Epigenetic changes shed light on biological mechanism of autism

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Scientists from King's College London have identified patterns of epigenetic changes involved in autism spectrum disorder (ASD) by studying genetically identical twins who differ in autism traits. The study, published in *Molecular Psychiatry*, is the largest of its kind and may shed light on the biological mechanism by which environmental influences regulate the activity of certain genes and in turn contribute to the development of ASD and related behaviour traits.

ASD affects approximately 1 in 100 people in the UK and involves a spectrum of disorders which manifest themselves differently in different people. People with ASD have varying levels of impairment across three common areas: deficits in social interactions and understanding, repetitive behaviour and interests, and impairments in language and communication development.

Evidence from twin studies shows there is a strong genetic component to ASD and previous studies suggest that genes that direct brain development may be involved in the disorder. In approximately 70% of cases, when one identical twin has ASD, so does the other. However, in 30% of cases, identical twins differ for ASD. Because identical twins share the same genetic code, this suggests non-genetic, or epigenetic, factors may be involved.

Epigenetic changes affect the expression or activity of genes without changing the underlying DNA sequence – they are believed to be one mechanism by which the environment can interact with the genome.

Importantly, epigenetic changes are potentially reversible and may therefore provide targets for the development of new therapies.

The researchers studied an epigenetic mechanism called DNA methylation. DNA methylation acts to block the genetic sequences that drive gene expression, silencing gene activity. They examined DNA methylation at over 27,000 sites across the genome using samples taken from 50 identical twin pairs (100 individuals) from the UK Medical Research Council (MRC) funded Twins Early Development Study (TEDS): 34 pairs who differed for ASD or autism related behaviour traits, 5 pairs where both twins have ASD, and 11 healthy twin pairs.

Dr Chloe Wong, first author of the study from King's College London's Institute of Psychiatry, says: "We've identified distinctive patterns of DNA methylation associated with both autism diagnosis and related behaviour traits, and increasing severity of symptoms. Our findings give us an insight into the biological mechanism mediating the interaction between gene and environment in autism spectrum disorder."

DNA methylation at some genetic sites was consistently altered for all individuals with ASD, and differences at other sites were specific to certain symptom groups. The number of DNA methylation sites across the genome was also linked to the severity of autism symptoms suggesting a quantitative relationship between the two. Additionally, some of the differences in DNA methylation markers were located in genetic regions that previous research has associated with early brain development and ASD.

Professor Jonathan Mill, lead author of the paper from King's College London's Institute of Psychiatry and the University of Exeter, says: "Research into the intersection between genetic and environmental influences is crucial because risky environmental conditions can sometimes be avoided or changed. Epigenetic changes are potentially

reversible, so our next step is to embark on larger studies to see whether we can identify key epigenetic changes common to the majority of people with autism to help us develop possible therapeutic interventions."

Dr Alycia Halladay, Senior Director of Environmental and Clinical Sciences from Autism Speaks who funded the research, says: "This is the first large-scale study to take a whole genome approach to studying epigenetic influences in twins who are genetically identical but have different symptoms. These findings open the door to future discoveries in the role of epigenetics – in addition to genetics – in the development of autism symptoms."

More information: Wong, C.C.Y et al. 'Methylomic analysis of monozygotic twins discordant for autism spectrum disorder and related behavioural traits' Molecular Psychiatry (2013) doi: 10.1038/mp.2013.41

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