January 2015

# Olanzapine differentially corrects altered NMDA receptor binding induced by prenatal polyIC and LPS

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## Abstract

Abstract of a poster presentation.


## Disciplines

Medicine and Health Sciences


## Publication Details

Bell, C. J., Boz, Z., Wang, H. Q., Yu, Y. H. & Huang, X. F. (2015). Olanzapine differentially corrects altered NMDA receptor binding induced by prenatal polyIC and LPS. Biological Psychiatry Australia (BPA) Conference: Abstract Book 2015 (pp. 122-122). Australia: Biological Psychiatry Australia.

**P064 - Abstract Title:** Olanzapine differentially corrects altered NMDA receptor binding induced by prenatal polyIC and LPS


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**Purpose:** Prenatal infection from bacterial or viral agents has been identified as an environmental risk factor for altered brain development in offspring, which contributes to the development of mental illness and schizophrenia. NMDA hypofunction is a known contributor to the neuropathology of schizophrenia. The prenatal infection animal model mimics schizophrenia-like symptoms and behaviours such as cognitive deficits and PPI inhibition. This study aims to examine if either prenatal polyIC or LPS alters NMDA receptor binding in the brain of adult offspring.
**Methods:** Maternal Sprague-Dawley rats were injected intraperitoneally with saline solution, LPS, or polyIC at embryonic days 15 and 16, comparable to the second trimester in human pregnancy; one of the critical periods for immunogen exposure relating to the development of schizophrenia symptoms. At postnatal day (PN) 126, NMDA receptor binding density was examined by in-vitro autoradiography with [$H^3$] MK-801 and MK-801 as specific and non-specific ligands, respectively. Furthermore, adult female offspring were treated with saline or olanzapine from PN 90 for five weeks.
**Results**: Prenatal exposure to polyIC produced a significant decrease in NMDA receptor binding density in the caudate putamen (CPu, 16%, $p<0.05$), nucleus accumbens (NAc, 20%, $p<0.05$), and amygdala (25%, $p<0.05$) of adult offspring. Prenatal LPS, however, produced a significant decrease in only the amygdala (30%, $p<0.01$); a trend decrease was observed in the NAc (15%, $p<0.1$). Olanzapine with prenatal polyIC significantly increased NMDA receptor binding density in the CPu (36%, $p<0.05$) and NAc (22%, $p<0.5$), but not the amygdala. Prenatal LPS offspring administered olanzapine exhibited increased NMDA receptor binding density in the amygdala (24%, $p<0.1$), but not the NAc.
**Conclusion:** While polyIC and LPS both reduce NMDA receptor binding density in the limbic system, only polyIC had an effect in the caudate putamen. Administration of olanzapine corrected the polyIC-induced changes in the caudate putamen and nucleus accumbens, but not the amygdala. Conversely, olanzapine administration corrected the LPS-induced change in the amygdala, but not the nucleus accumbens. These findings may explain why olanzapine administration can have different therapeutic effects in individuals, dependent on the specific aetiology of schizophrenia.