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Prenatal infection promotes olanzapine-induced obesity in rats: implications for antipsychotic-induced obesity in schizophrenia

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Abstract

Abstract of a poster presentation.

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Prenatal infection promotes olanzapine-induced obesity in rats: Implications for antipsychotic-induced obesity in schizophrenia

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Purpose: Atypical antipsychotic drugs such as olanzapine and clozapine induce significant weight gain and obesity in schizophrenia and allied disorders. Prenatal infection is considered to be a severe impact to brain development which can lead to offspring developing late onset behavioural abnormalities. These abnormalities resemble some aspects of schizophrenia. This study aims to develop a rodent model mimicking patients of schizophrenia with metabolic syndrome after chronic treatment with olanzapine.

Methods: Pregnant SD rats were injected with saline, PolyI:C (polyinosinic-polycytidylic acid, 8mg/kg), LPS (lipopolysaccharide, 100 microgram/kg) from gestation day 15 and 16. Each group was subdivided into a control and olanzapine group, and treated for 5 weeks from 13 weeks of age. All rats throughout the experiment were fed lab chow *ad libitum*. Body weight and food and water intake were measured twice a week.

Results: Prenatal PolyI:C and LPS rats gained weight quickly and developed obesity after olanzapine administration. The final body weight of the prenatal LPS group with olanzapine treatment was higher than the saline control ($p=0.002$) and LPS control groups ($p=0.004$) respectively. Prenatal infection with LPS in addition to olanzapine significantly increased peri-ovarian adipose weight ($p=0.001$). Analysis of hypothalamic neuropeptides relevant to body weight control and metabolism is currently ongoing.

Conclusion: For the first time, the viral and bacterial prenatal infection models successfully replicate antipsychotic drug induced obesity and metabolic syndrome in SD rats. This model represents the diseased condition in humans brought on by prenatal viral or bacterial infection. This animal model will be used to study the mechanism of antipsychotic drug induced obesity and metabolic side effects, and to identify therapeutic targets for treatment.