

Complex Relationship Between Parental Age, Autism Risk



The risk for autism spectrum disorder (ASD) is not only associated with increasing paternal age but also increasing maternal age and increasing age gaps between parents, a large study of children in five countries reveals.

Findings from the largest-ever study of parental age and autism risk reveal a complex relationship between parental age and autism risk. The researchers discovered that for both mothers and fathers, the risk for autism in their children increases with increasing age.

Moreover, the risk is even greater when both parents are older and when either the mother or the father is at least 10 years younger than the other parent.

"These results suggest that multiple mechanisms are contributing to the association between parental age and ASD risk," the authors, led by Sven Sandin, PhD, Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden, write.

The study was [published online](#) June 9 in *Molecular Psychiatry*.

International Study

Building on the International Collaboration for Autism Registry Epidemiology, the team examined data from Denmark, Israel, Norway, Sweden, and Western Australia on 5,766,794 children born between 1985

<http://www.medscape.com/viewarticle/846265>

and 2004 and followed-up until 2004 to 2009. Of these, 30,902 children were diagnosed with ASD, and 10,128 were diagnosed with autism disorder.

There was a monotonic increase in the risk for ASD with increasing paternal age, and a U-shaped association with maternal age.

Compared with men aged 20 to 29 years, paternal age of 40 to 49 years was associated with a relative risk of ASD in their offspring of 1.28; the relative risk for men aged ≥ 50 years was 1.66.

For women younger than 20 years, the relative risk for ASD in their offspring was 1.18 compared with women aged 20 to 29 years; the relative risk for women aged 40 to 49 years was 1.15. Similar patterns were seen for autism disorder.

The relative risks for ASD and autism disorder were higher when both parents were older. It was also higher with increasing age gaps between the parents. The highest risk for ASD was seen in couples with the following characteristics:

- The father was older than approximately 45 years, regardless of maternal age.
- The father was aged 35 to 44 years, and the mother was at least 10 years younger.
- The mother was aged 30 to 39 years, and the father was at least 10 years younger.

The results also indicated that the relative risk for ASD increased with increasing parental age difference in couples in which the father was younger than 45 years and the mother was younger than 40 years.

Dr Sandin told *Medscape Medical News* that the results suggest a complex relationship between parental age and autism.

However, he argued that if one looks back at previous studies of these factors, perhaps the complexity of the relationship is not so much of a surprise.

Age of Both Parents Influential

"In the first studies that were done, they mainly focused on maternal age, and then later studies also included paternal age, which some people thought was a bit odd: Why should there be effect with paternal age?," he said.

Initially, in epidemiologic studies, it was shown that paternal age had an effect on autism risk. This was later verified in biological studies.

<http://www.medscape.com/viewarticle/846265>

"For paternal age, we could also find mechanism, through these so-called de novo mutations, when new sperms are created in aging fathers," Dr Sandin noted.

"Then suddenly paternal age was the strongest risk factor, and maternal age was set aside a bit, but now we can show that there is actually an effect from both of them, independently of each other."

With both relatively advanced age and relatively young age of mothers associated with an increased autism risk, as well as a combined effect from both parents, Dr Sandin noted that it is a "more complex picture" than had been previously thought and that "this suggests that there may be several mechanisms that we see through the paternal and maternal age."

Another question that often comes up is whether the link between paternal age and autism risk is greater for the mother or for the father. The current results suggest that the risks are comparable for the sexes.

"When we look at mothers having the same age as the father, it looks like the risk is very similar. So a lot of the risk difference may come from the fact that fathers can reproduce at older ages compared to the mothers," Dr Sandin noted.

"I want to stress that, independent of all this, autism is actually quite a rare disease, and I think that needs to be emphasized," he added.

The study was funded by grants from Autism Speaks. The authors report no relevant financial relationships.

Mol Psychiatry. Published online June 9, 2015