Astroglial hemichannels and pannexons: The hidden link between maternal inflammation and neurological disorders

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Abstract

Maternal inflammation during pregnancy causes later-in-life alterations of the offspring's brain structure and function. These abnormalities increase the risk of developing several psychiatric and neurological disorders, including schizophrenia, intellectual disability, bipolar disorder, autism spectrum disorder, microcephaly, and cerebral palsy. Here, we discuss how astrocytes might contribute to postnatal brain dysfunction following maternal inflammation, focusing on the signaling mediated by two families of plasma membrane channels: hemi-channels and pannexons. $[Ca^{2+}]_i$ imbalance linked to the opening of astrocytic hemichannels and pannexons could disturb essential functions that sustain astrocytic survival and astrocyte-to-neuron support, including energy and redox homeostasis, uptake of K^+ and glutamate, and the delivery of neurotrophic factors and energy-rich metabolites. Both phenomena could make neurons more susceptible to the harmful effect of prenatal inflammation and the experience of a second immune challenge during adulthood. On the other hand, maternal inflammation could cause excitotoxicity by producing the release of high amounts of gliotransmitters via astrocytic hemichannels/pannexons, eliciting further neuronal dam-age. Understanding how hemichannels and pannexons participate in maternal inflammation-induced brain abnormalities could be critical for developing pharmacological therapies against neurological disorders observed in the offspring.

Author keywords

Astrocyte; Connexins; Excitotoxicity; Hemichannels; Lipopolysaccharide; Microglia; Neu rodegeneration; Neuroinflammation; Neuron; Pannexins; Pannexons