DUNEDIN STUDY CONCEPT PAPER FORM

Provisional Paper Title: Impact of cannabis on ocular structure and function

Proposing Author: Graham Wilson

Author's Email: graham.wilson@tdh.org.nz

P.I. Sponsor:
(if the proposing author is a student or colleague of an original PI)

Today's Date: 17th November 2021

Please describe your proposal in 2-3 pages with sufficient detail for helpful review.

Objective of the study:

To examine the role of smoking cannabis on ocular health within a New Zealand population. Specifically, the study will examine the effect of cannabis consumption on:

- Visual function (measured by visual acuity and contrast sensitivity)
- Intraocular pressure
- Optic nerve structure

Retinal microvasculature

Data analysis methods:

Data will be collected in an Excel spreadsheet and analysed using STATA. Data from both eyes of each subject will be utilized, with a generalized estimating equations approach to allow for clustering of eyes within subjects and accounting for inter-eye correlation. Analysis will be controlled for cigarette smoking and SES. A p value of < 0.05 will be considered statistically significant.

Variables needed at which ages:

Cannabis joint years (up to P45)
Smoking pack years (up to P45)
SES at P45
Eye examination parameters from Phase 45

- Pinhole visual acuity
- Contrast sensitivity
- Intraocular pressure
- Optic nerve retinal nerve fibre layer thickness and ganglion cell layer
- Retinal microvasculature – CRAE and CRVE

Significance of the Study (for theory, research methods or clinical practice):

There were an estimated 13.1 million people with cannabis dependence in 2010, accounting for around 2 million disability adjusted life years (DALYs) globally (Degenhardt, 2013). Cannabis consumption is common in New Zealand; and within the Dunedin Study, 72.3% of adults report having used cannabis, with 14.2% reporting regular cannabis use in at least one wave of the study (Meier et al., 2012). The debate regarding risks (or benefits) of marijuana has been intensified over the last few years, and the 2020 New Zealand cannabis referendum highlighted the many health, social, political, and legal issues surrounding the widespread use of this drug. This increases the importance of having accurate data on how cannabis use affects the population.

Cannabis has been reported previously to have mixed effects on the eye. Cannabis consumption results in a lowering of intraocular pressure, although the effect is transient (up to 4 hours; Bowen et al., 2018). It has been posited that cannabis may have a neuroprotective role, in part through the reduction in intraocular pressure, and also through action on COX-2 and EP2 receptors within retinal ganglion cells (Yazulla 2008). Conversely, however, a delay in transmission of retinal ganglion cells has been observed with marijuana use (Schwitzer et al., 2017), and a decline in neuropsychological function has been observed with cannabis use, suggestive of a neurotoxic effect on the brain (Meier et al., 2012). Further studies are required to determine whether cannabis has a neuroprotective, or neurotoxic effect on the optic nerve.

Within the retina, cannabinoids have been observed to depress dopamine release and also to pre-synaptically reduce transmitter release from cones and from bipolar cells (Yazulla, 2008). The functional effect of this on vision, however, has not been quantified. No difference in self-reported visual function has been observed in subjects that report heavy marijuana use compared to those that report light or no marijuana use (Akano, 2017) but relying on self-reported visual function has obvious draw backs,

and a more objective measure of visual function is warranted.

References:

Akano OF. Marijuana use and self-reported quality of eyesight. Optom Vis Sci 2017;94(5):630-633.

Bowen LL, McRae-Clark AL. Therapeutic benefit of smoked cannabis in randomized placebo-controlled studies. Pharmacotherapy 2018;38(1):80-85.

Degenhardt L, Ferrari AJ, Calabria B, Hall WD, Norman RE, McGrath J, Flaxman AD, Engell RE, Freedman GD, Whiteford HA, Vos T. The global epidemiology and contribution of cannabis use and dependence to the global burden of disease: results from the GBF 2010 study. PLoS One 2013;8(10):e76635.

Meier MH, Caspi A, Ambler A, Harrington H, Houts R, Keefe RS, McDonald K, Ward A, Poulton R, Moffitt T. Persistent cannabis users show neuropsychological decline from childhood to midlife. Poc Natl Acad Sci USA 2012;109(40):E2657-64.

Schwitzer T, Schwan R, Albuisson E, Giersch A, Lalane L, Angioi-Duprez KLaprevote V. Association between regular cannabis use and ganglion cell dysfunction. JAMA Ophthalmology 2017;135(1):54-60.

Yazulla S. Endocannabinoids in the retina: from marijuana to neuroprotection. Progress in Retinal and Eye Research 2008;27:501-526.

DATA SECURITY AGREEMENT

Provisional Paper Title	Impact of marijuana on ocular structure and function
Proposing Author	Graham Wilson
Today's Date	17th November 2021

Please keep one copy for your records and return one to the PI Sponsor

Please initial your agreement: (customize as necessary)

	I am current on Human Subjects Training [CITI www.citigrogram.org] or equivalent.
	My project is covered by the Dunedin Study's ethics approval OR I have /will obtain ethical approval from my home institution (please specify).
	I will treat all data as "restricted" and store in a secure fashion. My computer or laptop is: • encrypted (recommended programs are FileVault2 for Macs, and Bitlocker for Windows machines) • password-protected • configured to lock-out after 15 minutes of inactivity AND • has an antivirus client installed as well as being patched regularly.
	I will not "sync" the data to a mobile device.
	In the event that my laptop with data on it is lost, stolen or hacked, I will immediately contact my PI Sponsor or Study Director, Richie Poulton (richie.poulton@otago.ac.nz).
	I will not share the data with anyone, including my students or other collaborators not specifically listed on this concept paper.
	I will not post data online or submit the data file to a journal for them to post. *Some journals are now requesting the data file as part of the manuscript submission process. The Dunedin Study Members have not given informed consent for unrestricted open access, so we have a managed-access process. Speak to your PI Sponsor or Richie Poulton for strategies for achieving compliance with data-sharing policies of journals.*
	I will delete all data files from my computer after the project is complete. Collaborators and trainees may not take a data file away from the office. The data remains the property of the Study and cannot be used for further analyses without an approved concept paper for new analyses.

Signature: _____