Project Details	
Project Code	MRCNMH25Ba Fairchild
Title	Understanding the impact of childhood maltreatment on brain structure and connectivity in Conduct Disorder
Research Theme	Neuroscience & Mental Health
Summary	Childhood maltreatment is a major risk factor for Conduct Disorder (CD), a condition characterized by antisocial and aggressive behaviours. The 'ecophenotype hypothesis' suggests that maltreatment-related CD differs from non-maltreatment-related CD in severity, developmental course, treatment response, and neurobiological mechanisms. This PhD project aims to explore these differences using various large-scale datasets, including data from the recently-established ENIGMA-Antisocial Behavior Working Group (https://enigma.ini.usc.edu/ongoing/enigma-antisocial-behavior/). The research will compare maltreated and non-maltreated youth with CD in clinical profiles, developmental trajectories, brain structure and connectivity. The findings could inform the development of diagnostic criteria (DSM/ICD) and lead to personalized treatments for maltreated youth with CD.
Description	Childhood maltreatment is a key risk factor for the development of Conduct Disorder (CD), a psychiatric diagnosis involving antisocial and aggressive behaviour (Green et al., 2010; Bauer et al., 2022). Furthermore, maltreatment-related CD may differ from non-maltreatment-related CD in ways that are important for prognosis and treatment. This idea, termed the 'ecophenotype hypothesis', has been developed by Teicher and colleagues and outlined in several high-profile review articles in which they argued that maltreatment-related disorders may differ in clinical severity, developmental course, responsiveness to treatment and neurobiological correlates/mechanisms from non-maltreatment-related forms of the same disorder (Teicher et al., 2013, 2016, 2022). Key implications of the ecophenotype hypothesis are that clinicians should assess for maltreatment history as part of the diagnostic workup for CD, and the diagnostic criteria for CD (and other disorders) should include maltreatment as an additional specifier. However, this hypothesis has not been tested empirically in relation to CD, with the exception of two relatively small-scale studies in single cohorts. One of these was conducted by a former PhD student in my lab; they found more extensive alterations in cortical structure in maltreated youth with CD compared to their non-maltreated counterparts (Staginnus et al., 2023; Biological Psychiatry: CNNI). This PhD project will extend this preliminary work by investigating differences between maltreatment-related and non-maltreatment-related CD in terms of clinical symptoms, patterns of comorbidity, developmental trajectories and brain structure and connectivity. Our long-term aim is to inform the development of the main diagnostic and classification systems (DSM and ICD) and guide future research in psychiatry and clinical psychology. We will use data from the recently established ENIGMA-Antisocial Behavior Working Group (Gao, Staginnus et al., 2024, Lancet Psychiatry; https://enigma.ini.usc.edu/ongoing/enigma-antisocial-behavior/), which is jointly chaired by the lead supervisor and includes clinical and

	neuroimaging data from 20 international cohorts (N=3636). We will also use several other large-scale or prospective longitudinal datasets (ABCD, Imagen, ALSPAC, Generation R) to investigate these issues and ensure our findings are robust and generalizable across samples and countries. We will explore differences between maltreatment-related and non-maltreatment-related CD in clinical presentation, developmental course and patterns of comorbidity using LASSO regression to identify the factors or variables that best differentiate between these subgroups. We will also investigate whether these subgroups differ in brain structure or connectivity by analysing structural MRI and diffusion tensor imaging data. We will use neuroimaging mega-analysis methods developed by the ENIGMA Consortium (https://enigma.ini.usc.edu/) and the dataset generated during the first ENIGMA-Antisocial Behavior case-control project to investigate cortical structure and subcortical volume differences between maltreated and non-maltreated CD youth. Critically, we will include data from maltreated youth without CD to disentangle the brain alterations associated with maltreatment-related CD from the effects of maltreatment in general. As well as treating maltreatment as a categorical/dichotomous variable, we will investigate dimensional relationships between continuous measures of maltreatment and brain structure and connectivity using Childhood Trauma Questionnaire data (available for 7+ cohorts in ENIGMA-Antisocial Behavior; estimated sample size, n=1284). Identifying unique clinical profiles or brain alterations in maltreated youth with CD versus their non-maltreated counterparts would strengthen the case for including maltreatment as a specifier in the diagnostic criteria for CD, as proposed by Teicher and colleagues. The proposed work has theoretical and practical implications: if compelling evidence for the ecophenotype hypothesis was obtained, this would suggest that current neurocognitive models of CD need to be modified accordingly. This research would also have implications for treatment studies of CD, as previous research has shown that maltreated individuals with depression are substantially less responsive to antidepressant treatment or cognitive behavioural therapy. Our work could lead to the development of personalized treatments, targeted to meet the unique needs of maltreated youth with CD. This project is expected to generate 3-4 open-access articles presenting: (1) differences between maltreatment-related and non-maltreatment-related CD in clinical profiles, patterns of comorbidity and demographic characteristics/environmental risk factors; (2) 2-3 neuroimaging studies (brain structure and structural connectivity differences between maltreated and non-maltreated CD subgroups). The student is also expected to contribute to a review article summarizing their findings, ensuring they are accessible to a general audience and that clinicians and researchers in other fields are aware of our results and their implications. Beyond the first study, which will use ENIGMA data (i.e., a mega-analysis of structural MRI data comparing maltreated and non-maltreated youth with CD in cortical thickness, surface area and subcortical volumes), the student could go in many different directions with this project. They

	would be able to learn advanced methods such as normative modelling through our extensive network of international collaborators and links with the central ENIGMA team at the University of Southern California, potentially visiting USC to do this. It would also be possible for them to gain experience of primary data collection (e.g., qualitative interviews with young people with CD with versus without maltreatment or EEG data collection).
Supervisory Team	
Lead Supervisor	
Name	Dr Graeme Fairchild
Affiliation	Bath
College/Faculty	Humanities and Social Sciences
Department/School	Psychology
Email Address	gf353@bath.ac.uk
Co-Supervisor 1	
Name	Dr Janet Bultitude
Affiliation	Bath
College/Faculty	Humanities and Social Sciences
Department/School	Psychology
Co-Supervisor 2	
Name	Dr Xavier Caseras
Affiliation	Cardiff
College/Faculty	Medicine
Department/School	Division of Psychological Medicine and Clinical Neurosciences
Co-Supervisor 3	
Name	Dr Tom Lancaster
Affiliation	Bath
College/Faculty	Humanities and Social Sciences
Department/School	Psychology