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Prenatal Infections and Long-Term Mental Outcome

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Disturbances directed at the maternal host during pregnancy can lead to direct physiological changes in the fetal environment and negatively affect the normal course of early brain development in the offspring. This can have long-lasting consequences for the development of postnatal brain dysfunctions, in which the primary cerebral insult or pathological process occurs during early brain development long before the illness is clinically expressed. Two prominent examples of such neuropathological outcomes are schizophrenia and autism: Both disorders seem to be associated with aberrations in early neurodevelopmental processes caused by a combination of environmental and genetic factors, which predispose the organism to long-lasting neuropathology and psychopathology. A large body of human epidemiological data shows that maternal infection during pregnancy is one of the relevant environmental factors increasing the risk of these of neurodevelopmental brain dysfunctions in the offspring. Even though the precise neuroimmunological mechanisms involved still need to be delineated, one prevalent hypothesis suggests that infection-induced disruption of fetal neurodevelopmental processes may predispose the organisms to long-lasting changes in subsequent brain and behavioral development, thereby facilitating the expression of postnatal brain dysfunctions relevant to schizophrenia and autism. This hypothesis has been substantiated by numerous investigations in experimental rodent models demonstrating the emergence of altered fetal brain development and multiple long-term brain and behavioral abnormalities relevant to schizophrenia and autism following prenatal exposure to infection and/or immune activation. These experimental models provide indispensable experimental tools to test the hypothesis of causality in human epidemiological associations, and to explore the critical neuroimmunological and developmental factors involved in shaping the vulnerability to infection-induced neurodevelopmental disturbances in humans. Experimental models of prenatal immune challenge also offer a unique opportunity to establish and evaluate early preventive interventions aiming to reduce the risk of long-lasting brain dysfunctions following prenatal exposure to infection. The present talk will highlight the advances in modeling the epidemiological link between prenatal immune challenge and neurodevelopmental brain dysfunctions and will discuss the relevance of experimental findings to the prenatal infectious etiologies of human mental illness.

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