Investigating the effects of cesarean delivery and antibiotic use in early childhood on risk of later attention deficit hyperactivity disorder


Abstract

BACKGROUND:
Increasing attention deficit hyperactivity disorder (ADHD) incidence has been proposed to be caused by factors influencing microbiota in early life. We investigated the potential causality between ADHD and two surrogate markers for changes in children's microbiota: birth delivery mode and early childhood antibiotic use.

METHOD:
This population-based, prospective cohort study linked nationwide registers of data for native Danish singleton live births in Denmark from 1997 to 2010. Exposure variables were delivery mode and antibiotic use during the first 2 years of life. The main outcome measure was ADHD diagnosis or redeemed ADHD medication prescriptions. For statistical analysis, we used both advanced sibling models and a more traditional approach.

RESULTS:
We included 671,592 children, followed from their second birthday in the period 1999-2014 for 7,300,522 person-years. ADHD was diagnosed in 17,971. In total, 17.5% were born by cesarean delivery, and 72% received antibiotic treatment within their first 2 years of life. In the adjusted between-within sibling survival model, mode of delivery or antibiotics had no effect on ADHD when compared with vaginal delivery or no antibiotic treatment as hazard ratios were 1.09 (95% confidence interval 0.97-1.24) for intrapartum cesarean, 1.03 (0.91-1.16) for prelabor cesarean, 0.98 (0.90-1.07) for penicillin, and 0.99 (0.92-1.06) for broader spectrum antibiotics. In a sibling-stratified Cox regression, intrapartum cesarean was associated with increased ADHD risk, but other exposures were not. In a descriptive, nonstratified Cox model, we found increased risk for ADHD for all exposures.

CONCLUSIONS:
Detailed family confounder control using the superior between-within model indicates that cesarean delivery or use of antibiotics during the first 2 years of life does not increase ADHD risk. Therefore, our study suggests that changes in children's microbiota related to cesarean delivery or antibiotic use, do not cause ADHD.