Project Details	
Project Code	MRC23PHSEx Caramaschi
Title	The role of prenatal inflammation on neurodevelopmental disorders
Research Theme	Population Health Sciences
Summary	Inflammation during pregnancy as a result of stress and infection is linked could increase the risk of autism and attention-deficit hyperactivity disorder in the child, potentially by influencing their brain development. In this project, the aim is to decipher this link by analysing large datasets from human population studies, including genetic and other molecular markers.
Description	Background. Several environmental factors and health conditions, including mental health, lead to a chronic inflammatory status, which in pregnant women could affect the development of the unborn baby. Some studies have suggested a link between the prenatal inflammatory system and brain development, potentially leading to atypical neurodevelopment. Molecular phenotypes may provide useful biomarkers of inflammation for identifying at-risk infants and perhaps even a mechanistic link between inflammation and neurodevelopment and therefore therapeutic targets. Aim. Investigate the capacity of molecular phenotypes such as genotype, DNA methylation and protein abundance as biomarkers of maternal inflammation in pregnancy with potential roles in mediating its apparent effect on atypical neurodevelopment. The project will be comprising a wealth of bioinformatic and statistical secondary analyses on rich datasets based in the UK and internationally. Objective 1. Inflammatory biomarker discovery in maternal blood. Epigenome-wide association studies and machine learning approaches will be applied to genome-wide data from pregnancy cohort studies such as the Avon Longitudinal Study of Parents and Children (ALSPAC) and Born In Bradford mothers to derive accurate biomarkers of maternal inflammation in prenatal blood samples. Specifically, it will consist of deriving predictive epigenetic scores for prenatal inflammatory status and evaluating their validity against measured circulating inflammatory markers such as C-reactive protein and interleukins. Objective 2. Inflammatory exposure biomarker discovery in cord blood. Epigenome-wide association studies and machine learning approaches will be applied to genome-wide data from ALSPAC and Born In Bradford children to derive accurate biomarkers of exposure to maternal inflammation in cord blood samples. Objective 3. Neurodevelopment biomarker discovery. Epigenome-wide association studies and machine learning approaches will be applied to genome-wide data from ALSPAC and Born In Bradford to derive accurate biomarkers of neurodevelopment, including longitudinal modelling of neurodevelopmental measures obtained repeatedly through childhood. Objective 4. Causal molecular mediation of inflammatory exposure on neurodevelopment. Causal inference studies using Mendelian randomization will be carried out to estimate the mediating role of DNA methylation in the link between prenatal inflammation and neurodevelopment. Alternative directions. Due to the availability of various datasets and the broad range of expertise across the supervisory team and collaborators, the student will be able to refine their own project according to their interests and career aims and steer the focus

	towards other objectives. For instance, the project could investigate mechanisms by comparing the findings obtained in peripheral tissues with brain tissue or investigating sex-specific pathways in a new molecular dataset on autistic children from the US-based Simons Foundation. Alternatively, state-of-the-art epigenomic sequencing data, specific antigens and inflammatory protein levels from ALSPAC will be available to determine the impact of maternal immune activation on the offspring's immune system according to neurodevelopmental traits, should this be the focus identified by the student.
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