Explaining the Relationship between Three Eye Diseases and Depressive Symptoms in Older Adults

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Purpose. The purpose of this study is to examine whether patients with age-related eye diseases, like age-related macular degeneration (AMD), glaucoma, or Fuchs corneal dystrophy, are more likely to show signs of depression compared to a control group of older adults with good vision, and to determine whether reduced mobility mediates these relationships.

Methods. We recruited 315 eligible patients (81 with AMD, 55 with Fuchs, 91 with glaucoma, and 88 controls) from the ophthalmology clinics of a Montreal hospital from September 2009 until December 2011. Depressive symptoms were assessed using the Geriatric Depression Scale Short Form (GDS-15). Life space was measured using the Life Space Assessment. Logistic regression was used to adjust for demographic, health, and social factors, and mediation was assessed using the methods of Baron and Kenny.

Results. There were 78 people (25%) meeting the criteria for depression in the cohort. All three groups with eye disease were more likely to be depressed than the control group after adjusting for age, sex, ethnicity, education, cognitive score, limitations in activities of daily living, social support, and lens opacity ($P < 0.05$). Life space and limited activities due to a fear of falling appeared to mediate the relationship between eye disease and depression.

Conclusions. Visually limiting eye disease is associated with depression in older adults. Further research on interventions to prevent depression in patients with eye disease is warranted and should consider strategies to alleviate mobility limitation. Greater attention from families, physicians, and society to the mental health needs and mobility challenges of patients with eye disease is needed. (*Invest Ophthalmol Vis Sci.* 2012;53:2308–2313) DOI:10.1167/iovs.11-9330

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Prior research has found consistently that patients with age-related macular degeneration (AMD) have high rates of depression,[1–3] while results for glaucoma are less convincing or null.[4–7] Few studies have attempted to explain why patients with eye disease would be more likely to be depressed,[8] which is important to provide appropriate treatment and to design effective non-medical interventions. Much remains to be explained to understand the pathways by which age-related eye disease may affect mental health.

We found recently that patients with AMD, Fuchs corneal dystrophy, and glaucoma have greatly reduced life space (16, 13, and 12 points lower than controls, on average) compared to a control population of patients with good vision after adjusting for several demographic and health factors.[9] We chose these three age-related eye diseases because they have very different profiles of vision loss that we thought might impact mobility in different patterns. Life space refers to the spatial extent of a person over the last month and takes into account their need for assistance.[10] Conceptually, eye disease may lead to reduced life space due to a variety of factors, such as driving limitations,[11,12] fear of falling,[13,14] and worse balance,[15] which may then cause depression. Therefore, reduced mobility, especially as captured by the concept of life space,[10] may explain (mediate) part of the relationship between eye disease and depression. A mediator, also called an intervening variable, is a variable that is related statistically to the independent and dependent variable and also is hypothesized to be in the causal pathway.[16] Although we must be cautious in inferring causality from observational data, the search for mediators is important because the identification of factors lying in the causal pathway can lead to additional targets for intervention.

Our first objective was to examine the relationship between patients with different types of visually impairing eye disease and depression. Based on previous research showing consistent relationships between AMD and depression,[1–3] and because of our prior results that AMD and Fuchs patients had the largest decrements in life space,[9] we hypothesized that patients with central vision loss (AMD and Fuchs) would be more likely to be depressed than patients with primarily peripheral vision loss (glaucoma). Our second objective was to examine whether reduced mobility mediated these relationships.

Methods

Study Population

All participants were recruited from the ophthalmology clinics at Maisonneuve-Rosemont Hospital in Montreal, Canada between September 2009 and December 2011. Three members of the research team (MP, SM, and FD) reviewed all the patient files every day for five

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retinal specialists, five glaucoma specialists, four corneal specialists, and six general ophthalmologists to check for eligible patients.

Participants were required to be 65 years or older. Furthermore, the patients with a clinical diagnosis of AMD, Fuchs, or glaucoma were required to have at least some vision loss because we thought it would be unlikely that these diseases would cause depression unless they had begun to affect vision. Specifically, the AMD and Fuchs patients were required to have bilateral disease and to have visual acuity of worse than 20/40 in their better eye. Glaucoma patients were required to have bilateral disease and to have a visual field mean deviation worse than or equal to −4 decibels (dB) in their worse eye. This would be considered "early" visual field loss according to prior literature.[17] All glaucoma types were recruited. The three groups with eye disease were allowed to have other eye diseases, which also may have impaired vision. However, a person was not included if he/she met the visual inclusion criteria for multiple groups (i.e., AMD and Fuchs). Finally, the controls were required to have visual acuity of 20/40 or better in the better eye and a visual field mean deviation in the worse eye better than −4dB. Controls either had no current eye disease (65%) or they had non-visually impairing conditions, such as early cataract (15%), early AMD (5%), ocular hypertension (6%), blepharitis (3%), or other (6%). People who had received eye surgery, laser, or an intra-vitreal injection in the last 3 months were enrolled after a 2 to 3 month delay so that their data would be less affected by their treatment. Patients had to score 10 or better on the Mini-Mental State Exam (MMSE) Blind Version to optimize the reliability of the collection of the self-reported data.[18] The Blind version of the MMSE omits eight items that rely on vision and has been validated against the original version. A score of 10 on the Blind version is equivalent to a score of 18 on the original version, which was the cutoff used in previous vision research on older adults.[19]

Of 555 patients who appeared to meet eligibility criteria from a review of the medical records, 378 (68%) accepted our invitation to be in the study, 152 (27%) refused, and 25 (5%) were not capable of responding for themselves. Of the 378 who accepted 315 met final eligibility criteria, including 81 with AMD, 91 with glaucoma, 55 with Fuchs corneal dystrophy, and 88 without significant eye disease. Participants were paid $10 for their participation and signed a consent form. The project was approved by the Ethics Committee of the Hospital and the research conformed to the tenets of the Declaration of Helsinki.

Data Collection

Data were collected in a 1 to 1.5-hour session by one of three trained research personnel. Participants first answered questions on demographics, mobility, and health, and then they performed vision tests. The medical chart also was reviewed.

Mobility

The Life Space Assessment (LSA) was used to measure the spatial extent of participants in a given month.[10] The LSA takes into account the frequency of going to different life space levels (bedroom, driveway, within neighborhood, outside neighborhood but within town, and out of town), and whether personal or technical assistance was required to get to those levels. A composite score (LS-C, range 0–120) was calculated, which combined information on the life space level, assistance required, and frequency. Higher life space scores indicated greater life space. The reliability and construct/criterion validity of this questionnaire have been reported previously.[10] Patients also were asked if they limited their activities due to a fear of falling.

Depression, Health, and Social Support. Depressive symptoms were assessed using the Geriatric Depression 15-item Scale.[20] A score of 5 or greater was used to indicate depression. This threshold had 93% sensitivity and 65% specificity compared to a clinical diagnosis of depression using ICD-10 criteria.[20] Participants were asked if they had any limitations in activities of daily living (ADL) with the following question: "Because of any physical or health problem, do you need the help of another person with present care needs, such as eating, bathing, dressing, or getting around the home?" Cognitive status, as mentioned previously, was measured using the MMSE Blind Version, which excludes eight items that rely heavily on vision for a total maximum score of 22.[18] Social support was assessed by asking, "When you need help, can you count on someone who is willing and able to meet your needs?" Responses were always, sometimes, and never.

Vision and Eye Disease. Binocular habitual visual acuity was measured using the ETDRS chart with illuminated light box at 2 meters or at 1 meter if the participant could not read any letters at 2 meters.[21,22] Letter by letter scoring was performed with scores at 2 meters converted to scores at 1 meter by adding 15. Scores were converted to logMAR. Contrast sensitivity was measured using the Pelli-Robson chart at 1 meter for each eye.[23] Forced choice letter-by-letter scoring procedures were used until a participant read all 3 letters of a triplet incorrectly. Visual field was measured using the Humphrey FDT with full threshold N-30 testing in each eye.[24] The FDT measures 30° horizontally and 24° vertically. In addition, the medical record was reviewed, and further detail on the patient's eye disease and any coexisting eye disease (such as lens opacity) was recorded. Those who could not perform the FDT test because of advanced eye disease had their last visual field exam results taken from the medical record.

Statistical Analyses

Descriptive statistics were calculated including means, standard deviations, and percentages. In preliminary analyses, vision, demographic, health, social, and mobility variables were compared for the three eye disease groups and the control group using ANOVA or chi square tests. Next, to determine if eye disease was associated independently with depression, logistic regression was used to adjust for potential confounding. The different disease groups (AMD, glaucoma, and Fuchs dystrophy) were entered as indicator variables in the regression model with the control group as the reference. We adjusted for demographic and health variables, including age, sex, ethnicity, education, cognitive status, social support, ADL limitations, and lens opacity. These variables were chosen based on research showing the importance of these variables for depression.[25–27] The Baron and Kenny approach was used to determine evidence for mediation.[28] Briefly, relationships between eye disease and depression should be reduced once a mediator is in the model. Analyses were done in Stata Version 11.0 (College Station, TX).

Results

We recruited 315 patients who resided in the community (82%), in assisted living (10%) or in a retirement home (8%). Characteristics of the four groups are compared in Table 1. The groups with eye disease were older than the control group ($P < 0.001$). The AMD and Fuchs groups had a higher percentage of women than the glaucoma or control groups ($P = 0.001$) and the glaucoma group had a higher percentage of those from an African descent than the other groups. The groups with eye disease had worse cognitive scores, were more likely to have ADL limitations and lens opacities, had worse life space, and were more likely to limit activities due to a fear of falling than the control group ($P < 0.05$).

Visual acuity and contrast sensitivity were worst in the AMD and Fuchs groups, while visual field was worst in the glaucoma group, as expected ($P < 0.001$, Table 1). The binocular visual acuity was 0.74 logMAR (∼20/90 Snellen) in the AMD group, 0.62 logMAR (∼20/80 Snellen) in the Fuchs group, 0.32 logMAR (∼20/45 Snellen) in the glaucoma group, and 0.04 logMAR (∼20/20 Snellen) in the control group. Most of the glaucoma patients (83%) had primary open-angle glaucoma.

Table 1. Description of Four Study Groups

	AMD $n = 81$	Fuchs $n = 55$	Glaucoma $n = 91$	Controls $n = 88$	*P* Value*
Mean age, years (SD)	82.4 (5.9)	79.1 (7.2)	76.4 (7.6)	73.1 (4.5)	<0.001
Female, %	75%	84%	57%	59%	0.001
Ethnicity, %					
Caucasian	100%	100%	88%	98%	<0.001
African descent	0%	0%	12%	2%	
Education, mean years (SD)	9.2 (3.3)	11.0 (4.4)	10.7 (4.3)	11.6 (3.9)	0.001
Binocular visual acuity, mean logMAR (SD)	0.74 (0.40)	0.62 (0.32)	0.32 (0.32)	0.04 (0.06)	<0.001
Contrast sensitivity in better eye, mean letters correct (SD)	24.5 (8.6)	25.7 (7.4)	28.9 (7.3)	39.2 (2.7)	<0.001
Visual field in better eye, mean MD in dB (SD)	−2.9 (3.8)	−2.8 (3.7)	−9.7 (6.3)	0.5 (2.0)	<0.001
Lens opacity, %	36%	25%	25%	15%	0.019
Mean (SD) Mini-Mental Blind Version (max 22)	18.8 (2.8)	19.5 (2.5)	19.4 (2.5)	20.7 (1.4)	<0.001
ADL limitations, %	12%	7%	13%	1%	0.016
Social support available, %					
Always	68%	73%	69%	75%	0.734
Sometimes/never	32%	27%	31%	25%	
Mean life space score (SD)	38.1 (17.7)	46.2 (24.1)	54.4 (25.7)	73.3 (19.7)	<0.001
Limit activities due to fear of falling, %	49%	49%	41%	15%	<0.001

MD = mean deviation.
* *P* value derived from ANOVA for continuous variables or chi-square test/Fisher's exact test for categorical variables.

Other types included secondary glaucoma (7%), angle closure glaucoma (2%), pseudoexfoliation glaucoma (1%), not specified (3%), or mixed (4%). The mean pachymetry value in the worse eye of the Fuchs patients was 687 μm (SD = 104).

The three groups with eye disease were more likely to be depressed than the control group ($P < 0.001$, Table 2). The rates of depression in those with eye disease ranged from 29–39% compared to 8% in the control group. Other variables

Table 2. Characteristics of Participants by Depression Status

	Depressed $n = 78$*	Not Depressed $n = 229$	*P* Value†
Eye disease group, %			
AMD	39%	61%	<0.001
Fuchs	30%	70%	
Glaucoma	29%	71%	
Control	8%	92%	
Mean age (SD)	80.5 (7.5)	76.2 (6.7)	<0.001
Female, %	20%	80%	0.133
Male, %	28%	72%	
Ethnicity, %			0.269
Caucasian	25%	75%	
African descent	38%	62%	
Education, mean years (SD)	9.7 (3.7)	11.0 (4.1)	0.021
Mean (SD) Mini-Mental Blind Version (max 22)	18.8 (2.8)	19.9 (2.4)	0.001
ADL limitations, %			<0.001
No	22%	78%	
Yes	68%	32%	
Social support available, %			
Always	23%	77%	0.096
Sometimes/never	32%	68%	
Lens opacity, %			
No	22%	78%	0.031
Yes	35%	65%	
Mean life space score (SD)	38.3 (20.9)	60.4 (24.5)	<0.001
Limit activities due to fear of falling	64%	28%	<0.001

* Eight people were missing data on depression status.
† *P* value derived from *t* test for continuous variables or chi-square test for categorical variables.

Table 3. Logistic Regression Results Showing Adjusted Relationship between Eye Disease and Depression without (Model 1) and with (Models 2 and 3) Proposed Mobility Mediator

	Model 1 N=304 Depression		Model 2 N=302 Depression		Model 3 N=302 Depression	
	OR	95% CI	OR	95% CI	OR	95% CI
Control	1.00		1.00		1.00	
AMD	4.19	1.53, 11.46	2.50	0.86, 7.26	2.20	0.74, 6.55
Fuchs	3.41	1.19, 9.74	2.16	0.71, 6.54	1.66	0.53, 5.23
Glaucoma	2.66	1.01, 6.96	2.06	0.76, 5.54	1.80	0.65, 4.95
Age	1.04	0.99, 1.09	1.02	0.97, 1.07	1.01	0.96, 1.06
Sex						
Male	1.00		1.00		1.00	
Female	1.01	0.52, 1.96	0.80	0.40, 1.61	0.85	0.41, 1.73
Ethnicity						
Caucasian	1.00		1.00		1.00	
African descent	2.61	0.67, 10.12	2.06	0.49, 8.57	1.74	0.40, 7.66
Education	0.99	0.91, 1.07	0.99	0.91, 1.08	0.99	0.91, 1.08
MMSE Blind Version	0.96	0.85, 1.08	0.97	0.85, 1.10	0.96	0.84, 1.09
ADL limitations	4.59	1.74, 12.10	2.50	0.89, 7.00	2.20	0.77, 6.28
Social support available						
Always	1.00		1.00		1.00	
Sometimes/never	1.68	0.90, 3.11	1.56	0.83, 2.95	1.46	0.76, 2.80
Lens opacity	1.47	0.79, 2.75	1.54	0.81, 2.91	1.49	0.78, 2.85
Life space score			0.97	0.96, 0.99	0.98	0.96, 0.99
Limit activities due to fear of falling					2.51	1.34, 4.70

related to depression in unadjusted analyses included age, education, cognitive status, ADL limitations, lens opacity, life space, and the limitation of activities due to a fear of falling ($P < 0.05$).

In logistic regression models adjusting for age, sex, ethnicity, education, cognitive status, ADL limitations, social support, and lens opacity, patients with AMD (odds ratio, OR, = 4.19, 95% confidence interval, CI, 1.53, 11.46), Fuchs (OR = 3.41, 95% CI 1.19, 9.74), and glaucoma (OR = 2.66, 95% CI 1.01, 6.96) were more likely to be depressed (Table 3, Model 1).

We then sought to determine whether mobility limitations summarized by life space could explain the relationship between eye disease and depressive symptoms (Table 3, Model 2). With life space in the regression model, the OR dropped from 4.19 to 2.50 for AMD, from 3.41 to 2.16 for Fuchs, and from 2.66 to 2.06 for glaucoma. The ORs for AMD, Fuchs, and glaucoma were no longer statistically significant with life space in the model, indicating evidence for partial mediation. We also added limitation of activities due to a fear of falling to the model and this variable further reduced the odds ratios for eye disease, also indicating evidence of partial mediation (Table 3, Model 3).

Discussion

Those older adults with AMD, Fuchs corneal dystrophy, and glaucoma were more likely to be depressed than the controls. The relationships with depression were strongest for AMD and Fuchs, which affect primarily central vision, providing support for our hypothesis. Furthermore, we found evidence that life space and the limitation of activities due to a fear of falling act as partial mediators of the relationship between eye disease and depression. These cross-sectional data are consistent with our conceptual model that eye disease acquired at an older age results in loss of mobility, which may then cause or exacerbate depressive symptoms.

Our data agree with literature finding high prevalence rates and incidence rates of depression in AMD patients.[1–3] To our knowledge, no prior studies have been done examining depression in Fuchs patients. Other studies on glaucoma and depression either did not have a control group,[4] did not adjust for factors other than age[6] or were null.[7] We included only people with a certain severity of glaucoma, as our inclusion criteria for glaucoma required bilateral disease and a mean deviation visual field in the worse eye of at least −4dB. We required glaucoma patients to have bilateral disease due to other research reporting that only bilateral disease affected mobility.[29]

We calculated our sample size to have enough statistical power to detect fairly large (OR > 2.5) relationships between the three eye diseases and depression. However, we had limited power to detect relationships between other factors and depression. For example, social support, which is an established risk factor for depression,[30,31] was not statistically significant in our data, although the trend is in the expected direction in that those who only sometimes or never have social support available had a higher odds of depression (OR = 1.68, 95% CI 0.90, 3.11).

A limitation of our study is that we do not have longitudinal data to investigate mediation more conclusively. Longitudinal data are necessary to establish the temporality of the onset of eye disease, loss of life space, and onset of depression. We used a cutoff of 5 on the Geriatric Depression Scale, which was reported to have a 93% sensitivity and 65% specificity.[20] This lower specificity probably resulted in some false positives for depression but it should not have differed by eye disease status and, therefore, should not have biased our results. Furthermore, it is possible that some of the relationship between eye disease and depression is due to the ongoing treatments that patients with eye disease must undergo. We tried to limit this

by delaying data collection by 2–3 months for those who had recently had eye surgery, an intravitreal injection, or laser. Strengths of this study include a good response rate in eligible patients (68%); use of a validated depression scale suitable for older adults; inclusion of several potential confounders including social support, cognitive status, and ADL disability; measurement of visual function, and the investigation of mediation. Another important strength of our study is that controls were recruited from the same clinics as the patients with eye disease, minimizing the chances of selection bias. Our rate of depression in the control population (8%) was similar to what was reported in similarly aged US population-based studies (11%),[32,33] giving us greater confidence that our control sample was representative of the greater population of older adults.

Some randomized clinical trial work has been done in AMD patients to try to prevent depression. Brody et al. found that a 12-hour self-management session reduced emotional distress over a 6-month period in AMD patients,[34] while Rovner et al. found that six problem-solving treatment sessions resulted in a lower 2–month incidence rate of depressive symptoms but that these results were not maintained by 6 months.[35] Further research on interventions to prevent depression in patients with eye disease is warranted and should consider strategies to alleviate mobility limitation. Greater attention from families, physicians, and society to the mental health needs and mobility challenges of patients with eye disease is needed.

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