Project Details	
Project Code	MRCPHS24Ba Walton
Title	Bridging the gap: combining epigenetics and neuroimaging to shed new light on brain development and mental health in a population-based context
Research Theme	Population Health Sciences
Summary	Epigenetic processes (e.g., DNA methylation) play a key role in healthy development and function. Epigenetic alterations have been linked to neurodevelopmental, psychiatric and neurological conditions. The student will lead a unique, large and international set of studies to systematically characterize age-specific associations between peripheral DNA methylation extracted from blood and structural variation in the brain across development.
Description	Significance: This project is uniquely embedded within the global MIND consortium, which aims to shed light on the relationship between DNA methylation patterns and brain structure across development. Findings will help identify epigenetic biomarkers of typical and atypical neurodevelopment. Challenge: So far, studies in this field have been very heterogeneous in terms of design, characteristics, and methodology, with few shared practices. Furthermore, results so far have been typically based on single, cross-sectional studies with small sample sizes (n<100) – which raises issues of statistical power, low reproducibility and unclear direction of effects. Originality: The student will work with the MIND consortium, which comprises a global set of researchers and datasets (sample n>5000), including groups from the USA, UK, South Africa, Finland, Brazil, the Netherlands and more. The MIND consortium was specifically established to advance the new field of Neuroimaging Epigenetics by (i) promoting collaborative science via multi-cohort analyses; (ii) increasing scientific rigor through data harmonization and the establishment of shared practices; and (iii) elucidating directionality of associations between methylation and the brain via the use of prospective, longitudinal studies across development. Approach: The student will combine information on DNA methylation with a wide range of neuroimaging phenotypes from cohorts spanning pregnancy to adulthood. Through a meta-analytic approach, they will then pool results from individual studies that feature this unique combination of data; thereby maximizing statistical power, enabling to identify robust associations and fostering reproducible science. Project Objectives: 1) Systematically characterize associations between peripheral DNA methylation extracted from blood and structural variation in the brain across development 2) Carry out functional characterization analyses on these associations, using data from brain-tissue biobanks 3) Examine developmental dynamics from birth to adulthood 4) Test whether individual differences in brain structures mediate the association between DNA methylation and psychiatric symptoms (e.g, internalizing, externalizing and substance use disorder symptomatology) Student Ownership: The student is encouraged to explore their own ideas in pursuing each of the objectives. E.g., they can: a) Choose between various neuroimaging methods of their interest (e.g., surface- or volume-based, DTI – partially informed by their PREP period experience) b) Decide how best to assess

	ancestry diversity (given the global, ethnically diverse datasets), c) Select which developmental time points to focus on (e.g., neonatal, childhood, adolescence). d) Identify mental health outcomes of their own interest (e.g., in- or externalizing). Feasibility: The project relies on data that has already been collected and a network that is already set up. Hence, this project is highly feasible. Added-value features: This project connects a truly global set of research teams and datasets (n>8 countries across 5 continents) with the GW4 partnership. The high-impact output of this project is further secured through the collaboration across the University of Bath and University of Bristol. Knowledge transfer: The project aims to provide important new insights into the relationship between DNA methylation and brain development, using novel and ethnically diverse datasets. The student will work with the Research and Innovation Services at the University of Bath to evidence any impact arising from the project.
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