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Genes link growth in the womb with adult metabolism and disease

Researchers have identified four new genetic regions that influence birth weight, providing further evidence that genes as well as maternal nutrition are important for growth in the womb. Three of the regions are also linked to adult metabolism, helping to explain why smaller babies have higher rates of chronic diseases later in life.

It has been known for some time that babies born with a lower birth weight are at higher risk of chronic diseases such as type 2 diabetes and cardiovascular disease. Three genetic regions have already been identified that influence birth weight, two of which are also linked to an increased susceptibility to type 2 diabetes.

The latest study analysed almost 70,000 individuals of European descent from across 43 separate studies of pregnancy and birth. Their findings confirmed the three regions previously identified and also revealed four new genetic regions that are associated with birth weight. The study was part-funded by the Wellcome Trust, the Netherlands Organisation for Scientific Research, the European Union, the Medical Research Council (UK), the Academy of Finland and the National Institute of Health (USA).

One of the new genetic regions is also associated with blood pressure in adulthood, providing the first evidence of a genetic link between birth weight and blood pressure. Two of the regions are known to be linked to adult height, showing that genes involved in growth begin to take effect at a very early stage.

Professor Mark McCarthy, a co-author of the study from the Wellcome Trust Centre for Human Genetics, said: "Our findings add to the growing evidence that events during early growth in the womb can have a significant impact on our health as adults. However, these genes tell only part of the story. It's important that we understand how much is down to genetics and how much is due to the environment in which we grow so that we can target efforts to prevent disease later in life."

It's not clear how the genetic regions identified affect both birth weight and adult metabolism, although the findings do offer

some clues as to the biological pathways involved. For example, the two genetic regions linking birth weight with type 2 diabetes risk are also associated with reduced levels of insulin. Insulin is the hormone responsible for regulating sugar levels in the blood, but it is also known to have an important role in early growth.

Dr Rachel Freathy, co-lead author and a Sir Henry Wellcome Postdoctoral Fellow from the University of Exeter Medical School, said: "These discoveries give us important clues to the mechanisms responsible for the control of a baby's growth in the womb, and may eventually lead to a better understanding of how to manage growth problems during pregnancy."

Together, the newly identified genetic regions have a surprisingly large effect on birth weight when compared with known environmental influences. Dr Inga Prokopenko, co-lead author from the University of Oxford explained: "Birth weight is subject to powerful influences from many environmental factors. It was a surprise to see that the genetic effects in combination have a similar impact to that of maternal smoking in pregnancy, which itself is well known to lead to lower birth weight babies."

Dr Nic Timpson, a co-author from the University of Bristol's School of Social and Community Medicine, added:"Of the intriguing findings in this work, the notion of shared biological underpinnings of early life experience and later health is one we are beginning to demonstrate with real evidence from studies like this. A fascinating extension of this work will be the dissection of the association signals reported here and working out their relevance for later life health."

The findings are published online today in the journal Nature Genetics. The international research team was led by scientists from the UK, Finland, the Netherlands and the United States.

Struan F.A. Grant, associate director of the Center for Applied Genomics at The Children's Hospital of Philadelphia and one of the co-authors on the study, said: "This study demonstrates that genes acting early in development have important effects on health both in childhood and beyond. While we continue to learn more about the biology, an important implication is that designing prenatal interventions to improve birth weight could have lifelong health benefits."

Source: Bristol University

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