**DNA study shows link between schizophrenia and memory processes**

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Genetic mutations that cause schizophrenia could be linked to systems in the brain responsible for learning and memory, a study suggests.

Researchers from Cardiff University and the University of Edinburgh have identified changes to genes – genetic mutations – in patients with schizophrenia who had not inherited the condition.

The study, published in the journal Molecular Psychiatry, showed that these mutations occurred among a set of proteins that play a key role in memory function.

The scientists took samples of DNA from more than 650 patients with schizophrenia and compared these with DNA from their parents – who did not have the condition – to identify the genetic differences.

Professor Michael Owen of Cardiff University, who led the research with colleague Professor Michael O’Donovan, said: "By studying such a large sample we have been able to provide the first clear insights into the sorts of basic biological processes that underlie schizophrenia.

"We hope that by identifying these mutations our findings will help us understand more clearly how schizophrenia arises and ultimately identify new targets for treatments."

The task of identifying what causes schizophrenia is difficult because the disorder does not occur as a result of a single genetic mutation, but reflects a large number of different risk genes.

Professor Seth Grant, of the University of Edinburgh, whose laboratory previously discovered dozens of proteins linked to learning and memory, said: "Although it has been known for some time that DNA mutations predispose individuals to the development of schizophrenia, it has remained a puzzle as to how these genes cause behavioural problems.

"The surprising finding was that DNA mutations that cause schizophrenia are interfering with the same proteins in the molecular machinery that controls learning and memory.

The findings will help research into new drug therapies and in developing new diagnostic tests."

The genetic mutations disrupt the production of proteins found at synapses, which are the connections between different brain cells.

The proteins are normally assembled together and process information that is passed from the environment to the memory systems in the brain.

Disrupting the fundamental information processing systems in synapses results in behavioural disorders.

Professor Michael O’Donovan from Cardiff University added: "The main importance of the finding is that the new mutations were not randomly occurring in genes, instead they were concentrated in a relatively small number of genes which are crucial to the way nerve cells communicate with each other at junctions called synapses."

The study was funded by the Medical Research Council, the Wellcome Trust and the European Union.

Professor George Kirov also from Cardiff University and the study’s first author, said: "We already know that genetic factors increase the risk of schizophrenia, as well as non-genetic factors.

However, we assumed that because schizophrenia sufferers are less likely than average to have children, genes with quite large effects on risk will be removed from the population by the process of natural selection.

"If this is true, this loss of disease genes must be compensated for by new mutations or the disease would no longer exist."

Rare genetic mutations that occurred either prior to or at fertilisation - do novo mutations – were found to occur among patients with schizophrenia.

Schizophrenia is a severe disorder affecting approximately one per cent of the population.

Signs can be present from childhood, but usually the disorder is diagnosed in early teens and has an impact on adult life.

**Notes to Editor**

A copy of De novo CNV analysis implicate specific abnormalities of postsynaptic signalling complexes in the pathogenesis of schizophrenia published in Molecular Psychiatry, published online before print at doi:10.1038/mp.2011.154, is available, on request.

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