood. Children with congenital esotropia were slightly more likely to have an increased total number of mental health disorders ($P = .06$) and to use psychiatric medications ($P = .06$). However, the findings for each of those variables might be attributable to chance alone, and numbers were too small to allow any definitive conclusions. Moreover, the

findings might be attributable in part to the association of premature birth, which was more prevalent among patients with congenital esotropia than control subjects or subjects with other forms of strabismus, and ADHD, which was diagnosed for 17.2% of the patients with congenital esotropia and none of their control subjects.²⁰ ADHD, in turn, is associated with increased risk of developing other psychosocial and psychiatric disorders,^{21,22} which may explain the weak link between congenital esotropia and an increased number of mental health disorders.

The findings from this study may raise questions regarding the level of mental illness that constitutes normalcy in human society. We found that 30.7% of control subjects without strabismus were diagnosed as having some form of mental illness by the beginning of the third decade of life. This finding seems abnormally high, and we have no other Olmsted County data with which to compare this finding. However, a psychiatric diagnosis was made for 20.3% of randomly selected children 9, 11, and 13 years of age who were living in a rural community in the southeastern United States.²³ Our prevalence of 30.7% among patients ~1 decade older seems congruent. Moreover, children with exotropia in this study had a greater number and severity of illnesses, such as major depression and illicit drug use; these diagnoses tend to have significantly greater adverse effects on daily life, compared with many of the disorders diagnosed among control subjects.

There are a number of limitations to this study. First, this investigation was performed in a racially homogeneous population in a single geographic area. Extrapolating the findings from this study to groups not represented within our community is problematic. Second, some forms of strabismus were relatively uncommon in our community. The cohort size of 29 patients with congenital esotropia, for example, hindered our ability to examine the role of potential confounders or statistical significance. Moreover, the numbers for some of the reported variables were so small that reported associations might have been the result of chance alone, as was possible for the elevated occurrence of eating disorders among children with esotropia. Caution is therefore warranted regarding some of the reported factors until results are confirmed in other populations. Third, given the stigma of mental illness, some patients from our community might have sought diagnosis and care of their condition outside our geographic area. For example, some routine Mayo Clinic patients had their mental illness managed at the other medical facility in our community, Olmsted Medical Group, and vice versa. However, we would expect the numbers of case and control subjects who did seek outside care to be similar between the 2 groups. Fourth, follow-up monitoring for the control subjects with esotropia was longer than that for the case subjects with esotropia. This difference might result in underrepresentation of the number of children with esotropia who would develop mental illness. Moreover, the children with esotropia were monitored to a mean age of 15.8 years, compared with 20.3 years for those with exotropia. Such a difference might explain the

lower prevalence of mental illness among children with esotropia, because some forms of mental illness that develop in late adolescence might not have been adequately represented. Finally, because the follow-up monitoring in this study ended by late adolescence or early adulthood, we were unable to detect an association with disorders that tend to develop later in life, such as schizophrenia.

This population-based, nested-control study found that children with exotropia had a threefold increased risk of developing mental illness by early adulthood, compared with control subjects. Patients with intermittent exotropia, the most prevalent form of exotropia, also were significantly more likely to have a greater number of mental health disorders, a greater number of mental health emergency department visits or hospitalizations, and suicidal or homicidal ideation. Children with esotropia, however, were no more likely than control subjects to develop mental illness when monitored for a similar period.

ACKNOWLEDGMENT

This study was supported in part by an unrestricted grant from Research to Prevent Blindness (New York, NY).

REFERENCES

1. Frandsen AD. Occurrence of squint: a clinical-statistical study on the prevalence of squint and associated signs in different groups and ages of the Danish population. *Acta Ophthalmol Suppl.* 1960;62:9–157
2. Graham PA. Epidemiology of strabismus. *Br J Ophthalmol.* 1974;58(3):224–231
3. Chew E, Remaley NA, Tamboli A, et al. Risk factors for esotropia and exotropia. *Arch Ophthalmol.* 1994;112(10):1349–1355
4. Govindan M, Mohny BG, Diehl NN, Burke JP. Incidence and types of childhood exotropia: a population-based study. *Ophthalmology.* 2005;112(1):104–108
5. Tollefson M, Mohny BG, Diehl NN, Burke JP. Incidence and types of childhood hypertropia: a population-based study. *Ophthalmology.* 2006;113(7):1142–1145
6. Greenberg A, Mohny BG, Diehl NN, Burke JP. Incidence and types of childhood esotropia: a population-based study. *Ophthalmology.* 2007;114(1):170–174
7. Yu CBO, Fan DSP, Wong VWY, Wong CY, Lam DSC. Changing patterns of strabismus: a decade of experience in Hong Kong. *Br J Ophthalmol.* 2002;86(8):854–856
8. Toyota T, Yoshitsugu K, Ebihara M, et al. Association between schizophrenia with ocular misalignment and polyalanine length variation in *PMX2B*. *Hum Mol Genet.* 2004;13(5):551–561
9. Schiffman J, Maeda JA, Hayashi K, et al. Premorbid childhood ocular alignment abnormalities and adult schizophrenia-spectrum disorder. *Schizophr Res.* 2006;81(2–3):253–260
10. Kurland LT, Molgaard CA. The patient record in epidemiology. *Sci Am.* 1981;245(4):54–63
11. Satterfield D, Keltner JL, Morrison TL. Psychosocial aspects of strabismus study. *Arch Ophthalmol.* 1993;111(8):1100–1105
12. Coats DK, Paysse EA, Towler AJ, Dipboye RL. Impact of large angle horizontal strabismus on ability to obtain employment. *Ophthalmology.* 2000;107(2):402–405
13. Menon V, Saha J, Tandon R, Mehta M, Khokhar S. Study of the psychosocial aspects of strabismus. *J Pediatr Ophthalmol Strabismus.* 2002;39(4):203–208
14. Eustis S, Smith DR. Parental understanding of strabismus. *J Pediatr Ophthalmol Strabismus.* 1987;24(5):232–236
15. Weissberg E, Suckow M, Thorn F. Minimal angle horizontal strabismus detectable by lay observers. *Optom Vis Sci.* 2004;81(7):505–509
16. Reinecke RD, Sterling R, Wizov S. Accuracy of judgments of the presence or absence of eccentric (non-primary) gaze and the presence or absence of strabismus. *Binocul Vis Strabismus Q.* 1991;6:189–196
17. Uretmen O, Egrilmez S, Kose S, et al. Negative social bias against children with strabismus. *Acta Ophthalmol Scand.* 2003;81(2):138–142
18. Olitsky SE, Sudesh S, Graziano A, et al. The negative psychosocial impact of strabismus in adults. *J AAPOS.* 1999;3(4):209–211
19. Engle EC. Genetic basis of congenital strabismus. *Arch Ophthalmol.* 2007;125(2):189–195
20. Bhutta AT, Cleves MA, Casey PH, Cradock MM, Anand KJS. Cognitive and behavioral outcomes of school-aged children who were born preterm. *JAMA.* 2002;288(6):728–737
21. Klassen AF, Miller A, Fine S. Health-related quality of life in children and adolescents who have a diagnosis of attention-deficit/hyperactivity disorder. *Pediatrics.* 2004;114(5). Available at: www.pediatrics.org/cgi/content/full/114/5/e541
22. Biederman J, Newcom J, Sprick S. Comorbidity of attention deficit hyperactivity disorder with conduct, depressive, anxiety, and other disorders. *Am J Psychiatry.* 1991;148(5):564–577
23. Costello EJ, Angold A, Burns BJ, et al. The Great Smokey Mountains Study of Youth: goals, design, methods, and the prevalence of DSM-III-R disorders. *Arch Gen Psychiatry.* 1996;53(12):1129–1136
24. Donahue SP. Pediatric strabismus. *N Engl J Med.* 2007;356(10):1040–1047

Mental Illness in Young Adults Who Had Strabismus as Children

Brian G. Mohnney, Jeff A. McKenzie, Jason A. Capo, Kevin J. Nusz, David Mrazek
and Nancy N. Diehl

Pediatrics 2008;122;1033

DOI: 10.1542/peds.2007-3484

Updated Information & Services

including high resolution figures, can be found at:
<http://pediatrics.aappublications.org/content/122/5/1033.full.html>

References

This article cites 23 articles, 3 of which can be accessed free at:
<http://pediatrics.aappublications.org/content/122/5/1033.full.html#ref-list-1>

Citations

This article has been cited by 3 HighWire-hosted articles:
<http://pediatrics.aappublications.org/content/122/5/1033.full.html#related-urls>

Subspecialty Collections

This article, along with others on similar topics, appears in the following collection(s):
Ophthalmology
http://pediatrics.aappublications.org/cgi/collection/ophthalmology_sub

Permissions & Licensing

Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at:
<http://pediatrics.aappublications.org/site/misc/Permissions.xhtml>

Reprints

Information about ordering reprints can be found online:
<http://pediatrics.aappublications.org/site/misc/reprints.xhtml>

PEDIATRICS is the official journal of the American Academy of Pediatrics. A monthly publication, it has been published continuously since 1948. PEDIATRICS is owned, published, and trademarked by the American Academy of Pediatrics, 141 Northwest Point Boulevard, Elk Grove Village, Illinois, 60007. Copyright © 2008 by the American Academy of Pediatrics. All rights reserved. Print ISSN: 0031-4005. Online ISSN: 1098-4275.

American Academy of Pediatrics

DEDICATED TO THE HEALTH OF ALL CHILDREN™

