Advanced paternal age increases risk of bipolar disorder in offspring

**QUESTION**

**Question:** Does advanced paternal age increase the risk of bipolar disorder in offspring?

**People:** 7,739,202 individuals were identified through linkage of the Hospital Discharge Register and the Multigeneration Register. From this study base of over 7 million individuals, 13,428 cases (42% male) with two known biological parents and at least two separate hospital admissions for bipolar disorder (using ICD codes) were identified. Exclusions: people diagnosed with bipolar disorder but with only one hospitalisation (to avoid inclusion of people who were misdiagnosed); people diagnosed with unipolar depression.

**Controls:** (67,140 people; five randomly selected for each case) were people without a diagnosis of bipolar disorder and matched to cases for sex and age. Controls had to be alive at the date of the case’s first hospitalisation to allow for an equal period of risk.

**Outcomes:** Bipolar disorder (defined as diagnosis of bipolar disorder at hospital discharge on two or more occasions).

**METHODS**

**Design:** Nested case control study.

**Follow-up period:** Up to 59 years (assessed retrospectively).

**MAIN RESULTS**

The risk of bipolar disorder in the offspring increased with advancing paternal age (see online table). Compared with offspring of men aged 20–24 years, the risk of bipolar disorder was highest in offspring of men aged 55 years and older (unadjusted odds ratio (OR) 1.38, 95% CI 1.04 to 1.84). This increase remained significant after adjustment for a family history of psychotic disorders, maternal age, socioeconomic status and parity (OR 1.37, 95% CI 1.02 to 1.84).

For cases with early onset bipolar disorder (715 cases and 3,575 controls included in the analysis), the risk of bipolar disorder was highest in offspring of men aged 50 years and older compared with offspring of men aged 20–24 years (OR 2.63, 95% CI 1.19 to 5.81; adjusted for maternal age). Increasing maternal age was also associated with an increased risk of bipolar disorder. However, after controlling for paternal age, family history of psychotic disorders, parity and socioeconomic status, the increase only remained significantly higher in offspring of women aged 30–34 years (OR 1.08, 95% CI 1.01 to 1.16) and 35–39 years (OR 1.16, 95% CI 1.06 to 1.26) compared with offspring of women aged 20–24 years. After adjusting for paternal age, the associations between maternal age and risk for early onset bipolar disorder were not statistically significant (OR 1.24, 95% CI 0.71 to 2.19).

**CONCLUSIONS**

Advanced paternal age is a risk factor for bipolar disorder in offspring.

**ABSTRACTED FROM**


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Advanced paternal age has historically been examined in association with psychiatric disease in the offspring. However, most studies have suffered from methodological shortcomings and the “new wave” started in 2001 when Malaspina and colleagues, based on a large cohort, described an almost three times increased risk for comings and the “new wave” started in 2001 when Malaspina and colleagues, based on a large cohort, described an almost three times increased risk for...