Maternal immune activation and neuroinflammation in human neurodevelopmental disorders

Velda X Han , Shrujna Patel , Hannah F Jones , Russell C Dale

Nat Rev Neurol. 2021 Aug 2.
DOI: 10.1038/s41582-021-00530-8.

Abstract

Maternal health during pregnancy plays a major role in shaping health and disease risks in the offspring. The maternal immune activation hypothesis proposes that inflammatory perturbations in utero can affect fetal neurodevelopment, and evidence from human epidemiological studies supports an association between maternal inflammation during pregnancy and offspring neurodevelopmental disorders (NDDs). Diverse maternal inflammatory factors, including obesity, asthma, autoimmune disease, infection and psychosocial stress, are associated with an increased risk of NDDs in the offspring. In addition to inflammation, epigenetic factors are increasingly recognized to operate at the gene-environment interface during NDD pathogenesis. For example, integrated brain transcriptome and epigenetic analyses of individuals with NDDs demonstrate convergent dysregulated immune pathways. In this Review, we focus on the emerging human evidence for an association between maternal immune activation and childhood NDDs, including autism spectrum disorder, attention-deficit/hyperactivity disorder and Tourette syndrome. We refer to established pathophysiological concepts in animal models, including immune signalling across the placenta, epigenetic 'priming' of offspring microglia and postnatal immune-brain crosstalk. The increasing incidence of NDDs has created an urgent need to mitigate the risk and severity of these conditions through both preventive strategies in pregnancy and novel postnatal therapies targeting disease mechanisms.