

Children of older men have more gene abnormalities: study

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Do older fathers doom their children to genetic disease?

This is the question raised by a new study that says [older men](#) produce more gene [mutations](#) in the children they sire, boosting their risk of schizophrenia and autism and possibly other diseases.

A father's age is by far the biggest factor determining the rate of new, uninherited [genetic mutations](#) in his offspring, according to a paper published Wednesday in the journal *Nature*.

From a man's peak reproductive years in adolescence, the rate of new or "de novo" gene mutations triggered at conception in his children rises by about two per year, the study found.

The rate doubles every 16 years, meaning that the baby of a 36-year-old father would have twice as many new mutations than that of a 20-year-old.

"The age of the father is the most important factor to determine the number of new mutations that happen when a child is conceived," study co-author Kari Stefansson from Iceland's [DeCODE genetics](#) company told AFP.

Though de novo mutations are not necessarily harmful, it can take only one change in a key gene to cause some types of disease -- and the more mutations the higher the risk.

The results from what is claimed to be the biggest-ever study of its kind suggest that disproportionate attention has been paid to the age at which women give birth.

"We have in a very unjust manner been pointing the finger at the old mother when we should have been careful when it comes to the old father. It is clearly dangerous to have an old father," said Stefansson.

[Maternal age](#) is linked to Down's syndrome and other chromosomal diseases that develop through a process that is different to the type of genetic mutation described in this study.

The mutations in the Nature report are caused by cell division during processes like sperm production.

Stefansson and a team in Iceland, Denmark and Britain sequenced the genomes of 78 parent-child trios, as well as hundreds of [control subjects](#), looking for variants in the sequence of a child's genetic code that did not exist in the parents.

They found that the rate of increase in de novo mutations could be ascribed to the tune of 97.1 percent, "maybe entirely", to the age of the father -- an outcome that "surprised" the researchers.

The remaining 2.9 percent was ascribed to environmental factors and other random influences, Stefansson said, adding there was "no connection" between the mother and age-related increase in the rate of mutations.

The average newborn today has about 60 new small-scale mutations -- ranging from 25 in the child of a 20-year-old man to 65 in that of a 40-year-old, Alexey Kondrashov of the University of Michigan's department of ecology and evolutionary biology wrote in an analysis of

the study.

The number of de novo mutations ascribed to the mother always remains roughly 15, regardless of her age.

Previous research has shown a link between de novo mutations and autism and schizophrenia, and also a statistical link between the diseases and paternal age.

"Our contention is that a part of the increase in the diagnosis of autism that is being made these days is accounted for by increase in the age of the father," said Stefansson.

And he added further research is likely to show a similar link to other genetic illnesses, especially diseases of the brain.

In a comment also carried by Nature, Kondrashov said the study suggested a rethink of the advisable age to have children. It might be a "wise individual decision" for young men to cold-store their sperm for later use.

The age of new fathers in the Western world has been climbing in recent decades, and the number of first-time dads over 40 is growing. Official statistics show that in Iceland, the average [age](#) of fathers at conception rose from 27.9 in 1980 to 33 in 2011.

Contrary to de novo mutations which occur during cell division, inherited gene mutations are transferred at an equal rate by the father and mother, are more common and thus more commonly responsible for disease.

Scientists believe that both inherited and new mutations are responsible for diseases like autism and schizophrenia, but have not worked out the

ratio of blame.

On the positive side, de novo gene mutations are a necessary element of human evolution, allowing us to adapt to our changing environment.

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