Maternal infection requiring hospitalization during pregnancy and attention-deficit hyperactivity disorder in offspring: a quasi-experimental family-based study

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Abstract

BACKGROUND:
Maternal infection during pregnancy (IDP) has been associated with increased risk of attention-deficit/hyperactivity disorder (ADHD) in offspring. However, infection is associated with social adversity, poor living conditions and other background familial factors. As such, there is a need to rule out whether the observed association between maternal IDP and ADHD might be attributed to such confounding.

METHODS:
This nationwide population-based cohort study using a family-based, quasi-experimental design included 1,066,956 individuals born in Sweden between 1992 and 2002. Data on maternal IDP (bacterial or viral) requiring hospitalization and ADHD diagnosis in offspring were gathered from Swedish National Registers, with individuals followed up through the end of 2009. Ordinary and stratified Cox regression models were used for estimation of hazard ratios (HRs) and several measured covariates were considered. Cousin- and sibling-comparisons accounted for unmeasured genetic and environmental factors shared by cousins and siblings.

RESULTS:
In the entire population, maternal IDP was associated with ADHD in offspring (HR = 2.31, 95% CI = 2.04-2.61). This association was attenuated when accounting for measured covariates (HR = 1.86, 95% CI = 1.65-2.10). The association was further attenuated when adjusting for unmeasured factors shared between cousins (HR = 1.52, 95% CI = 1.12-2.07). Finally, the association was fully attenuated in sibling comparisons (HR = 1.03, 95% CI = 0.76-1.41).

CONCLUSIONS:
This study suggests that the association between maternal IDP and offspring ADHD is largely due to unmeasured familial confounding. Our results underscore the importance of adjusting for unobserved familial risk factors when exploring risk factors for ADHD.