

Older grandfathers pass on autism risk through generations, study says

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Men who have children at older ages are more likely to have grandchildren with autism compared to younger grandfathers, according to new research. This is the first time that research has shown that risk factors for autism may accumulate over generations.

The study led by King's College London's Institute of Psychiatry, Karolinska Institutet in Sweden and the Queensland Brain Institute in Australia is published today in *JAMA Psychiatry*.

By using Swedish national registers, researchers identified 5,936 individuals with [autism](#) and 30,923 healthy controls born in Sweden since 1932. They had complete data on each individual's maternal and paternal grandfathers' age of reproduction and details of any psychiatric diagnosis.

The study found that the risk of autism in the grandchild increased the older the age of the grandfather at the time his son or daughter was born. Men who had a daughter when they were 50 or older were 1.79 times more likely to have a grandchild with autism. Men who had a son when they were 50 or older were 1.67 times more likely to have a grandchild with autism, compared to men who had children when they were 20-24.

Dr Avi Reichenberg, from King's Institute of Psychiatry and co-author of the paper says: "We tend to think in terms of the here and now when we talk about the effect of the environment on our [genome](#). For the first time in psychiatry, we show that your father's and grandfather's [lifestyle](#)

[choices](#) can affect you. This doesn't mean that you shouldn't have children if your father was old when he had you, because whilst the risk is increased, it is still small. However, the findings are important in understanding the complex way in which autism develops."

Emma Frans, lead author of the study from Karolinska Institutet says: "We know from previous studies that older [paternal age](#) is a risk factor for autism. This study goes beyond that and suggests that older grandpaternal age is also a risk factor for autism, suggesting that [risk factors](#) for autism can build up through generations."

In the UK, approximately 1 in 100 adults have an autism spectrum disorder (ASD), with the condition affecting more men than women. The condition affects people in very different ways: some are able to live relatively everyday lives, while others will require a lifetime of specialist support. People with ASD have difficulty communicating with and relating to other people, and making sense of the world around them.

Autism is known to be caused by a combination of genetic and environmental factors. Previous studies have shown that older paternal age is a risk factor for autism in children: fathers aged 50 or older have a more than doubled risk to have a child diagnosed with autism compared to younger fathers.

The mechanism behind this link is unknown, but may be explained by mutations occurring in the male sperm cells. Sperm cells divide over time, and on each division the genome is faced by the possibility of new mutations being introduced.

However, most genetic mutations do not result in the child developing autism. The new findings suggest that these 'silent' mutations are passed on to the otherwise healthy child, but may influence the risk of future generations developing autism. The authors suggest that genetic risk

could accumulate over generations, or could interact with other risk factors, until it reaches a threshold resulting in the disorder manifesting itself.

More information: Frans, E.M. et al. 'Autism risk develops across generations: a population based study advancing grandpaternal and paternal age', *JAMA Psychiatry* March 20, 2013

Provided by King's College London

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