Maternal exposure to bacterial endotoxin during pregnancy in rats: implications for aetiopathogenesis of schizophrenia

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Increasing evidence associates schizophrenia with prenatal exposure to infection. Our attempt to study the link between prenatal immunological challenge and subsequent pathology has led to the establishment of a rat model demonstrating the emergence and maintenance of several schizophrenic-like symptoms following prenatal immunological challenge. In this model, pregnant rats are exposed to the bacterial endotoxin lipopolysaccharide (LPS) throughout gestation and the offspring are examined by evaluating the prepulse inhibition of the acoustic response (PPI), dopaminergic function, brain protein expression, and cytokine serum levels. Both, sensory information processing deficits and immune anomalies induced by prenatal LPS exposure were accompanied by alterations in dopaminergic neurotransmission and synaptophysin expression. Histopathological features in brain areas related with PPI circuitry were also observed. Even more, PPI disruption as well as the increases in the levels of serum cytokines induced by prenatal LPS were reversed by the typical antipsychotic haloperidol. From an ontogenic point of view, prenatal LPS exposure induced a deficit in PPI that emerged at “puberty” and that persisted throughout adult life. This prenatal insult caused age-specific changes in dopamine levels in the nucleus accumbens and in synaptophysin expression in the frontal cortex. Moreover, serum cytokine levels were altered in an age- and cytokine-dependent manner. Our results illustrate the critical influence of prenatal immune events upon adult nervous and immune systems functioning, in association with a putative role of the immune system in the development and maintenance of neurobehavioral alterations relevant to schizophrenia.