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DNA tags key to brain changes in mental disorders

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(Medical Xpress) -- Researchers from the Institute of Psychiatry at King's College London have found a relationship between molecular tags on our DNA and the weight of a particular region of the human brain called the cerebellum. The findings may provide important clues for understanding the causes of schizophrenia and autism.

The researchers focussed on a gene called Insulin-like Growth Factor 2 (IGF2) as its activity is known to be controlled by a specific process called DNA methylation. The IGF2 gene is important in regulating growth and development, principally by controlling the size of the placenta which affects the flow of nutrients from mother to foetus.

Previous studies have examined patterns of DNA methylation on the IGF2 gene in animals and human placenta samples. However, the new

study, published in *Epigenetics* is the first time that researchers have taken a detailed look at IGF2 methylation in human brain tissue. Changes in cerebellum weight are important as the size of the cerebellum is altered in some psychiatric disorders, including autism and schizophrenia.

Ruth Pidsley, from the IoP at King's who led the research, says: 'DNA methylation can be thought of as a molecular switch, helping to control the activity of genes in different parts of our bodies. New techniques allow us to accurately measure DNA methylation and investigate how it relates to measurable traits. Using these techniques we have shown that variation in DNA methylation at IGF2 is associated with cerebellum weight.'

People inherit two copies of almost every gene: one from the mother and one from the father. The activity, or expression, of a gene is controlled by DNA methylation, and in most cases this activity comes from both copies. However, in the case of IGF2, the copy we inherit from our father is methylated, and gene expression is silenced.

Using this information the researchers found that genetic sequence changes in the IGF2 gene showed a different association with cerebellum weight depending on whether the copy was maternally- or paternally-inherited. The average difference in cerebellum weight between individuals who inherited the genetic variant from just their mother and those who inherited it just from their father was considerable at 30g, roughly the weight of a kiwi fruit!

Dr Jonathan Mill, Head of the Psychiatric Epigenetics group at the MRC Social, Genetic and Developmental Psychiatry (SGDP) Centre adds: 'Given the link between structural brain abnormalities and neuropsychiatric disease, an understanding of the factors influencing brain morphology provides important clues about the etiology of

disorders such as schizophrenia and autism.'

Postmortem brain tissue was donated by the UK Medical Research Council (MRC) London Neurodegenerative Diseases Brain Bank and the Stanley Medical Research Institute. The research was supported by grants from the US National Institutes of Health and funds from the London University Central Research Fund.

More information: Pidsley, R. et al. 'Epigenetic and genetic variation at the IGF2/H19 imprinting control region on 11p15.5 is associated with cerebellum weight' *Epigenetics* (Feb 2012) doi: 10.4161/epi.7.2.18910

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