Genetic changes involved in learning disability identified

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Dr Caleb Webber and colleagues set out to identify the types of genes involved in learning disability

(PhysOrg.com) -- The first comprehensive effort to pinpoint the genetic causes of learning disability has narrowed down the genes involved from a potential list of thousands to several dozen key genes.

The study by scientists at Oxford University and Radboud University Nijmegen Medical Centre in The Netherlands could lead to diagnostic testing and genetic counselling being offered as an option to people with learning difficulties and their families.

The 78 genes identified by the research are involved in the nervous system. This is the first time that evidence from across the human genome has shown that learning disability is a disorder of the brain and nervous system.

The study was funded by the Medical Research Council and the Netherlands Organisation for Health Research and Development, and the findings are published in the journal PLoS Genetics.

'We have found a set of key genes in which changes or variations could lead to learning disability,' says Professor Chris Ponting of the MRC Functional Genomics Unit at the University of Oxford. 'This could be a first step towards offering people the option of having a genetic diagnostic test for learning difficulties, should they want it.

'For example, if I had a child with learning difficulties, I might choose to know whether I had passed on a genetic change or if such a change had arisen spontaneously by chance. Such knowledge might remove worries I might have about wanting further kids. But proper genetic counselling and support would be needed to help in making such choices.'

Learning disability is defined by having an IQ less than 70, with 1.5 million people in the UK falling into this category. People with learning difficulties can have problems with skills needed for daily life, social interaction and communication. It can result from different environmental causes (such as injuries in car crashes or childhood illness) and genetic factors.

The genetic causes of learning disability are poorly understood. Because the condition is so generally defined, the symptoms are so broad and the brain is so complex, it is estimated that thousands of genes could be associated with learning difficulties. However, there is little evidence available to back up this assumption.

The team from Oxford University and Radboud University Nijmegen Medical Centre set out to identify the types of genes that, when changed, can result in learning disability.

First, they looked at large-scale changes in the DNA of over 1,000 people with learning disabilities. These were deletions or duplications of whole chunks of DNA that had arisen spontaneously and were not found in their unaffected parents, with each chunk often containing as many as 40 individual genes.

To understand which of the many genes in these long lengths of DNA might be involved in learning disability, the researchers turned to the vast amount of genetic information available from mice. Over 5,000 genes have been individually disrupted in mice to see what role they play in the body. This means that data exist on the mouse equivalents of roughly one in four human genes.

Putting all this together, the researchers found that the DNA changes associated with learning disability contained greater than expected numbers of genes whose loss in mice affected the nervous system. This suggests that the loss or disruption of these genes could result in learning difficulties.

'Now that we have shown how powerful this technique of combining human and mouse genetic data can be, we intend to look at the genetic basis of autism and schizophrenia next,' says Dr Caleb Webber, also of the MRC Functional Genomics Unit at Oxford University.

More information: Webber C, Hehir-Kwa JY, Nguyen D-Q, de Vries BBA, Veltman JA, et al. (2009) Forging Links between Human Mental Retardation-Associated CNVs and Mouse Gene Knockout Models. *PLoS Genet* 5(6): e1000531. doi:10.1371/journal.pgen.1000531, www.plosgenetics.org/article/i … journal.pgen.1000531