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Greater physical activity is associated with slower visual field loss in glaucoma

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Abstract

Objective: To determine the association between physical activity levels and the rate of visual field (VF) loss in glaucoma.

Design: Longitudinal, observational study.

Participants: Older adults with suspect or manifest glaucoma.

Methods: Participants wore accelerometers for one week to define average steps per day, minutes of moderate-to-vigorous activity (MVPA) and minutes of non-sedentary activity. All available VF measurements before and after physical activity assessment were retrospectively analyzed to measure rates of VF loss.

Main Outcome Measures: Pointwise changes in VF sensitivity associated with physical activity measures.

Results: One hundred forty-one participants (mean age 64.9 ± 5.8 years) were enrolled. Eye mean deviation (MD) at the time of physical activity assessment was −6.6 dB and average steps per day was 5613 ± 3158. The unadjusted average rate of VF loss as measured by pointwise VF sensitivity was 0.36 dB/year (95% CI: −0.37, −0.35). In multivariable models, slower VF loss was observed for patients demonstrating more steps (+0.007 dB/year/1000 daily steps, p<0.001), more moderate-to-vigorous activity (+0.003 dB/year/10 more minutes of MVPA per day, p<0.001), and more non-sedentary activity (+0.007 dB/year/30 more minutes of non-sedentary time per day, p=0.005). Factors associated with a faster rate of VF loss included older age, non-Caucasian race,

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glaucoma surgery, cataract surgery, and moderate baseline VF damage (−6 dB≥MD>– 12 dB) as opposed to mild VF damage (MD>−6 dB). Similar associations between baseline accelerometer-measured physical activity and rates of VF loss were observed over other time periods (e.g., within 1, 3 and 5 years of activity assessment).

Conclusions: Increased walking, greater time spent doing moderate-to-vigorous physical activity and more time spent in non-sedentary activity were associated with slower rates of VF loss in a treated population of glaucoma patients, with an additional 5,000 daily steps or 2.6 hours of non-sedentary physical activity decreasing the average rate of VF loss by roughly 10%. Future prospective studies are needed to determine if physical activity can slow VF loss in glaucoma and/or if progressive VF loss results in activity restriction. If the former is confirmed, this would mark physical activity as a novel modifiable risk factor for preventing glaucoma damage.

Introduction

Adults with poor vision demonstrate a striking degree of physical activity restriction.[1,2] For example, individuals with bilateral visual field (VF) loss walked less and restricted their physical activity as much as, or even more than, those with chronic obstructive pulmonary disease, arthritis, or diabetes.[2] Furthermore, VF loss due to glaucoma is also associated with less physical activity, as judged by less time in higher levels of activity and fewer daily steps walked.[3] One proposed explanation for the observed lower activity levels with glaucoma damage is perceived mobility difficulty, i.e. from prior falls/fear of falling.[4] However, in one study of glaucoma patients, fear of falling did not mediate the association between severity of VF damage and time spent in physical activity, suggesting alternate explanations for this association.[5]

A growing body of evidence exploring the causal relationship between VF damage and activity levels has suggested that physical activity may protect against glaucoma damage. In one study, animals forced to engage in physical activity suffered less optic nerve damage due to high intraocular pressure (IOP).[6] In a study of male runners, rigorous physical activity reduced glaucoma risk, particularly for runners with faster performance and longer running distances.[7] However, no longitudinal studies examining rates of VF loss and the development of glaucoma following physical activity measurement (i.e., the exposure status) have been conducted. Here, we retrospectively analyze VFs before and after physical activity assessment in patients with known or suspected glaucoma in an effort to better understand the potential causal, bidirectional, or reverse causal relationship between physical activity and VF loss. If physical activity is indeed a risk factor for glaucoma, it would be only the second identified modifiable risk factor for glaucoma (other than intraocular pressure).

In this study, we examined the association between physical activity levels measured with a one-week accelerometer trial at a single point in time with longitudinal rates of change in VF damage. We hypothesized that more active individuals would demonstrate slower rates of VF damage.

Methods

The Johns Hopkins Medicine Institutional Review Board approval was obtained, and all study participants provided written informed consent.

Study Participants

Subjects between the ages of 60 and 80 were recruited at the Glaucoma Center of Excellence at the Wilmer Eye Institute at Johns Hopkins Hospital between July 2009 and June 2011. Participants included: (1) individuals with a chart diagnosis of glaucoma suspect or ocular hypertension, and (2) individuals with bilateral VF loss from glaucoma. Patients were included in the glaucoma group if they had a physician diagnosis of primary open angle glaucoma, primary angle closure glaucoma, pseudoexfoliation glaucoma, or pigment dispersion glaucoma. Other inclusion criteria included proficiency in English and a willingness to wear an accelerometer for one week. Exclusion criteria included a history of laser procedure within 1 week, hospitalization or non-ophthalmic surgery within the last 2 weeks, and intraocular surgery within the previous 2 months of the accelerometer trial to assess physical activity.

Evaluation of Physical Activity

An omnidirectional accelerometer (Actical, Respironics Inc) was used to measure physical activity over 1 week. Subjects were asked to wear the accelerometer on their waistband during all waking hours except when bathing or swimming.

To maximize compliance with accelerometer wear, participants were called daily over the course of the week of accelerometer wear and reminded to wear their device. Days with less than 8 hours of accelerometer wear (estimated by time stamps of recorded activity) were excluded from analysis as measurements on these days may not have captured total daily activity.[8] Individuals with fewer than 2 valid days of physical activity assessment were also excluded from analysis. A total of 17 individuals were excluded due to missing data with regards to cataract surgery status, glaucoma surgery status or IOP (n=16) or a number of steps well above the rest of the cohort (n=1).

Motion detected by the accelerometer was converted into electrical activity through the piezoelectric crystal within the device, and this activity was expressed as unit-less “count” data. The accelerometer also interpreted motion data to calculate steps. Count data were then summarized as average total daily counts (a measure of total activity considering both time and intensity), as well as minutes of sedentary, light, moderate, and vigorous physical activity using previously-validated cutpoints.[9] Given the paucity of time spent in vigorous activity, time spent in moderate and vigorous physical activity were combined.

Collection of Visual Field Data

All available VF data from study patients were downloaded from a clinical server. VF data ranged from 13.2 years prior to 6.7 years following the physical activity assessment. VF tests were limited to Automated perimetry using the 24–2 pattern of the Humphrey Field Analyzer (HFA-II, Carl Zeiss Meditec, Dublin, CA), a size III stimulus and one of the

Swedish interactive threshold algorithms (SITA). A graphical representation of VF point-wise sensitivities over time for each hemifield for one subject is shown in **Fig. 1.** Selected VFs were reviewed by a glaucoma specialist (PR) and were excluded from analysis if the VF measurement was likely to be affected by artifact.[10] Visual fields were reviewed if the false positive rate was ≥15%, the mean deviation (MD) was positive (>0 dB), or if there was a >3 dB difference in MD for any two consecutive VF measurements based on the expected variability in MD across repeated tests within the same eye of the same individual.[10] Using these criteria and excluding individuals with missing covariate data, a total of 304 VF tests out of 2849 were excluded from analysis.

Measurement of Covariates

Variables abstracted from patient charts included IOP (Goldmann tonometry) at the time of activity assessment and history of glaucoma surgery and/or cataract surgery prior to or over the course of VF testing. At the time of activity assessment, participants were interviewed and self-identified their race and ethnicity. Participants also reported any previous diagnoses made by a physician out of a list of 15 comorbid conditions including: arthritis, previous hip fracture, back problems, previous heart attack, angina/chest pain, congestive heart failure, peripheral vascular disease, hypertension, diabetes, emphysema, asthma, stroke, Parkinson's, non-skin cancer, or vertigo/Meniere's.[11] The number of comorbid conditions was summed and considered in analyses. Seasonality was assessed not included as a covariate based on its lack of association with physical activity in prior analyses.

Statistical Methods

The average rate of VF loss and interquartile range (IQR) summary statistics were calculated by running a regression model for each individual VF point for every eye if the eye had at least 5 VFs. Multilevel linear mixed effects regression models included all eyes and were carried out to examine the factors that affect the rates of change in threshold sensitivity at each VF test coordinate. Random effects at four levels were included: patient, eye, superior vs. inferior hemifield, and VF coordinate. This type of hierarchical model allowed for the inclusion of both eyes of the same subject, while accounting for the correlation among points in the same hemifield and the correlation among repeated measures from the same coordinate. It also took into account the correlation between residuals, making it more adequate than an ordinary least squares models in this longitudinal dataset. Random effects within models included random intercepts for the patient, eye (right vs. left), region (superior vs. inferior hemisphere) and VF coordinate to account for clustering at each level. Random slopes for the superior and inferior hemispheres were also included to allow for different variance components in the two regions with respect to the rate of change. An unstructured variance-covariance structure was used, allowing for correlation between the random slope and the random intercept. The VF points were correlated within clusters. The statistical models used in the analysis attempted to address the clustering by employing a random intercept and a random slope by hemisphere, but it is beyond the capacity of statistical models and current knowledge to include a correlation structure at an even lower level of clustering.

Due to collinearity between accelerometer variables, separate multivariable models were used for each measure of physical activity. Co-variates in the models included age, race, history of cataract surgery, history of glaucoma surgery, baseline severity and IOP. Two-way interactions between co-variates that could potentially change the rate of progression and time (reflected through the patient's age) were included in the models to capture the factors that affect the rates of change. The covariates with an interaction term with age were: race, history of cataract surgery, history of glaucoma surgery, hemifield, baseline severity and IOP. Statistical significance was defined at p<0.05.

Results

One hundred forty-one patients were enrolled in the study and completed the study procedures. Participants had an average age of 65 years (standard deviation, SD: 5.8), and had high levels of comorbid disease (**Table 1**). Approximately one third of the participants were non-Caucasian and 57% were female. The mean baseline eye MD was −6.6 (SD: 8.4) dB. Subjects had an average of 6.7 (SD: 0.9) valid days of physical activity measurement. During their accelerometer trial, subjects took an average of 5,613 (SD: 3,158) steps per day and averaged 148 minutes/day of non-sedentary activity and 11 minutes/day of moderate-to-vigorous physical activity. Overall, the interquartile range (IQR) for the average rate of VF loss overall was −0.49 dB/year to −0.04 dB/year. For individuals with baseline MD >−6 dB, the IQR for average rate of VF loss was −0.44 dB/year to −0.06 dB/year. For individuals with baseline MD≤−6 dB and greater than −12 dB, and baseline MD≤−12 dB, the IQR for average rate of VF loss was −0.67 dB/year and −0.09 dB/year, and −0.63 dB/year and 0 dB/year, respectively.

Association of daily steps with trajectories of VF damage

In mixed effects linear regression models, VF sensitivities in the reference group (inferior points in 65-year-old non-White males with IOP of 14.6 mmHg, mild damage [MD>−6 dB] and no prior glaucoma or cataract surgery) decreased by 0.33 dB per year beginning with the first VF measurement (95% CI: −0.38 to −0.28, p<0.001). Each incremental increase of 1000 steps per day was associated with less sensitivity loss over time (+0.007 dB/year, p<0.001). Factors associated with a faster rate of decline in sensitivity included age (−0.03 dB/year/10-year increment in age, p<0.001), non-Caucasian race (−0.116 dB/year for non-Caucasians vs Caucasians, p<0.001), moderately worse baseline severity (−0.048 dB/year for −6 dB≥MD>−12 dB compared to MD>−6 dB, p=0.001), history of glaucoma surgery (−0.181 dB/year, p<0.001) and history of cataract surgery (−0.037 dB/year, p<0.001) (**Table 2**). Subjects with baseline MD between −12 dB and −20 dB had a slower annual decline in sensitivity by +0.095 dB/year compared to subjects with baseline MD>−6 dB (p<0.001) and individuals with more co-morbid conditions had a slower annual decline by +0.007 dB/year (p=0.037). Variables that were not significantly associated with rate of progression included baseline IOP and VF hemifield (p>0.05).

Association of minutes of non-sedentary activity and moderate-to-vigorous physical activity with trajectories of VF damage

In separate multivariable models, each incremental 30-minute increase in non-sedentary activity per day was associated with less average visual field sensitivity loss over time (+0.007 dB/year, p=0.005). In addition, each 10-minute increase in moderate-to-vigorous physical activity was associated with a slower annual rate of decline (+0.003 dB/year, p<0.001). Covariates in both models also associated with a faster rate of decline in sensitivity included age, non-Caucasian race, history of glaucoma surgery, history of cataract surgery and worse baseline severity (**Table 2**).

Relationship between physical activity and VF loss over varying time periods

Additional analyses were performed to address concerns that cross-sectional measurement of physical activity may be less strongly associated with VFs that are further away in time, and to better establish the temporality of the association between physical activity and VF loss. Stratification of the VF data based on time away from the physical activity assessment showed significantly less VF loss over time with higher levels of physical activity for all of the time periods assessed, including times more proximate to the assessment (i.e. within 1, 3 or 5 years of the activity assessment), as well as time periods following the physical activity assessment (i.e. 3 or 5 years after physical activity assessment) (**Fig. 2**). When the sensitivities over each hemisphere were averaged, physical activity variables affected progression similarly, but were no longer statistically significant.

Discussion

Greater levels of physical activity are associated with statistically significant slower rates of VF loss in persons with glaucoma. All measures of physical activity, including average steps per day, minutes of non-sedentary activity and moderate-to-vigorous physical activity, were associated with slower rates of decline. It is currently unclear which measure and what type of physical activity is most associated with health outcomes, thus we investigated the association between 3 different measures/types of activity and VF loss. Our results suggest that any type of activity, including light activity, may be beneficial. Of note, however, the observed effects were small. Walking an additional 5000 steps/day, an extra 2.6 hours in non-sedentary activity, or an extra 120 minutes of moderate-vigorous physical activity were associated with a change in the rate of observed progression of about 10% from the average rates of decline. Associations of greater activity with slower rates of VF loss were also noted in models in which the exposure (physical activity) preceded the outcome (change in VF sensitivity). These data raise the possibility that physical activity may, to some extent, influence the rate of progressive glaucoma damage, though our data from models only assessing VFs prior to the activity assessment also support the possibility that progressive VF damage may lead to activity restriction. Further work is needed to establish whether physical activity is a reversible risk factor that may protect against VF loss in glaucoma.

Cross-sectional studies have demonstrated decreased levels of activity in association with glaucoma-related VF damage. One study reported significant reductions in time spent in physical activity and walking as measured by steps, with greater levels of VF loss.[3]

Individuals with glaucoma also had fewer daily excursions, were less likely to travel far from home and less likely to leave the home on any given day compared to individuals with normal vision.[12] Our study examines longitudinal changes in VF damage and their association with levels of activity and suggests a potential causal role of physical activity in glaucoma progression, particularly given that models looking at VF loss only after physical activity assessment showed less loss with greater activity, demonstrating a temporal association between greater activity and slower VF loss. However, models looking at VF loss only before physical activity assessment also showed less loss with physical activity, suggesting that causality may be bidirectional, or that VF loss may result in restriction of physical activity. We found that several measures of increased activity (more steps, greater time spent in non-sedentary activity and moderate-to-vigorous physical activity) were all associated with a slower rate of VF loss, suggesting that multiple forms of activity may be relevant.

The positive effects of physical activity on VF loss may be expected given previous research suggesting the protective role of activity on the optic nerve, IOP[13], and other neurologic systems. Animal models have shown that forced exercise can protect the optic nerve against injury caused by high IOP and reduce retinal inflammatory responses.[6] Other studies have also shown that exercise may be protective in neurologic disease. For example, increased recreational activity was associated with a lower risk of Parkinson's disease.[14] Mechanisms suggested by previous work include a decrease in striatal dopamine loss, increased neural growth factors and increased plasma urate resulting in increased protection of neurons and DNA from damage.[14–16] Physical activity is also beneficial with regards to dementia, where it may slow cognitive decline and reduce the likelihood of developing dementia.[17–19] This may be due to decreased cerebral atrophy and increased neuroprotective factors such as brain derived neurotrophic factor.[20,21] Physical activity also protects against ischemic stroke by reducing cerebral infarct size, improving vasorelaxation and increasing cerebral blood flow.[22] Thus, a neuroprotective role of physical activity has been widely demonstrated, making it easy to believe that it's effects may also extend to pathologic processes affecting the optic nerve.

As our study did not follow a prospective design, we examined whether the effects of physical activity were different for VF measurements further away from the time of activity assessment. In our analysis, we observed similar rates of change after stratifying the interaction terms based on the period of time between the VF measurement and physical activity assessment, and thus included all collected VF measurements in our primary analyses. Of particular note, the rate of VF loss assessed only for times following physical activity assessment suggest that physical activity may protect against future glaucoma damage. However, the rate of VF damage was also associated with activity levels in models evaluating VFs only over the 5-year period prior to activity assessment, suggesting that progressive VF damage may also result in physical activity restriction. Similar results over all assessed time periods may reflect stable physical activity patterns over the time periods studied and, indeed, research has shown that physical activity levels for adults between the ages of 30–64 do not change dramatically.[23] At 65 years of age, activity levels generally remain stable or improve slightly and absolute rates of change in physical activity for adults are small.[23] In addition, earlier physical activity has been cited as one of the most important determinants of physical activity at an older age; thus our cross-sectional measurement may also be modestly reflective of earlier activity levels.[24]

While average steps per day was used as the primary measure of activity, the activity that is most related to health is unknown. Previous studies have examined the role of aerobic exercise, resistance exercise, flexibility exercises and water based exercises in health, yet there is no consensus on which activity measure is most correlated with health outcomes.[25–27] In addition to the type of activity (i.e., running, weight training, swimming), it is unclear which aspect of physical activity (i.e., time spent in activity, intensity of activity, frequency of activity) has the greatest impact on health. In our study of older adults, we used a previously validated accelerometer to record information on intensity, steps, and time spent in sedentary and physical activity.[9,28,29] We captured 7 days of activity including both weekdays and weekend days during all waking hours, which has been routinely used in previous studies.[30] In addition, we assessed walking as one of our physical activity measures, which is not only reliable, but also highly applicable to older adults as walking is one of the most common types of physical activity undertaken by older individuals. In fact, many physical activity recommendations emphasize walking as a cost-friendly, effective way to engage in activity and interventions to increase walking may be a feasible way to substantially increase physical activity levels.[31–33]

In addition to physical activity, our analyses revealed several other factors associated with the rate of decline in sensitivity. Older age, non-Caucasian race and moderate baseline severity (as compared to mild baseline severity) were associated with a faster rate of VF loss in all analyzed models. This was expected given that numerous studies have identified these factors as prognostic markers of visual field worsening in glaucoma.[34–36] In our study, baseline IOP was not associated with rate of visual field loss. This may be due to the collection of IOP data at a single time point at the time of physical activity, the potential use of more aggressive treatment in response to elevated IOP and the tendency for less VF progression in those with the highest IOP. Studies investigating different IOP parameters as a prognostic factor of glaucomatous visual field progression have had conflicting results, likely as the goal of treatment is to eliminate this risk factor, such that failure to identify IOP as a risk factor reflects effective treatment.

Strengths of this study include the use of an accelerometer to measure physical activity, which has been shown to be more strongly associated with health outcomes such as blood sugar and body composition, as compared to subjective measurements (i.e. self-report).[37–39] Another strength is our statistical approach for this longitudinal dataset, which not only accounts for levels of correlation at the patient, eye, and hemifield level but also between VF test points. It also remains possible that our findings reflect the effects of unmeasured confounders such as socioeconomic status, health awareness levels, medication adherence, and overall health behavior, with more active patients also engaging in other beneficial behaviors which accounts for their better VF outcomes. We attempted to account for overall health status by controlling for the total number of comorbidities. Although different comorbidities may potentially have differing confounding effects, it is currently unclear which medical conditions have true confounding effects on the association between physical activity and rate of VF loss in glaucoma. Thus, the total number of comorbid conditions was used as a metric to capture the potentially more rapid biologic aging of individuals who have multiple comorbidities, which may interact with each other.[40] Additionally, this approach was taken given that the number of individuals with some covariates was small, such that the true impact of this covariate on the outcome (progression rate) was highly uncertain, and could introduce bias if the regression coefficient was inaccurate. Our study is limited in generalizability due to the older study population. Individuals excluded from analyses based on missing covariate data had a higher proportion of severe baseline disease compared to individuals included in the analysis (44% vs. 22%). This may have potentially introduced bias into our results if physical activity has different associations with rates of VF loss in individuals with more severe disease (i.e., physical activity may not be as impactful in severe disease or conversely, may have a greater impact). There are also several limitations with the use of accelerometer data. Accelerometers do not capture upper body movement, certain low ambulatory exercises and water based exercises.[41] They also do not provide any contextual information on the purpose of movement and cannot differentiate between leisure activity and daily activities.[30,41] Finally, validity of the correlation matrix cannot be ensured, it is not clear that our findings would have persisted if the true optimal correlation structures were used. Of note, however, similar regression coefficients were obtained when each hemifield was examined, though results were no longer statistically significant, possibly from the more limited statistical power.

In conclusion, our study found physical activity was associated with less VF progression in patients with glaucoma. Specifically, increased steps per day, minutes of non-sedentary activity and minutes of moderate-to-vigorous physical activity were associated with slower rates of decline. We also confirmed that other factors including older age, worse baseline severity, and non-Caucasian race are associated with a faster rate of VF loss. These findings suggest the need for clinical trials examining the association between physical activity and glaucomatous VF loss to determine if interventions to increase physical activity may have a beneficial role in patients with glaucoma.

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Precis:

Increased levels of physical activity are associated with slower rates of visual field loss in glaucoma patients.

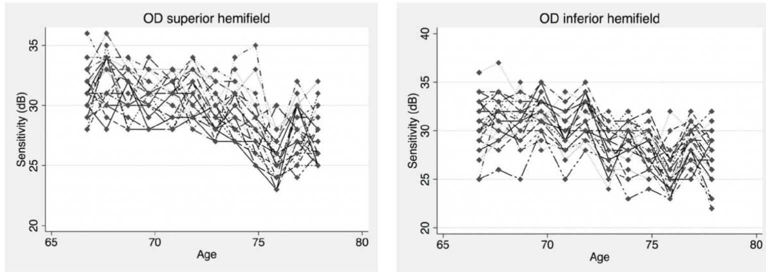

Figure 1.

Example of VF data

Pointwise sensitivity for each VF test coordinate in the superior and inferior hemifields for one eye.

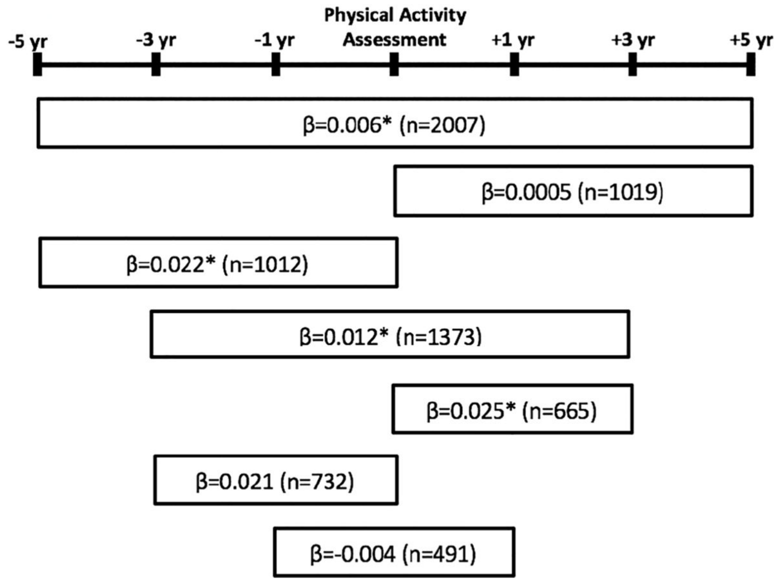

Figure 2:
Rate of VF loss in association with 1000 average steps/day at varying times from physical activity assessment
Note: n=number of VFs within each time period
*Denotes significance at α=0.05

Table 1.

Baseline characteristics of participants

Demographics	**Mean ± SD or n (%)**
Number of participants [n]	141
Age (years)	64.9 (5.8)
Non-Caucasian race, [n(%)]	46 (32)
Female [n(%)]	80 (57)
Education (years)	15 (3)
Currently employed [n(%)]	56 (40)
Health	
Number of co-morbid illnesses, [n(%)]	2.3 (1.6)
Arthritis, [n (%)]	73 (52)
Back pain, [n (%)]	54 (38)
Hypertension, [n (%)]	81 (57)
Eye Health level characteristics	
Baseline eye MD (dB)	−6.6 (8.4)
Baseline MD > −6 dB [n (%)]	175 (64)
−6 dB ≥ Baseline MD > −12 dB [n (%)]	39 (14)
−12 dB ≥ Baseline MD >−20 dB [n (%)]	61 (22)
History of glaucoma surgery [n (%)]	97 (39)
History of cataract surgery [n (%)]	113 (45)
Physical Activity	
Total days of physical activity measurement	6.7 ± 0.9
Steps/day	5613 ± 3158
Total minutes of non-sedentary activity	148 ± 65
Total minutes of moderate-to-vigorous physical activity	11 ± 16

Table 2.

Factors influencing rate of decline in sensitivity, multivariate analysis

Variable	Interval/Reference	Steps/day*	Min. of nonsedentary activity*	Moderate-tovigorous activity*
Steps/day	1000 steps	**0.007 (0.002)**	--	--
Min. of non-sedentary activity	30 minutes	--	**0.007 (0.003)**	--
Moderate-to-vigorous activity	10 minutes	--	--	**0.003 (0.000)**
Co-variates				
Age	1 year older	**−0.003 (0.000)**	**−0.003 (0.000)**	**−0.003 (0.000)**
Race	Caucasians vs. Non-Caucasians	**0.116 (0.011)**	**0.120 (0.011)**	**0.101 (0.011)**
Co-morbid conditions[a]	1 more co-morbidity	**0.007 (0.004)**	0.005 (0.003)	**0.009 (0.003)**
Ocular Health				
History of glaucoma surgery	Present vs. non-Present	**−0.181 (0.011)**	**−0.183 (0.011)**	**−0.178 (0.011)**
History of cataract surgery	Present vs. non-Present	**−0.037 (0.011)**	**−0.036 (0.011)**	**−0.035 (0.011)**
Baseline severity	$-6 \geq MD > -12$ vs. $MD > -6$	**−0.048 (0.015)**	**−0.046 (0.015)**	**−0.048 (0.015)**
Baseline severity	$-12 \geq MD > -20$ vs. $MD > -6$	**0.095 (0.014)**	**0.095 (0.015)**	**0.093 (0.014)**
IOP	1 mm Hg higher	−0.001 (0.001)	−0.001 (0.001)	−0.000 (0.001)
Hemifield	Superior vs. Inferior	−0.005 (0.010)	−0.005 (0.010)	−0.005 (0.010)

*Each analyzed in a separate regression model

[a]Co-morbid conditions include: arthritis, back pain, hypertension, previous hip fracture, previous heart attack, angina or chest pain, congestive heart failure, peripheral vascular disease, diabetes, emphysema, asthma, stroke, Parkinson's disease, nonskin cancer, vertigo or Ménière's disease.

Bolded **β (standard error)** values denote significance ($p<0.05$).