Mental disorders affect one in four people at some point in their lives, with 450 million patients worldwide currently suffering from such a condition. Globally, mental illness is projected to cost $6 trillion per year by 2030. Therefore, it is crucial that preventative measures are developed.

For many complex diseases, we have a good understanding of early risk processes within the general population during childhood that may contribute to disease development. Dietary and lifestyle risks, for example, are strongly associated with coronary heart disease. This knowledge is vital for informing development of targeted public health strategies aimed at reducing the risk of developing disease later in life. In contrast, early risk processes that may influence development of mental disorders are poorly understood. Late presentation of illness, heavy reliance on retrospective (‘in-hindsight’) patient reports and a lack of biological tests for mental conditions all hinder development of early management and treatment.

Step in Dr Lucy Riglin and colleagues. By exploring the contribution of genetic risk variants to mental illness in the general population, the team aim to better identify early risk processes for mental illness.

UNLOCKING THE ORIGINS OF MENTAL ILLNESS
As part of the Child and Adolescent Psychiatry and MRC Centre for Neuropsychiatric Genetics and Genomics research group at Cardiff University, Dr Riglin defines and assesses common genetic variants or “alleles” from very large studies of patients with illnesses that appear to be risk factors in mental disorders.

Much of the focus of her research tests what effect these risk alleles have on childhood development and mental health in a healthy population. This may in the future offer clues toward identifying the early risks for mental disorders, as has been done for other complex diseases.

SCHIZOPHRENIA: EARLY INDICATORS OF INCREASED RISK
Numerous mental illnesses, such as schizophrenia, are highly heritable. Although they typically start after puberty, they may be preceded by childhood problems. A recent study led by Dr Riglin set out to examine the relationship between schizophrenia risk alleles and early childhood developmental impairments. Among some of the early developmental issues experienced by those who go on to develop schizophrenia are cognitive and social as well as mood and behavioural problems.

Polygenic risk scores or PRS, represent an individual’s total number of risk alleles. PRS are being used as useful measures of genetic liability for different disorders. Dr Riglin and her colleagues have identified a connection between schizophrenia PRS with behaviour, learning ability, mood, social and other impairments in young children (pre-puberty). Importantly, the team’s work proposes that...
These problems could be early indicators of a genetic liability to schizophrenia. In addition, the study suggests that these schizophrenia liability traits may be present from the age of just four years old.

ADHD: UNRAVELLING THE DETERMINANTS OF SYMPTOM PERSISTENCE

Attention Deficit Hyperactivity Disorder (ADHD) is another disorder which has a strong inherited component. The condition is common in children, in whom symptoms such as hyperactivity, inattention and impulsivity can decline over time. Yet in roughly 65% of cases, symptoms continue into adulthood. Until now, the determinants of symptom persistence and decline have been poorly understood. Investigating the connection between genetic risk (indexed by PRS) and developmental trajectories of ADHD symptoms from childhood to puberty, Dr Riglin shows that an increased ADHD PRS is linked to persistence of ADHD symptoms into adulthood, within the general population.

Two key groups of individuals were identified as having a high probability of initially elevated ADHD symptoms in childhood – of these, an estimated 40% showed persistence of symptoms with increased ADHD traits at 17 years, compared to 60% whose ADHD traits were limited to childhood. Uniquely, the study also suggests that ADHD persistence can be associated with ‘multi-morbidity’ (the presence of multiple disorders) including lower IQ, behaviour problems, social issues and language impairments. Given that multi-morbidity was more common for those with persistent compared to childhood-only ADHD symptoms, this finding has clinical relevance since it may help identify potentially persistent ADHD. Importantly, it also suggests that multi-morbidity deserves more attention than received so far, particularly since there is a need to improve the prediction value of current clinical diagnoses.

THE IMPACT OF MENTAL DISORDER RISK ALLELES ON CHILDHOOD NEURODEVELOPMENT

Working with researchers Anita Thapar, Michael O’Donovan, Stephan Collishaw, Aja K. Thapar and Barbara Maughan, Dr Riglin’s latest project examines PRS across childhood neurodevelopmental and mental health areas. Importantly, the research group is also interested in examining what happens over time (longitudinal studies) to see whether polygenic risk scores can be linked to increased or declining symptoms / trajectories of mental health symptoms. The team also raise the need to investigate the effect of environmental factors in relation to the development of mental illness and assessment of neurodevelopmental issues.

Further work is needed but this is certainly an exciting area for development that will help us to better understand mental illness, how it may develop especially early on in life, and, ultimately, identify opportunities for prevention.

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