Project Details	
Project Code	MRC21NMHBa Taylor
Title	Cannabis, Tobacco and Psychiatric Disease: Examining the impact of single and combined-use on functional and structural brain functioning
Research Theme	Neuroscience & Mental Health
Summary	This PhD project will ask: Can we isolate the relationships between cannabis use, tobacco use and psychiatric disease through triangulation of data from multiple data sources (Cohort data, brain imagining data), and across statistical methods that differ in their ability to make causal links?
Description	Smoking is the world's leading cause of preventable illness and death. One in every two smokers will die because of their addiction unless they quit. In the UK, smoking prevalence has decreased from 46% during the 1970s to about 16% in recent years. However, smoking prevalence has not reduced in people with mental disorders, in 2015 it was 32%. Cannabis is gaining increasing acceptance as a medicinal and recreational drug and prevalence of use is rising worldwide. There are concerns about the adverse associations of cannabis and tobacco with risk of psychiatric disease, including severe and chronic disorders such as psychosis. The association between cannabis and psychiatric disease may be confounded by tobacco-use. Here we propose an innovative approach to explore the impact of single- and combined-use of tobacco and cannabis on brain function and structure, between people with and without psychiatric illness(anxiety, depression, psychosis). Understanding the impact of single and combined use on brain regions will inform conclusions about the impact of these substances on psychiatric disease. Question: Can we isolate the relationships between cannabis, tobacco and psychiatric disease through analysing functional and structural brain functioning data? Aims and method Study 1)Systematic review and meta-analysis of imaging studies exploring the association between cannabis, tobacco use and psychiatric disease. Exposure will be tobacco/cannabis use profile. The primary outcome will be change in functional and architecture of structural brain regions. Estimates will be compared between different cannabis/tobacco use profiles, and psychiatric groups(anxiety, depression, psychosis). Study 2)A cross-sectional and longitudinal analysis using pre-existing data from cohort studies with imaging data(IMAGEN, UK Biobank) to examine the association between dual and single cannabis/tobacco use and its impact on functional and structural brain regions. Exposure will have four levels: sole-administered tobacco, sole-administered cannabis, co-administered cannabis and tobacco, and the reference category will be never tobacco/cannabis-use. The primary outcome will be patterns in functional and architecture of structural brain regions, i.e.,ventral striatum response to reward anticipation in the monetary incentive delay task as this is disrupted in psychiatric disorders, and in cannabis and tobacco smokers. Estimates will be compared between different cannabis/tobacco use profiles, and psychiatric groups. Study 2 will identify a priori regions of interest to attempt to replicate in Study 3. To address confounding, selection bias and reverse causation(i.e., people with psychiatric disease are more likely to use cannabis and tobacco) using a novel approach, the student will triangulate evidence across

	three different analytical techniques: i)multivariable adjusted regressions, ii)propensity score matched regressions, and iii)Mendelian randomisation(MR). The student will use multivariable MR, to partition the effects of tobacco and cannabis smoking on outcomes and estimate the unique contribution of cannabis and tobacco. Study 3)Results from Study 2 will determine a-prior regions of interest to attempt to replicate in this study. For Study 3 the student will work at University of Exeter's state of the art MRI Mirielle Gillings Research Centre to collect cross-sectional data to examine the association between single- and dual-cannabis/tobacco use and brain functioning and structure, in people with and without psychiatric diseases. Exposure will have four levels: sole-administered tobacco, sole-administered cannabis, co-administered cannabis and tobacco, and the reference category will be never tobacco/cannabis-use. The primary outcome will be patterns in functional and architecture of structural brain regions. Estimates will be compared between different cannabis/tobacco use profiles, and psychiatric groups.
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