Project Details	
Project Code	MRC23NMHBa Freeman
Title	Effects of cannabis on the adolescent brain and epigenetic aging
Research Theme	Neuroscience and Mental Health
Summary	Adolescence is a critical neurodevelopmental period which may confer greater vulnerability to the harmful effects of cannabis. To test this hypothesis, you will apply a range of advanced methods (structural MRI, diffusion MRI, brain aging, epigenetic aging) to a recently completed longitudinal study. You will work with young people to create a novel video resource for drugs education and to encourage youth engagement with science.
Description	Cannabis is used by approximately 200 million people worldwide. This number is set to increase further as cannabis becomes available as a legal drug in the USA, Canada and beyond. One of the key public health concerns arising from this is the potential adverse impact of cannabis use on the developing brain. Advances in our understanding of the endocannabinoid system show that it plays a key role in adolescent neurodevelopment. Cannabinoid receptors are abundantly expressed in brain regions which change rapidly during adolescence and are highly interconnected with white matter fibers. Because cannabis acts on cannabinoid receptors, adolescence could mark a crucial developmental window of heightened vulnerability to the effects of cannabis. This studentship will provide exclusive access to data from a major MRC-funded project: "How does cannabis use affect teenagers' brains, cognitive functions and psychological wellbeing? (CannTeen)", registered on the Open Science Framework: https://osf.io/2sbx3/ As the project was fully funded by the MRC and completed in 2021, resourcing arrangements are highly feasible. The student will work with an unprecedented dataset including neuroimaging, genetic, clinical, cognitive, and biological marker data, supervised by international experts in cannabinoid psychopharmacology (Dr Freeman, Bath), neuroimaging (Prof Jones, Cardiff; Dr Walton, Bath) and epigenetics (Dr Walton, Bath; Dr Dempster, Exeter). The student will have full opportunity and capacity to learn diverse analysis techniques from these multiple disciplines, creating a good degree of challenge. The CannTeen study consists of four groups (adolescent cannabis users, adolescent controls, adult cannabis users, adult controls) followed up every three months for one year. The student will address the following research questions: 1) Are adolescents more vulnerable to the effects of cannabis use on brain structure? Using structural MRI, it is predicted that cannabis users will show a reduction in hippocampal and orbitofrontal cortex volume, and this reduction will be greater among adolescent users. 2) Are adolescents more vulnerable to the effects of cannabis use on white matter microstructure? Using diffusion MRI, it is predicted that cannabis users will show altered microstructure in the forceps minor (connecting bilateral frontal brain regions) and the corpus callosum (connecting bilateral cerebral hemispheres). 3) Are adolescents more vulnerable to the effects of cannabis use on trajectories of brain aging? Accelerated brain aging has been found for a range of psychiatric disorders but has never been investigated for cannabis use. Brain-PAD (predicted brain age – chronological brain age)

	will be estimated using structural MRI. It is predicted that cannabis use will accelerate brain aging, and adolescents will be more vulnerable to this effect. 4) Are adolescents more vulnerable to the effects of cannabis use on trajectories of epigenetic aging? Genome-wide DNA methylation data will be used to estimate epigenetic age acceleration, based on three methods (Horvath, Zhang, Shireby). It is predicted that cannabis use will accelerate epigenetic aging, and adolescents will be more vulnerable to this effect. As the first longitudinal study to directly compare how adolescents and adults differ in response to cannabis use on the brain and aging, this studentship will generate world-first findings, with the potential to inform policy (e.g. minimum age restrictions for cannabis sales). Knowledge transfer: In the final six months, the student will engage with young people from local schools to create a video resource using results from research questions 1-4. The video will be designed to play a dual role: an evidence-based drugs education resource, and to encourage engagement with science among young people. It will be shared on social media to generate wide international reach and impact.
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