Parental autoimmune and autoinflammatory disorders as multiple risk factors for common neurodevelopmental disorders in offspring: a systematic review and meta-analysis

Classification：etiology

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Abstract

Epidemiological studies have raised concerns about the risk of neurodevelopmental disorders (NDD) in children of patients with autoimmune or inflammatory disorders (AID). The pathophysiological pathways underlying this association are still unknown and little is known about the specific and distinct risk of each AID. To explore these questions, we investigated the association between the occurrences of several NDD in the offspring of mothers or fathers with different IDA. We conducted a meta-analysis-PROSPERO (CRD42020159250)-examining the risk of NDD in the offspring of mothers or fathers with AID. We performed specific analyses separately in fathers or mothers of NDD patients as well as subgroup analyses for each NDD and AID. We searched MEDLINE, Embase, PsycINFO, Cochrane Central Register of Controlled Trials, and Web of Science Core Collection published until December 2021. From an initial pool of 2074 potentially relevant references, 14 studies were included, involving more than 1,400,000 AID and 10,000,000 control parents, 180,000 children with NDD and more than 14,000,000 control children. We found AID in mothers (Adjusted OR 1.27 [95% CI 1.03; 1.57] p = 0.02, [I2 = 65%, Tau2 = 0.03 p = 0.01] and adjusted OR 1.31 [95% CI 1.11; 1.55] p = 0.001, [I2 = 93%, Tau2 = 0.13 p = 0.001] and, although in a lesser extent, in fathers (adjusted OR 1.18 [95% CI 1.07; 1.30] p = 0.01, [I2 = 15.5%, Tau2 = 0.002 p = 0.47]) and adjusted OR 1.14 [95% CI 1.10; 1.17] p < 0.0001, [I2 = 0%, Tau2 = 0 p = 0.29]) to be associated with ASD and ADHD in the offspring. This difference in the strength of the association was found in the AID-specific analyses, suggesting that AID increase the risk of NDD by a shared mechanism

but that a specific maternal route appears to represent an additional excess risk. Inflammatory bowel disease were not associated with an additional risk (neither in fathers nor in mothers) of NDD in offspring. Our results suggest that complex and multiple AID-specific pathophysiological mechanisms may underlie the association of AID and NDD in offspring. Further, comprehensive studies of the different AID and NDD are needed to draw definitive conclusions about the pathophysiological links between parental AID and NDD in children.