

# Twin study reveals epigenetic alterations of psychiatric disorders

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In the first study to systematically investigate genome-wide epigenetic differences in a large number of psychosis discordant twin-pairs, research at the Institute of Psychiatry (IoP) at King's College London provides further evidence that epigenetic processes play an important role in neuropsychiatric disease. Published in *Human Molecular Genetics*, the findings may offer potential new avenues for treatment.

Previous quantitative [genetic analyses](#) of [schizophrenia](#) and [bipolar disorder](#) reveal strong inherited components to both. However, although [heritability](#) for schizophrenia and bipolar disorder is estimated at 70%, disease concordance between twin-pairs is far from 100%, indicating that non-genetic factors play an important role in the onset of the diseases.

Dr. Jonathan Mill, lead author of the study at the IoP says, 'We studied a group of 22 identical twin-pairs, so 44 individuals in all, one of the largest twin studies performed for any complex disease to date. In each twin-pair, one had either schizophrenia or bipolar disorder. Because we know that twins are genetically identical, we can rule out any [genetic cause](#) of illness in the affected twin - the aim of our study was to investigate epigenetic variations associated with these disorders.'

Epigenetic mechanisms are linked to heritable, but reversible, changes in gene expression without a change in the underlying DNA sequence. This happens principally through alterations in DNA methylation and chromatin structure. Epigenetic changes in the brain have previously

been associated with a range of biological and cognitive processes, including neurogenesis, drug addiction and neurodegeneration. It has also been suggested that epigenetic changes in the brain may be involved in a spectrum of psychiatric disorders including psychosis.

The researchers looked at differences in DNA methylation across the genome using DNA taken from both the affected and unaffected twins in each monozygotic twin-pair. The findings were then compared to DNA samples taken from post-mortem brain material from psychosis patients and controls.

Whilst the researchers found no alterations in overall DNA methylation content between affected and unaffected twins, there were considerable disease-associated differences between twins at specific sites across the genome. The findings confirmed previously known sites implicated in psychiatric disorders as well as revealing previously unknown ones.

Dr. Mill adds, 'Our findings suggest that it is not only genetic variations that are important. The epigenetic differences we see may tell us more about the causes of schizophrenia and bipolar disorder, as some alterations were specific to either disease. Importantly, epigenetic processes are potentially reversible meaning that our research could open up new avenues for the development of novel therapeutic drugs.'

**More information:** Dempster, E. et al. 'Disease-associated epigenetic changes in monozygotic twins discordant for schizophrenia and bipolar disorder', *Human Molecular Genetics* [doi: 10.1093/hmg/ddr416](https://doi.org/10.1093/hmg/ddr416)

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