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Differential cognitive and behavioural impacts of LPS and PolyI:C prenatal infections on adult female offspring

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Differential cognitive and behavioural impacts of LPS and PolyI:C prenatal infections on adult female offspring

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Purpose: Maternal infection during pregnancy is a risk factor for offspring developing schizophrenia. Behavioural changes reported in adult offspring in animals studies are inconsistent due to variations in type, dose and timing of immunogen administration during gestation, and postnatal age examined. In this study, two different prenatal infection modes, bacterial (lipopolysaccharide; LPS) and viral (polyinosinic-polycytidylic acid; PolyI:C), were investigated to determine the impacts on cognitive functioning of adult rat offspring.

Methods: Maternal Sprague-Dawley rats were injected intraperitoneally with saline solution, LPS, or PolyI:C at embryonic days 15 and 16, to approximate the second trimester in human pregnancy; a critical period for immunogen exposure in schizophrenia aetiology. Adult female offspring (n=12) were treated with saline or olanzapine from postnatal day (PN) 90 for five weeks. From PN 118, cognition and behaviour of adult female offspring were examined by open field (OF) and novel object recognition (NOR) tests. Cognitive functioning investigated in the NOR test was expressed as a discrimination index reflecting recognition memory.

Results: Adult prenatal LPS offspring showed a 74% decrease in discrimination index compared to saline control (p=0.011) in the NOR test. Prenatal PolyI:C infection had no significant effect on discrimination index in the NOR test. Prenatal injection of PolyI:C significantly increased peripheral rearing activity of adult offspring in the OF test (p=0.034). However, prenatal LPS had no significant effect on peripheral rearing activity. Olanzapine administration significantly decreased peripheral rearing activity during the OF test for prenatal saline (p<0.001), LPS (p<0.001), and PolyI:C (p<0.001) offspring.

Conclusion: Bacterial and viral prenatal infection produce differing cognitive and behavioural effects in offspring. Cognitive deficit observed in prenatal LPS offspring suggests a risk of disrupted neurodevelopment. Prenatal PolyI:C-induced hyperlocomotor activity, indicative of schizophrenia-like symptoms, is reversed by chronic olanzapine treatment.