Immune dysfunction possibly linked to schizophrenia

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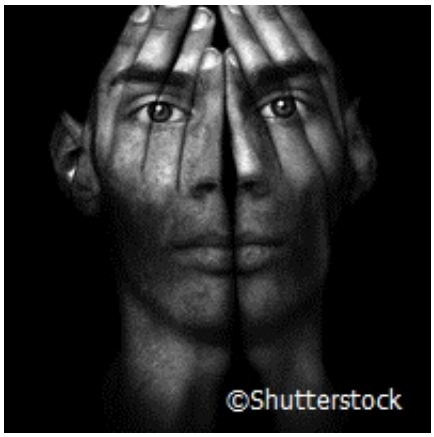

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Schizophrenia is a complex illness; among other characteristics, sufferers often find it difficult to tell the difference between what is real and not real and have trouble thinking clearly. Its symptoms could develop over months or years and mental health experts are still not entirely sure what causes it, though it is suspected that genes play a role.

A new study has discovered that a region of the genome involved in immune system function, called the major histocompatibility complex (MHC), is involved in the genetic susceptibility to schizophrenia.

Approximately seven in every thousand in the adult population are affected by schizophrenia which is among the most disabling psychiatric disorders. It is estimated that 80 per cent of the risk for developing schizophrenia is heritable, but there has been slow progress in identifying genetic variation that contributes to the risk for schizophrenia.

Two internationally renowned groups of scientists - the Wellcome Trust Case Control Consortium 2 and the Irish Schizophrenia Genomics Consortium - collaborated for this new study. It contributes to a growing literature by identifying variants of genes that influence the function of the immune system which may contribute to the heritable risk for schizophrenia.

Their findings, which were based on multiple datasets and approaches, lend further support for the involvement of the MHC genes in schizophrenia susceptibility. 'In this large collaborative effort, we have replicated evidence for specific risk and protective alleles at the MHC locus - a critical step teasing apart the genetic risk mechanisms involved,' commented Dr Aiden Corvin, one of the lead authors and a professor at Trinity College Dublin. 'However, pinpointing specific risk genes or alleles has been challenging because this is a region of great genomic variation within and between populations.'

The researchers began their work by conducting a discovery scan. They analysed over 6 million genetic variants in schizophrenia patients and controls from Ireland. This allowed them to compile a list of variants that showed the strongest association signals with schizophrenia.

They then performed similar work in an independent sample of 13,195 cases and 31,021 controls from around the world to look for the same top 'hits'. This wealth of data was provided by the international schizophrenia genetics community. The replication work is an important scientific strategy, particularly in the field of genetics, to strengthen and support the original findings.

The team's genetic findings also highlight an important gap in understanding of the biology of schizophrenia. There is a long history of interest in immunologic contribution to schizophrenia, including wide ranging observations linking viral infection, gluten sensitivity, changes in cytokine levels in blood and cerebrospinal fluid, and other

factors to schizophrenia.

'Despite this, we have relatively little understanding how alterations in immune function are involved in the etiology and pathophysiology of this disorder,' commented Dr John Krystal, Editor of *Biological Psychiatry*. 'Immunologic studies in schizophrenia that illuminate the nature of the contribution of variation in immune system genes to schizophrenia will be an important new direction in schizophrenia research.'

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