

Press release: European College of Neuropsychopharmacology

The U-curve: children born to younger or older parents have an increased risk of bipolar disorder

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Peer reviewed/observational study/people*

Children of either younger or older parents carry an increased risk of bipolar disorder. This risk is greater if you were born to a mother or father younger than 20 years old, if your mother was older than 35, or your father was older than 45. This tendency gives a 'U-Shaped Curve', showing increased risks for younger and older parents. This work is presented at the ECNP Congress in Vienna, after recent publication in the peer-reviewed journal European Neuropsychopharmacology.

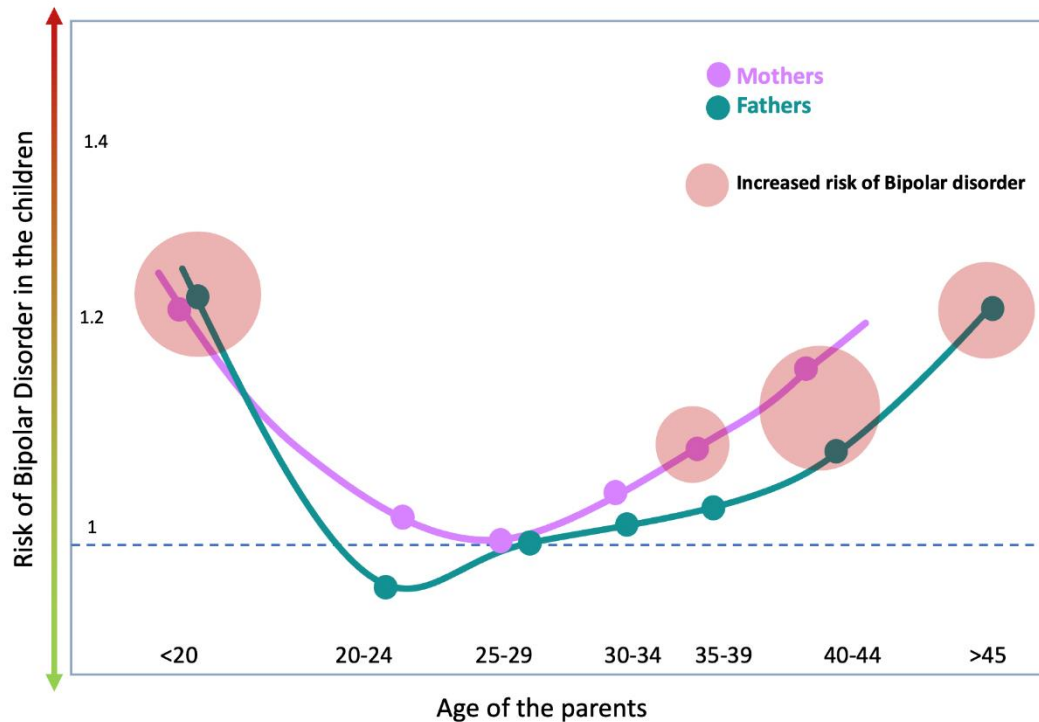
Bipolar disorder, where sufferers can swing from moods of elation to moods of extreme depression, is one of the most common serious mental illnesses, affecting around 2% of people, and carries a high risk of suicide and premature death. It is known to have high heritability; if one parent has bipolar disorder there's a 15% to 30% chance that this will be passed on to their children.

Study leader Dr Giovanna Fico, of the University of Barcelona, said:

"Parental age is a factor which affects many conditions, such as fertility and some neuropsychiatric disorders. What we have found is slightly unusual because both younger and older parents carry an increased risk of having a child with bipolar disorder. The increased risk is moderate, but real. We can speculate that younger parents may be affected by environmental factors, such as socio-economic problems, lack of support, but also stress or immunological factors, and that older parents may have genetic factors coming into play, but the truth is we don't really know".

The researchers, from Spain, Italy, Australia and the Netherlands, undertook a systematic review of studies from various countries which relate bipolar disorder to age. In total the studies included 13,424,760 participants, of whom 217,089 had bipolar disorder. They found that older men were more at risk than other groups of having a child with bipolar disorder. These men had 29% higher odds of having a baby with bipolar disorder than fathers aged 25 to 29 while older women had 20% higher odds than mothers aged 25 to 29. In parents younger than 20 years the increased odds were 23% (for mothers) to 29% (for fathers). All analyses were corrected for biasing factors, like familial history for bipolar disorders and the age of the other parent.

Giovanna Fico said *"Again, we must stress that this risk is moderate, and it must be kept in perspective. However, for those already at risk, age is another factor that should be taken into consideration, and so it may be that doctors need to counsel both younger and older couples if they have a risk of bipolar disorder. We also see this U-shaped curve in some other conditions, such as autism and some cardiovascular diseases".*



Note: the above graph is adapted from the published original. Y-axis indicates odds ratio. Credit Giovanna Fico.

She continued:

“We are planning to study several environmental factors which might be related to the risk of bipolar disorder, but also to its course of illness. For example, we would like to explore how the exposure to pollution, climate changes, urbanization might affect the risk of some psychiatric disorders, and we want to try to understand if these factors help or worsen the course of the disorder”.

Commenting, Professor Maj Vinberg (University of Copenhagen) said:

“This interesting systematic review article shows that children of young parents (up to 20 years) have a greater risk of developing bipolar affective disorder. The same pattern is seen in older parents, defined as fathers over 45 and mothers over 35.

The study raises several exciting research questions, including the possibility of early prevention and intervention. For example, in the daily clinical settings, it is crucial to be aware that young individuals with BD in their manic phases have more risky sexual behavior, which can associate with an increased pregnancy risk”.

This is an independent comment, Professor Vinberg was not involved in this research.

This work is presented at the 35th European College of Neuropsychopharmacology annual conference, which takes place in Vienna and online from 15-18 October, see <https://www.ecnp.eu/Congress2022/ECNPcongress>. Up to 5000 delegates are expected to attend. The ECNP is Europe’s main organisation working in applied neuroscience.

The published paper, “*The U-shaped relationship between parental age and the risk of bipolar disorder in the offspring: A systematic review and meta-analysis*”, Fico et al. *Eur Neuropsychopharmacol* 2022 Jul;60:55-75. doi: 10.1016/j.euroneuro.2022.05.004, can be accessed at: <https://pubmed.ncbi.nlm.nih.gov/35635997/>

None of the comments in this press release are in the published paper. A copy of the paper is available to journalists on request to the press officer.

*Press release labelling system for journalists, see <https://tinyurl.com/3kww75hy> for details

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Notes for Editors

Conference Abstract: P.0468 The U-shaped relationship between parental age and the risk of bipolar disorder in the offspring: A systematic review and meta-analysis

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Background: Evidence has suggested that parental age at birth is a risk factor for several psychiatric disorders in the offspring, including bipolar disorder (BD). Also, advanced parental age has been associated with an earlier onset of schizophrenia, but its role in BD has been overlooked.

Aims: The first aim of this systematic review and meta-analysis is to determine whether advanced parental age is associated with an increased risk of BD in the offspring. Also, considering that early-onset BD displays homogeneous characteristics and that specific risk factors might operate in this subgroup, a secondary aim is to assess whether advanced parental age is associated with an earlier BD onset.

Methods: The present Systematic Review and Meta-analysis were conducted according to the PRISMA and MOOSE guidelines. The PubMed/MEDLINE, EMBASE, Scopus, and PsycINFO databases were systematically searched from inception until December 1st, 2021. The meta-analyses were conducted using a random-effect model (restricted maximum-likelihood estimator). Heterogeneity between studies was assessed by χ^2 test of fit (Cochrane Q test) and I² statistic. Sensitivity analyses were conducted by removing one study at time from the analysis; cumulative analyses were performed to evaluate the repercussions of the follow-up length on the effect size.

Results: The literature search identified a total of 712 titles. A final number of 16 articles fulfilled inclusion criteria and of these, 14 were included in the quantitative syntheses. Included studies comprised a total of 13424760 participants and 217089 individuals with BD. Of the 14 studies included in the meta-analyses, five reported only paternal age and the offsprings' risk of BD, one only maternal age and the offsprings' risk of BD, and eight both paternal and maternal age and the offspring's risk of BD. Parental age was reported as means or ranges. Paternal age was categorized into the following age groups: <20, 20–24, 25–29, 30–34, 35–39, 40–44, and \geq 45 years. Maternal age was categorized into the following age groups: <20, 20–24, 25–29, 30–34, 35–39, \geq 40. Compared with parents aged 25–29 years, an increased risk of BD in the offspring was present both in fathers [adjusted OR: 1.29 (95% CI: 1.13–1.48)] and mothers aged \leq 20 [(OR:1.23 (95% CI: 1.14–1.33)]; in fathers aged \geq 45 years [adjusted OR: 1.29 (95% CI: 1.15–1.46)] and in mothers aged 35–39 years [OR: 1.10 (95% CI: 1.01–1.19)] and \geq 40 years [OR: 1.2 (95% CI: 1.02–1.40)].

Conclusions: There is evidence that young and advanced parental age is associated with an increased risk of BD in the offspring. Recognition of this risk is of great importance in both clinical psychiatric

practice and as a public health issue. It is necessary to implement interventions to reduce psychosocial stressors in adolescent parents, to inform individuals about the risk of early or delayed reproductive age, and implement programs to follow up offspring at risk of developing BD. Further studies are needed to elucidate the cause-effect relationship and mechanism between parental age and increased risk of BD in the offspring.

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