American Journal of
Preventive Medicine

RESEARCH ARTICLE

Persistent Cannabis Use and Ocular Health in Midlife

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Introduction: Cannabis is widely used and is becoming legal in many countries. Although some acute ocular effects of cannabis are well known (e.g., reduced intraocular pressure, vasodilation), little is known about the consequences of long-term cannabis use for ocular health. The aim of this study was to examine the association between persistent cannabis use across adulthood and measures of ocular health in midlife.

Methods: Participants were members of the Dunedin Study (N=1,037), a longitudinal cohort followed since birth. Cannabis use has been measured by self-report at every assessment from age 18 years to age 45 years. Ocular health data were collected as part of a larger assessment at age 45 years (2017−2019). Statistical analysis was performed in 2022.

Results: Cannabis use and ocular health data were obtained from 887 study members. Generalized estimating equation analysis showed that higher cannabis use was associated with poorer visual acuity, wider retinal arterioles and venules, and a thicker inferior hemifield of the ganglion cell−inner plexiform layer. However, when controlling for tobacco smoking and SES (known to be associated with these ocular health domains), the associations with visual acuity, arterioles, and venules were no longer significant. The association with ganglion cell−inner plexiform layer remained significant in this adjusted model.

Conclusions: Persistent cannabis use appears to be neither harmful nor beneficial to the eye at age 45 years, although the thicker inferior ganglion cell−inner plexiform layer hemifield in users of cannabis suggests biologically plausible neuroprotection. Further assessments as this cohort ages will illuminate the relationship between persistent cannabis use and ocular neuroprotection.

INTRODUCTION

Cannabis is increasingly legalized or decriminalized around the world and is readily available and widely used, even in jurisdictions where it is illegal. The 2010 Global Burden of Disease study estimated that 13.1 million people were cannabis dependent globally, accounting for 2 million lost disability-adjusted life years.[1] In New Zealand (NZ), both the Dunedin Multidisciplinary Health and Development Study (Dunedin Study) and the Christchurch Health and Development Study have found that close to 80% of people born in the 1970s reported trying cannabis at least once by the time they reached their mid-twenties.[2] The argument for the legalization of medical and recreational cannabis has garnered a lot of attention in recent years, with particular focus on the many health, social, political, and legal issues surrounding its widespread use.

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0749-3797/$36.00
https://doi.org/10.1016/j.amepre.2025.107955

In spite of its ubiquity, studying the effects of cannabis on health is challenging owing to methodologic issues such as legality (and, consequently, honesty in self-reports), unstandardized doses, tolerance development, lack of a credible placebo, cognitive changes impacting reliability of measures, and the effect of the social setting and expectations.[3] Despite these difficulties, longitudinal studies have shown that persistent cannabis use is detrimental to some aspects of health (e.g., periodontal health, lung function, neuropsychological function, and psychosis[4–7]); yet, cannabis or cannabinoids are also used very successfully in the management of pain and nausea, and there is limited evidence of their benefits in the treatment of a number of neurologic and neuropsychiatric disorders, such as spasticity associated with multiple sclerosis, dementia, sleep disorders, and anxiety.[8–10] Although there is much to learn about cannabinoids and their role in health and disease, there is consistent evidence that they have at least short-term effects on every organ system, including the eye. Cannabinoid receptors are distributed in all ocular tissues,[3] and CB1 and CB2 receptors are expressed throughout the human retina, including CB1 receptors in the ganglion cell and inner plexiform layers (GC-IPL).[11] A recent comprehensive review highlights these effects and some ocular-associated dysfunction and toxicity.[12]

Acute ocular effects of smoking cannabis include vasodilation, conjunctival hyperemia, changes in pupillary diameter and reaction, alterations in color discrimination, increased photosensitivity, and decreased ocular motility.[3,12,13] Anecdotal reports and case studies have suggested that cannabis use improved both visual acuity and night vision[14]; however, empirical evidence shows that visual acuity, stereoacuity, contrast sensitivity, and night vision are all worsened under the influence of cannabis,[15,16] and none of the participants in a recent controlled experiment perceived these functions as improved.[15] The short-term intraocular pressure (IOP) lowering effect of smoking cannabis was first reported in 1971.[17] Increased IOP is a risk factor for glaucoma,[18] but the use of cannabis for managing glaucoma has not proved to be a viable option owing to systemic side effects, short duration of action, and tolerance, and in 2010, the American Glaucoma Society recommended against its use in any form.[19]

A recent comprehensive review by Bondok et al.[13] (2024) presents evidence that chronic users of cannabis exhibit deficits in oculomotor control and stereopsis and possible vision deficits.[13,20] Schwitzer and colleagues[21,22] have shown delays in retinal cell responses in long-term users of cannabis, suggesting slowed transmission of visual information to the brain. There is some evidence that cannabinoids may be neuroprotective in the retina; for example, a recent study found that patients with cannabis use disorder had increased retinal nerve fiber layer (RNFL) thickness compared with controls.[23] However, the evidence for retinal neuroprotection comes largely from studies in animals with various injuries (including IOP-induced ischemia), where cannabinoid intervention results in better outcomes for retinal ganglion cells.[24]

The short-term effects of cannabis use on ocular health are well studied. In contrast, few studies investigate if persistent cannabis use across the lifespan is associated with visual function and eye health in midlife, whether detrimental or beneficial. Given that cannabis use is widespread, hotly debated, and gaining legality in many countries, it is important to explore the links between long-term cannabis use and ocular health. Longitudinal studies that follow population-representative cohorts of individuals from birth and conduct repeated physiologic assessments across the life course provide one of the best opportunities to understand those links. Thus, the aim of this study was to use data from the longitudinal Dunedin Study to examine the association between persistent cannabis use (reported regularly between the ages of 18 and 45 years) and a number of measures of ocular health at age 45 years.

METHODS

Study Sample

Participants are members of the Dunedin Multidisciplinary Health and Development Study (Dunedin Study), a longitudinal investigation of health and behavior in a population-representative birth cohort of 1,037 individuals (91% of eligible births; 52% male) born between April 1, 1972, and March 31, 1973, in Ōtepoti/Dunedin, NZ. The longitudinal study was established at age 3 years on the basis of residence in the province.[25,26] Assessments were conducted at birth and at ages 3, 5, 7, 9, 11, 13, 15, 18, 21, 26, 32, and 38 years and, most recently, at age 45 years (2017–2019), when 94% of the 997 participants still alive took part. Each study member was brought to the research unit for a day of interviews and examinations. The cohort represents the full range of SES on NZ's South Island, and as adults, study members match the NZ National Health and Nutrition Survey respondents on adult health indicators, for example, BMI, smoking, general practitioner visits.[27] Study participants are primarily of NZ European ethnicity; 8.6% reported Māori ethnicity at age 45 years. Written informed consent was obtained from participants, and the study was approved by the New Zealand Health and Disability Ethics Committee.

Measures

Study members were questioned about their cannabis use as part of an interview at ages 18, 21, 26, 32, 38, and 45 years. Cumulative cannabis consumption was estimated by joint-years, estimated using self-reported frequency of cannabis use (in any form) over the past year, where 1 joint-year reflects the equivalent of daily cannabis use for 1 year. This variable was created to parallel pack-years, the most commonly used variable in tobacco studies.[28]

Eye assessments were carried out as part of the assessment day at age 45 years. Visual acuity was measured for each eye with logarithmic visual acuity charts[29] using Thomson Test Chart (2016) software calibrated for viewing on a Samsung 23" LCD Thin Client screen at a distance of 4 meters, with the other eye occluded. If study members could not read to the bottom line, a multiple pinhole was placed over the eye and the best corrected acuity was recorded. If study members usually wore distance glasses or contact lenses, these were worn during this test.

Contrast sensitivity was assessed with the Pelli-Robson chart,[30] using Thomson Test Chart (2016) software on a Samsung 23" LCD Thin Client screen at the standard distance of 1 meter. If study members correctly determined 2 of 3 letters on a line, the technician proceeded to the next line. When 1 or 0 letters were correctly determined by the study member, the technician recorded the number of letters to determine the contrast sensitivity score.

IOP was measured using the Tonoref III (Nidek, Japan). IOP was recorded as an average of 3 measurements taken from each eye using an airpuff technique, with the peak of the air pressure automatically controlled within the range of 1−40 mmHg.

RNFL thickness and GC-IPL thickness were measured from optical coherence tomography scans (Cirrus HD-OCT, model 5000; Carl Zeiss Meditec, Dublin, CA) (Fig. 1). Optical coherence tomography scans were assessed by trained graders at the Singapore Eye Research Institute, National University of Singapore and excluded if quality was poor (e.g., image artefacts, insufficient signal strength).

Arteriole and venule calibers were measured from fundus photographs. Digital photographs were taken after 5 minutes of dark adaptation, as previously described.[31] The same camera (Canon NMR-45 with a 20D SLR backing, Tokyo, Japan) was used for all photographs, thereby preventing artifactual variation from different cameras. Both the left and right eyes were photographed, and the 2 eyes were averaged. Retinal photographs were graded at the Singapore Eye Research Institute, using semiautomated computer software (SIVA [Singapore I Vessel Assessment], software version 3.0). Trained graders, masked to participant characteristics, used the SIVA program to measure the retinal vessel diameters according to a standardized protocol with high intergrader reliability.[32] Caliber (or diameter) denotes the size of the lumen, which is the internal space of the vessel. Measurements were made for arterioles and venules where they passed through a region located 0.50−2.00-disc diameters from the optic disc margin.[33] Vessel calibers were based on the 6 largest arterioles and venules passing though this region and were averaged across the 2 eyes and summarized as central retinal artery equivalent (CRAE) and central retinal vein equivalent (CRVE), using the revised Knudtson −Parr-Hubbard formula.[32,34]

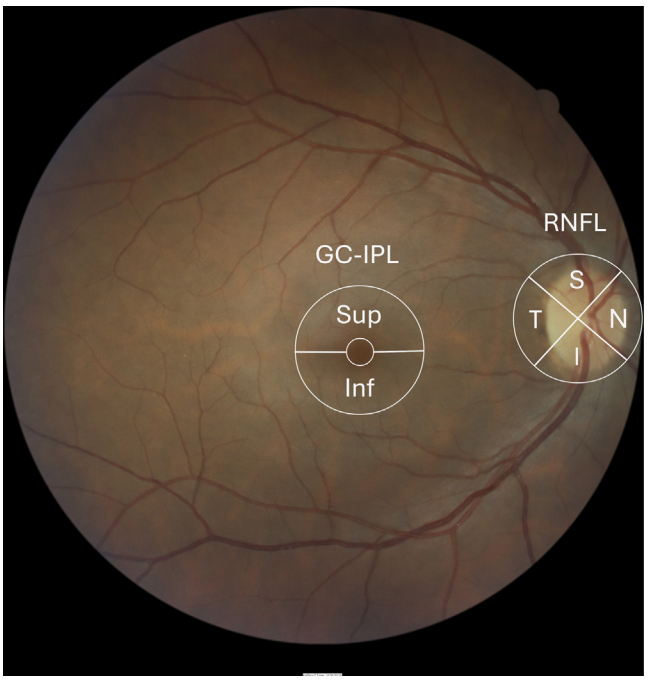

Figure 1. Representation of OCT-derived retinal measures used. *Note:* Sup denotes superior hemifield, and Inf denotes inferior hemifield. S denotes superior, N denotes nasal, I denotes inferior, and T denotes temporal. GC-IPL, ganglion cell and inner plexiform layer; OCT, optical coherence tomography; RNFL, retinal nerve fiber layer.

Tobacco exposure was calculated from the reported number of cigarettes smoked per day, divided by 20 (the number of cigarettes in a pack), and multiplied by the number of years smoked at that rate until age 45 years, to provide a measure of cumulative tobacco consumption. One pack-year reflects the equivalent of 20 cigarettes per day for 1 year.[28]

SES at age 45 years was measured according to the New Zealand Socioeconomic Index 2006,[35] a 6-group occupation-based measure (1=unskilled laborer; 6=professional). Homemakers and others not working in the

past year were assigned the SES of their most recent occupation, as reported at age 38 years. Study members who had been out of the work force since age 32 years were assigned the SES of their partner or, if they did not share a household with a partner, their education level.

Statistical Analysis

Study members were initially categorized into groups on the basis of joint-years (ranging from never used cannabis to 10+ joint-years) for descriptive purposes. To assess whether cannabis use was associated with ocular health in midlife, the associations between cannabis use in joint-years (a continuous variable) cumulatively from ages 18 to 45 years and various measures of ocular health at age 45 years were tested in Model 1, subsequently controlling for tobacco smoking and SES by adding tobacco pack-years from age 18–45 years and SES as covariates in Model 2. Generalized estimating equation analysis was used with eyes nested within subjects to allow for concordance of values between eyes. All analyses controlled for sex. A $p<0.05$ was considered statistically significant. Analyses were checked for reproducibility by an independent data analyst, who recreated the code by working from the manuscript and applying it to a fresh data set.

RESULTS

The analytic sample (n=857–883) included all participants aged 45 years with ocular health and cannabis data. Table 1 shows mean ocular health data for 4 groups of study members when categorized according to their self-reported cannabis use since age 18 years. The majority of study members reported that they have either never used cannabis (27.5% of the total study members assessed at age 45 years) or have used it for less than 2 joint-years (52.1% of study members assessed at age 45 years). Just over 10% of study members reported more than 10 joint-years of cannabis use. As indicated in Table 1, no systematic pattern of effects was detected, and there was little to no numerical difference between cannabis use groups in any of the domains assessed, even between nonusers and very high users.

Table 2 shows the associations between cannabis use from age 18 years to age 45 years and measures of ocular health at age 45 years. Long-term cannabis use had no effect on IOP, contrast sensitivity, or RNFL thickness when controlling for sex, and this effect was upheld when also controlling for tobacco pack-years and SES. Visual acuity was associated with cannabis use in Model 1 (i.e., heavy users had worse visual acuity); however,

Table 1. Means for Domains of Eye Health Assessed, With Study Members Grouped According to Cannabis Use

Ocular health	Never used cannabis (27.5%)	0–2 joint-years (52.1%)	2–10 joint-years (10.2%)	≥10 joint-years (10.1%)
Intraocular pressure (mmHg)				
IOP (n=883)	13.50	13.74	14.23	13.95
Contrast sensitivity				
Contract sensitivity (n=887)	2.00	2.01	2.02	1.99
Visual acuity				
Visual acuity (n=887)	−0.02	−0.02	−0.03	0.01
Visual acuity with pinhole (n=884)	−0.06	−0.06	−0.07	−0.05
RNFL thickness (μm)				
RNFL temporal (n=858)	64.83	63.77	63.68	61.90
RNFL superior (n=858)	114.47	113.74	115.56	114.88
RNFL nasal (n=858)	72.34	72.49	73.44	71.85
RNFL-Inferior (n=858)	120.17	120.85	119.60	121.65
RNFL average (n=858)	92.97	92.71	93.1	92.59
C-IPL thickness (μm)				
GC-IPL superior (n=855)	83.34	83.21	84.28	83.23
GC-IPL inferior (n=855)	80.68	80.96	81.22	81.88
GC-IPL average (n=855)	82.61	82.64	83.59	83.18
Arteriole and venule caliber				
CRAE (n=872)	139.05	138.76	139.08	140.78
CRVE (n=872)	192.98	192.99	196.41	197.81

Note: Where data were collected from each eye separately, these have been averaged across eyes.
CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; GC-IPL, ganglion cell and inner plexiform layer; IOP, intraocular pressure; RNFL, retinal nerve fiber layer.

Table 2. Associations Between Cannabis Use From Ages 18 to 45 Years and Ocular Health at Age 45 Years

	Model 1 (controlling for sex)		Model 2 (plus control for tobacco pack-years and SES)	
Ocular health	**β (95% CI)**	***p*-value**	**β (95% CI)**	***p*-value**
Intraocular pressure (mmHg)				
IOP (*n*=883)	0.026 (−0.008, 0.060)	0.128	0.007 (−0.033, 0.046)	0.736
Contrast sensitivity				
Contract sensitivity (*n*=887)	−0.000 (−0.002, 0.001)	0.401	0.000 (−0.001, 0.002)	0.636
Visual acuity				
Visual acuity (*n*=887)	0.002 (0.000, 0.003)	**0.027***	0.001 (−0.011, 0.022)	0.522
Visual acuity with pinhole (*n*=884)	0.000 (−0.001, 0.001)	0.704	−0.001 (−0.002, 0.000)	0.226
RNFL thickness				
RNFL temporal (*n*=858)	−0.031 (−0.155, 0.094)	0.630	0.016 (−0.130, 0.162)	0.828
RNFL superior (*n*=858)	0.105 (−0.076, 0.286)	0.257	0.073 (−0.139, 0.285)	0.502
RNFL nasal (*n*=858)	0.011 (−0.124, 0.147)	0.871	−0.035 (−0.193, 0.123)	0.664
RNFL inferior (*n*=858)	0.135 (−0.059, 0.330)	0.173	0.176 (−0.051, 0.404)	0.129
RNFL average (*n*=858)	0.056 (−0.058, 0.170)	0.331	0.058 (−0.075, 0.192)	0.392
GC-IPL thickness				
GC-IPL superior (*n*=855)	0.034 (−0.043, 0.111)	0.383	0.056 (−0.035, 0.147)	0.225
GC-IPL inferior (*n*=855)	0.096 (0.017, 0.174)	**0.017***	0.122 (0.030, 0.215)	**0.010***
GC-IPL average (*n*=855)	0.060 (−0.0126, 0.133)	0.105	0.082 (−0.004, 0.168)	0.061
Arteriole/venule caliber				
CRAE (*n*=872)	0.158 (0.032, 0.284)	**0.014***	0.013 (−0.134, 0.160)	0.863
CRVE (*n*=872)	0.291 (0.089, 0.493)	**0.005****	−0.027 (−0.241, 0.189)	0.813

Note: Boldface indicates statistical significance (*$p<0.05$ and **$p<0.01$).
CRAE, central retinal artery equivalent; CRVE, central retinal vein equivalent; GC-IPL, ganglion cell and inner plexiform layer; IOP, intraocular pressure; RNFL, retinal nerve fiber layer.

this effect was removed when controlling for tobacco pack-years and SES (Model 2).

Cannabis use was associated with a significantly thicker GC-IPL in the inferior hemifield; this effect remained after adjusting for tobacco pack-years and SES. There was no association between cannabis use and the superior hemifield thickness or average GC-IPL thickness. In Model 1, cannabis use appeared to be associated with both CRAE and CRVE, where the more cannabis people consumed, the wider the arteriole and venule calibers; however, this association was no longer significant after adjusting for tobacco pack-years and SES.

DISCUSSION

Cannabis has numerous short-term effects on many of the body's systems, including the eye[3,12] (e.g., vasodilation,[36] decreased IOP,[17] decreased ocular motility[13]), yet little is known about long-term effects that may result from persistent cannabis use across many years. The association between cannabis use since age 18 years and several aspects of ocular health was investigated in a birth cohort at age 45 years. Results suggest that persistent cannabis use does not have any positive or negative long-term effects on visual function (visual acuity and contrast sensitivity), IOP, retinal blood vessel caliber (CRAE and CRVE), or RNFL thickness by age 45 years. The only domain assessed that showed an association with cannabis use after controlling for tobacco use and SES was the thickness of the GC-IPL inferior hemifield.

Anecdotal reports have suggested that smoking cannabis leads to short-term improvements in visual acuity and night vision, but to date, there has been no empirical evidence of improvement of any visual function; in fact, in the majority of studies, visual function (e.g., contrast sensitivity, night vision, stereoacuity) is decreased.[15] Initial analysis suggested worse visual acuity with heavier use; however, this association was not upheld after controlling for tobacco smoking and SES (both known to have a negative effect on visual acuity[37,38]), providing evidence that even with very heavy cannabis use, the impairment to this function is temporary. Despite its transient effects, no long-term effects of cannabis use on contrast sensitivity were observed.

It has been known for half a century that smoking cannabis acutely lowers IOP, but this ocular hypotensive effect lasts for only a few hours,[17] and to date, there is no clinical evidence that cannabis could be an effective therapy for glaucoma. The results of this study show no

association between IOP at age 45 years and the amount of cannabis consumed across the adult lifespan, suggesting that even very frequent cannabis use does not result in chronically reduced IOP.

It is well understood that cannabinoids are acutely vasodilatory and increase blood flow in conjunctival arterioles, giving the consumer red eyes.[36] Hill et al.[39] (2020) assessed the retinal microvasculature of 55 people who used cannabis and 51 controls and found a significantly wider mean arteriolar diameter in users of cannabis. In this study, both the CRAE and CRVE were wider (vasodilated) in users of cannabis, but after controlling for SES and tobacco use, there was no association between cannabis use and retinal vessel caliber. Tobacco use has previously been shown to widen retinal arterioles and venules[40]; thus, the observed effects on CRAE and CRVE are potentially explained by tobacco rather than cannabis use.

Only 1 measure assessed showed a consistent association with cannabis use: thickness of the GC-IPL inferior hemifield. The GC-IPL layer naturally thins with aging,[41] and it is biologically plausible that this finding is due to a neuroprotective effect of cannabis in this region. This would align with what has previously been observed in animal studies; for example, it has been shown that delta-9-tetrahydrocannabinol (THC) lowers IOP and prevents retinal ganglion cell death in a rat model of glaucoma[42] and that it protects against retinal ganglion cell death induced by high IOP.[43] Conversely, Schwitzer and colleagues[21] found a delay in the transmission of action potentials in the retinal ganglion cells of regular cannabis users, suggesting that cannabis has a neurotoxic effect on this cell layer. In this study, there was no association between cannabis use and either average GC-IPL thickness or superior hemifield thickness, so it is possible that the thicker inferior hemifield in people with high cannabis use was an anomalous finding. However, the study members were aged only 45 years at the time of assessment, so it is also possible that early stages of neurologic protection are being observed. Future studies with the same cohort may elucidate whether there is a slower rate of GC-IPL layer thinning in those reporting chronic cannabis use.

Limitations

One limitation of this study is that it was not possible to control or measure the amount, dosage, or method of cannabis (or indeed tobacco) consumption, so measures relied on self-report, meaning that they are estimates. This is a methodologic limitation common to the field, owing to the illegality of cannabis in many countries. However, the close relationship and trust between the Dunedin Study members and the researchers built over 45 years has led to willingness to give honest reports, even regarding the use of illegal substances. In addition, study members were questioned about their cannabis use at 6 time points between ages 18 and 45 years, so they were not relying on retrospective memory for the previous 27 years. The high retention rate in the Dunedin Study (94.1% of the living cohort assessed at age 45 years) provides confidence that data collected are representative of the population in terms of substance use and means that robust SES and tobacco use data are provided.

A second limitation is that although study members were asked to abstain from drugs and alcohol in the 24 hours prior to their assessment day, this could not be enforced; therefore, it is possible that some were under the influence of cannabis during the vision assessment. On the basis of self-reported usage, only a very small number might be expected to have consumed cannabis in the hours prior to testing (study members arrived at the unit at 8AM, and visual assessments usually took place after 9:30AM), and this is most likely to be those reporting the heaviest use. However, if some study members were under the influence of cannabis during data collection, they were likely experiencing the aforementioned acute effects (e.g., lowered IOP, decreased visual function), and this was not reflected in the results. The use of any other drug (except tobacco) has not been controlled for in this study. Future research should explore the impact of other drugs on ocular health.

Finally, this study was conducted on a single cohort of a specific age: born in Dunedin, NZ, in the early 1970s, and results should be interpreted within that context. For example, the concentration of THC in cannabis has increased over the last few decades, with evidence, including NZ data, suggesting that THC concentrations increased by up to 0.29% each year from 1970 to 2017.[44] Furthermore, the Dunedin Study is under-representative of Māori and Pasifika compared with the NZ national population. Thus, the impact on the eye may be different in more diverse populations and at different points in time.

CONCLUSIONS

To date, the literature on the effects of persistent cannabis use across the lifespan on the eye has been sparse. This study found no relationship between cannabis use from ages 18 to 45 years and many domains of vision and ocular health at age 45 years, including IOP, suggesting that even very high cannabis use has no long-term negative or positive effects on the eye. Heavier cannabis use was associated with slightly increased GC-IPL

thickness in the inferior hemifield, providing some evidence that cannabis may have a weakly neuroprotective effect on the retina. Dunedin Study researchers are in the unique and privileged position to be collecting data as part of an ongoing longitudinal study, and the study members will be assessed again at the age of 52 years. Continuing to assess this cohort as they age will be important and, in time, may elucidate effects that cannot be seen at age 45 years, particularly with the potential for neuroprotection in the retina.

ACKNOWLEDGMENTS

The authors thank the Dunedin Study members and their families and friends for their long-term involvement. The Dunedin Multidisciplinary Health and Development Research Unit is based at the University of Otago within the Ngāi Tahu tribal area whom the authors acknowledge as first peoples, tangata whenua (translation: people of this land). The authors thank Professor David Mackey (Perth, Australia) for discussions contributing to this work. The authors also thank the Unit research staff and Dunedin Study founder Dr. Phil A. Silva. This work was conducted at Dunedin Multidisciplinary Health and Development Research Unit, Department of Psychology, University of Otago (Dunedin, New Zealand).

Disclaimer: Funding organizations had no role in study design; collection, analysis, and interpretation of data; writing of the report; or the decision to submit the report for publication.

Funding: The Dunedin Multidisciplinary Health and Development Research Unit is supported by the New Zealand Health Research Council (Grant Number 16-604) and has also received funding from the New Zealand Ministry of Business, Innovation, and Employment. Funding support was also received from the U.S. National Institute of Aging (Grant Numbers R01AG069936, R01AG032282, and R01AG049789) and the United Kingdom Medical Research Council (Grant Number MR/P005918/1). The authors also acknowledge the funding received from Anna Wilson; the Buchanan Trust; the Rapanui Trust; and the Department of Psychology, University of Otago for purchasing the optical coherence tomography machine.

Declaration of interest: None

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