Published in final edited form as:

Strabismus. 2015 ; 23(3): 105–110. doi:10.3109/09273972.2015.1070881.

Prevalence of Mental Health Illness Among Patients with Adult-onset Strabismus

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Abstract

Background—Children diagnosed with some forms of strabismus were recently found to have an increased risk of developing mental illness by early adulthood. The purpose of this case-controlled study was to determine if adults with non-paralytic forms of strabismus are similarly at an elevated risk for developing mental illness.

Methods—The medical records of all patients diagnosed as adults (≥ 19 years of age) with convergence insufficiency (CI, n=118), divergence insufficiency (DI, n=80), and small angle hypertropia (HT, n=99) from January 1, 1985, through December 31, 2004, were retrospectively reviewed. Each case was compared with a sex- and birthdate-matched non-strabismic control. The medical records were reviewed for mental health diagnoses, including inpatient and outpatient encounters, psychiatric ER visits, and medication use.

Results—Mental health disorders were diagnosed in 65 (55.1%) patients with CI compared to 54 (45.8%) controls ($p=0.15$), in 51 (63.8%) patients with DI compared to 42 (52.5%) controls ($p=0.15$), and in 63 (63.6%) patients with HT compared to 57 (57.6%) controls ($p=0.38$). CI patients were not more likely to have mental health disorders than their controls ($p=0.15$). Mental health hospitalizations ($p=0.02$), psychiatric medication use ($p=0.04$), and unspecified anxiety disorders ($p=0.03$) were higher in DI patients compared to controls. HT patients were found to have more generalized anxiety disorders ($p=0.003$) than controls.

Conclusions—Adults with some forms of strabismus (DI and HT) appear to have an increased risk of mental illness and its comorbidities, compared to age- and gender-matched non-strabismic controls.

Keywords

strabismus; mental disorders; ocular motility disorders

Introduction

Recent studies have demonstrated a link between strabismus and mental illness. Children diagnosed with some forms of strabismus (intermittent exotropia, convergence insufficiency and congenital esotropia) were recently found to have a three-fold increased incidence of developing mental illness by early adulthood compared to controls.^{1,2} Additionally, children with intermittent exotropia had more mental health emergency department visits, mental health hospitalizations, and suicidal or homicidal ideation when compared to their controls. Children with congenital esotropia were prescribed more psychotropic medications than their controls. In adults, constant exotropia, has recently been linked with schizophrenia as a result of polymorphisms in PMX2B, a gene that encodes a transcription factor found in neuroectodermal tissues.³ Studies have also suggested that, like children, adults with strabismus encounter negative psychosocial effects and report difficulties with employment, relationships, and self-image as a result of the negative bias associated with their ocular misalignment.⁴⁻⁶ Currently, there are no known reports that have analyzed the effects of these negative psychosocial factors on adults with strabismus, and it is unknown if these negative factors eventually progress to cause mental illness.

The lifetime risk for being diagnosed with adult-onset non-paralytic strabismus was recently reported to be 2.3%, with the most common forms being convergence insufficiency (CI), divergence insufficiency (DI), and small angle hypertropia (HT).⁷ The purpose of this population-based case-controlled study was to determine if adults with non-paralytic forms of strabismus are at an elevated risk for developing mental illness.

Methods

The medical records of all adults 19 years of age and older residing in Olmsted County and diagnosed with convergence insufficiency (CI), divergence insufficiency (DI), and small angle hypertropia (HT) between January 1, 1985 and December 31, 2004 were retrospectively reviewed⁷. Institutional review board approval was obtained for this study. The Rochester Epidemiology Project, a medical records linkage system designed to capture data on any patient-physician encounter in Olmsted County, Minnesota was used to identify the cases in this study.⁸ The racial distribution of Olmsted County residents in 1990 was 95.7% white, 3.0% Asian American, 0.7% black, 0.3% Native American, and 0.3% 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.⁸

The cases for this study were previously reported in a 20-year population-based study.⁷ Each of the strabismus cases was matched with a non-strabismic control from the same population. Controls were chosen by selecting Olmsted County residents who were of the same gender and whose year of birth and registration (within the 2 medical institutions) matched for each of the index case subjects. Residence status, 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. None of the 594 patients included in this study were related.

The medical records of the adults with strabismus and the matched controls were reviewed for a diagnosis of mental illness (*Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition Text Revision* 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, and substance abuse among case and control subjects were collected from mental health and self-reporting primary care records. The data for this study was collected via Research Electronic Data Capture (REDCap), an online application that allows for secure and portable data collection for research purposes.⁹

Comparisons between the incidence of mental illness in adults with strabismus and their sex- and age-matched controls without strabismus was completed by using a Chi-square test for independence, or Fishers exact test for rare risk factors. The two-sample t-test or Wilcoxon Rank-sum test was used to compare any continuous variables between the cases and controls.

Results

A total of 297 adults with new-onset non-paralytic strabismus [118 with convergence insufficiency (CI), 80 with divergence insufficiency (DI), and 99 with small angle hypertropia (HT)] were identified during the 20-year study period. Males represented 50 (42.4%) of the 118 adults with CI, 28 (35.0%) of the 80 adults with DI, and 36 (36.4%) of the 99 adults with HT. The 118 adults with CI, diagnosed at a median age of 69 years, were monitored to a median age of 82 years compared with 82 years for controls ($p=0.76$). Adults with DI were diagnosed at a median age of 74 years and followed to a median age of 85 years compared with 83 years for controls ($p=0.39$). Adults with HT were diagnosed at a median age of 72 years and were monitored to a median age of 82 years compared with 82 years for controls ($p=0.32$). Table 1 presents historical and initial clinical characteristics of the 297 cases with adult-onset non-paralytic strabismus. There were no significant differences between the 3 case groups and their controls, including family history of psychiatric disease or chemical abuse.

Table 2 shows the prevalence of specifically queried factors of mental illness among the 297 cases and their controls. A mental health disorder was diagnosed in 65 (55.1%) adults with CI compared with 54 (45.8%) of controls ($p=0.15$). In adults with DI, a mental illness was diagnosed in 51 (63.8%) compared with 42 (52.5%) of controls ($p=0.15$). A mental health disorder was diagnosed in 63 (63.6%) of hypertropic adults compared with 57 (57.6%) of

controls ($p=0.38$). Except for adults with DI, the 6 specifically queried factors of mental illness were no different between cases and controls. Adults with DI were significantly more likely to have psychiatric hospitalizations ($p=0.02$) and to use psychotropic medications ($p=0.04$) when compared to their controls.

Table 3 presents the types and total numbers of psychiatric disorders diagnosed among the 297 adults with strabismus and their controls. There were no significant differences in the prevalence of specific psychiatric disorders between adults with CI and their controls. Adults with DI were significantly more likely to be diagnosed with unspecified anxiety disorders when compared to their controls ($p=0.03$), while adults with HT were significantly more likely to be diagnosed with generalized anxiety disorder ($p<0.001$) when compared to their controls.

Table 4 presents the average prevalence of the queried factors in Table 2 among adults with strabismus and their controls. The number of CI adults diagnosed with mental illness was not significantly higher than the number of controls diagnosed with mental illness ($p=0.15$). Adults with DI, however, have a higher average number of psychiatric hospitalizations ($p=0.02$), maximum concurrent number of psychotropic medications ($p=0.03$), and total months on psychotropic medications ($p<0.01$) when compared to controls. There appear to be no significant differences between adults with HT and their controls.

Table 5 presents the timing of the initial mental health diagnosis among adults with strabismus, with regards to whether it was before or after their strabismus diagnosis. The majority of adults with CI (63.1%) and DI (58.8%) were diagnosed with a mental health disorder before they were diagnosed with strabismus, while the majority of adults with HT (57.1%) were diagnosed with a mental health disorder after their strabismus diagnosis.

Discussion

Adults with divergence insufficiency (DI) from Olmsted County, Minnesota, were significantly more likely to have psychiatric-related hospitalizations and psychotropic medication use than their controls, while adults with small angle hypertropia (HT) had a mild increase of specific mental health disorders compared to their controls. Those with convergence insufficiency (CI) did not have an increased risk of mental health illness when compared to their controls.. Adults with DI had significantly higher number of psychotropic medications and length of time on medications. Additionally, the DI cases had a significantly higher number of unspecified anxiety disorder diagnoses, while the HT cases had a significantly higher number of generalized anxiety disorder when compared to their controls.

Children with exotropia and congenital esotropia were recently found to be 3 times more likely to develop a psychiatric disorder when compared to their controls.^{1,2} These children also had significantly increased numbers of psychiatric diagnoses and children with exotropia had more psychiatric-related emergency department visits and hospitalizations, and suicidal and homicidal ideation than their sex- and birthdate-matched controls. Given that children with CI were found to be at an increased risk for developing mental illness,

adults with CI may similarly be expected to be at an increased risk. However, CI adults were no more likely than controls to develop a psychiatric illness or have other psych-related comorbidities.

Divergence insufficiency and small angle hypertropia, two forms of strabismus rarely observed in children, were associated with an increased risk of developing mental illness and its comorbidities (DI) or with specific psychiatric disorders (DI and HT). However, a cause and effect relationship seems unlikely given that the psychiatric illness predated the diagnosis of strabismus in 58.8% and 42.9% of DI and HT patients, respectively.

A link between constant exotropia and schizophrenia was found to be associated with polymorphisms in a gene encoding a transcription factor.³ Although the genetic and molecular basis of adult-onset non-paralytic strabismus is not yet known, it is possible that mutations could be responsible for the development and progression of both mental illness and strabismus. Potential etiologies for DI have been thought to include microvascular ischemia, paralysis of the sixth nerve, and even local degenerative changes.^{10,11} Similarly, HT is thought to be caused by hemorrhage or infarction of the brainstem, as well as other space occupying lesion causes like multiple sclerosis.¹² Mental illness and these two types of strabismus could both be a result of these insults to the brain. Alternatively, CI is thought to be linked with the decline in the ability to accommodate with aging.¹³ The degenerative etiology for adult-onset CI could explain why they are not at an increased risk for developing mental illness.

A mental health illness was diagnosed in 45.8% of the CI controls, 52.5% of DI controls, and 57.6% of HT controls in this study. The prevalence of mental health illness in controls appears elevated; however, in a study that interviewed more than 9,000 participants aged 18 and older using the National Comorbidity Survey between 2001 to 2003 (within the years of this study), the lifetime prevalence of at least 1 mental health disorder was found to be 46.4 %.¹⁴ The prevalence of mental health illness in the control groups of the current study is consistent with these findings, given that the CI, DI, and HT controls were followed to median ages of 82, 83, and 82 years, respectively.

There are a number of limitations to the findings of this study. The retrospective nature of this study is hampered by incomplete data and irregular follow-up. Moreover, some of the study patients may have sought medical care outside the 2 medical centers, particularly given the social stigma associated with mental illness, thereby further decreasing the prevalence of disease. However, both cases and controls would be expected to be affected similarly. A further limitation is that the general population from which the cases and controls were obtained is a racially homogeneous one. Making inferences to other populations, especially ones not well represented in this study, could be problematic. Third, we investigated the prevalence of many variables between the cases and controls in this study. This study should be viewed as hypothesis generating research. It is possible that some of the significant associations were based on chance alone and would need to be confirmed by reproducing this study in a different population.

Adults with DI were found to have a higher number of psychiatric-related hospitalizations and psychotropic medication use (both number and length of time), and were also diagnosed with unspecified anxiety disorder more than their controls in this population-based study. Adults with HT had a higher rate of generalized anxiety disorder, while adults with CI had no increased risk of mental health illnesses compared to controls.

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Table 1

Historical and Initial Clinical Characteristics of Adults with Non-paralytic strabismus (N=297) and Control Subjects (N=297)

Characteristic	Convergence Insufficiency			Divergence Insufficiency			Hypertropia		
	Case (N=118)	Control (N=118)	P	Case (N=80)	Control (N=80)	P	Case (N=99)	Control (N=99)	P
Male, n (%)	50 (42.4)	50 (42.4)	1.00	28 (35.0)	28 (35.0)	1.00	36 (36.4)	36 (36.4)	1.00
Family history of psychiatric disease, n/N (%)	25/102 (24.5)	21/83 (25.3)	0.90	16/55 (29.1)	12/54 (22.2)	0.41	13/84 (15.5)	12/70 (17.1)	0.78
Family history of chemical abuse, n/N (%)	28/102 (27.5)	19/85 (22.4)	0.42	19/57 (33.33)	14/54 (25.9)	0.39	20/84 (23.8)	19/70 (27.1)	0.64
Median age at last follow up, years	82	82	0.76	85	83	0.39	82	82	0.32

P: p-value

Table 2

Mental Health Characteristics of Adults with Non-paralytic strabismus (N=297) and Control Subjects (N=297)

	No. (%)							
Characteristic	Convergence Insufficiency			Divergence Insufficiency			Hypertropia	
	Case (N=118)	Control (N=118)	P	Case (N=80)	Control (N=80)	P	Case (N=99)	Control (N=99)
No. of patients with mental illness	65 (55.1)	54 (45.8)	0.15	51 (63.8)	42 (52.5)	0.15	63 (63.6)	57 (57.6)
No. of patients using psychiatric medications	59 (50.0)	46 (39.0)	0.09	51 (63.8)	38 (47.5)	0.04	49 (49.5)	46 (46.5)
No. of patients with psychiatric ER visits	14 (11.9)	11 (9.3)	0.53	10 (12.5)	7 (8.8)	0.54	10 (10.1)	11 (11.1)
No. of patients with psychiatric hospitalizations	18 (15.3)	13 (11.0)	0.34	13 (16.3)	4 (5.0)	0.02	8 (8.1)	10 (10.1)
No. of patients with suicide attempts	4 (3.4)	4 (3.4)	1.00	2 (2.5)	1 (1.3)	1.00	0 (0.0)	2 (2.0)
No. of patients with suicidal ideation	8 (6.8)	6 (5.1)	0.58	5 (6.3)	2 (2.5)	0.25	4 (4.0)	5 (5.1)

P: p-value

Table 3

Type and Prevalence of All Mental Illnesses Diagnosed Among Adults with Non-paralytic Strabismus (N=297) and Control Subjects (N=297)

Type of Diagnosis Reported	No. (%)							
	Convergence Insufficiency				Divergence Insufficiency		Hypertropia	
	Cases (N=118)	Controls (N=118)	P		Cases (N=80)	Controls (N=80)	P	
Major depression	28 (23.7)	18 (15.3)	0.10		11 (13.8)	4 (5.0)	0.06	12 (12.1)
Depression NOS	11 (9.3)	12 (10.2)	0.83		20 (25.0)	24 (30.0)	0.48	30 (30.3)
Adjustment disorder	16 (13.6)	13 (11.0)	0.55		12 (15.0)	5 (6.3)	0.07	16 (16.2)
Generalized anxiety	10 (8.5)	13 (11.0)	0.51		12 (15.0)	13 (16.3)	0.83	26 (26.3)
Anxiety NOS	4 (3.4)	2 (1.7)	0.41		8 (10.0)	1 (1.3)	0.03	1 (1.0)
Alcoholism	9 (7.6)	4 (3.4)	0.15		4 (5.0)	2 (2.5)	0.41	3 (3.0)
Personality disorder	5 (4.2)	4 (3.4)	0.73		4 (5.0)	4 (5.0)	1.00	5 (5.1)
Bipolar disorder	4 (3.4)	2 (1.7)	0.41		1 (1.3)	0 (0.0)	1.00	-
Somatoform/conversion disorder	3 (2.5)	3 (2.5)	1.00		1 (1.3)	1 (1.3)	1.00	1 (1.0)
Eating disorder	3 (2.5)	1 (0.8)	0.62		2 (2.5)	2 (2.5)	1.00	-
Schizophrenia	1 (0.8)	2 (1.7)	1.00		-	-	-	-
Schizoaffective disorder	-	-	-		1 (1.3)	0 (0.0)	1.00	-
Mood disorder NOS	1 (0.8)	1 (0.8)	1.00		-	-	-	-
Anxiety panic disorder	3 (2.5)	0 (0.0)	0.25		2 (2.5)	1 (1.3)	1.00	1 (1.0)
Dysthymia	0 (0.0)	2 (1.7)	0.50		2 (2.5)	1 (1.3)	1.00	1 (1.0)
Psychoses	1 (0.8)	0 (0.0)	1.00		0 (0.0)	3 (3.8)	0.25	-
Anxiety OCD	1 (0.8)	0 (0.0)	1.00		1 (1.3)	0 (0.0)	1.00	-
Anxiety phobia	-	-	-		-	-	-	1 (1.0)
Oppositional disorder	0 (0.0)	1 (0.8)	1.00		-	-	-	-
Post-traumatic stress disorder	1 (0.8)	0 (0.0)	1.00		-	-	-	-
Seasonal affective disorder	1 (0.8)	0 (0.0)	1.00		-	-	-	-
Other substance-related disorder	-	-	-		1 (1.3)	0 (0.0)	1.00	-
Dementia	24 (20.3)	19 (16.1)	0.40		17 (21.3)	16 (20.0)	0.85	27 (27.3)
								18 (18.2)
								0.13

P: p-value

Mental Health Characteristics of Adults with Non-paralytic Strabismus (N=297) and Controls (N=297)

Table 4

	mean (SD)								
Characteristic	Convergence Insufficiency				Divergence Insufficiency		Hypertropia		
	Cases (N=118)	Controls (N=118)	P	Cases (N=80)	Controls (N=80)	P	Cases (N=99)	Controls (N=99)	P
Avg total no. of disorders	0.9 (1.2)	0.7 (1.1)	0.05	1.1 (1.3)	0.8 (1.0)	0.24	1.0 (1.0)	0.7 (0.8)	0.12
Avg no. of documented psychiatric hospitalizations	0.4 (1.4)	0.2 (1.1)	0.30	0.5 (1.6)	0.1 (0.5)	0.02	0.1 (0.5)	0.2 (0.6)	0.62
Avg no. of psychiatric emergency room visits	0.3 (1.6)	0.3 (1.7)	0.54	0.3 (1.2)	0.2 (0.9)	0.38	0.2 (1.3)	0.2 (0.6)	0.86
Avg no. of reported suicide attempts	0.1 (0.5)	0.1 (0.3)	0.98	0.1 (0.4)	0.0 (0.1)	0.54	0.0 (0.0)	0.0 (0.2)	0.16
Avg no. or reported episodes of suicidal or homicidal ideation	0.2 (1.0)	0.1 (0.5)	0.59	0.2 (1.4)	0.0 (0.2)	0.22	0.1 (0.7)	0.2 (0.8)	0.73
Avg no. of max concurrent psychiatric medications	0.8 (1.0)	0.6 (0.9)	0.06	1.1 (1.2)	0.7 (0.8)	0.03	0.7 (0.9)	0.6 (0.8)	0.48
Avg no. of total months on medications	52.4 (95.3)	43.4 (91.8)	0.10	64.5 (94.2)	28.1 (61.8)	0.003	34.5 (66.7)	36.6 (70.4)	0.99

P: p-value

Timing of Mental Health Diagnosis in Adults with Non-paralytic Strabismus and 1 Mental Health Disorder

Table 5

Type of Strabismus	Before Strabismus	After Strabismus
CI, n (%)	41 (63.1)	24 (36.9)
DI, n (%)	30 (58.8)	21 (41.2)
HT, n (%)	27 (42.9)	36 (57.1)