



Concept Paper Form

Provisional Paper Title: Impact of cannabis on ocular structure and function
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P.I. Sponsor: (if the proposing author is a student or colleague of an original PI)
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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
- Ocular tear film parameters and dry eye

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. A p value of < 0.05 will be considered statistically significant.

Variables needed at which ages:

Maternal drug and smoking history

Gestational age at birth (exclude those born < 37 weeks)

Childhood vision at age 11 (subjects with poor best corrected vision in

childhood excluded from ongoing analysis)

Cannabis smoking history and frequency of use at each age (ages 9, 11, 13, 15, 18, 21, 26, 32, 38, 45)

Smoking status and pack years smoked at each age (ages 9, 11, 13, 15, 18, 21, 26, 32, 38, 45)

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
- OCT-angiography vessel density and foveal avascular zone parameters
- Dry eye parameters

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 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, with the possibility of an upcoming referendum on law reform with regard to legalizing cannabis. 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 drawbacks, and a more objective measure of visual function is warranted.

References:

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- 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. *Proc Natl Acad Sci USA* 2012;109(40):E2657-64.
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- Yazulla S. Endocannabinoids in the retina: from marijuana to neuroprotection. *Progress in Retinal and Eye Research* 2008;27:501-526.