

## Clozapine attenuated mitochondrial dysfunction, inflammatory gene expression, and behavioral abnormalities in an animal model of schizophrenia

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**Objectives:** Beyond abnormalities in neurotransmitter hypothesis, recent evidence suggests that mitochondrial dysfunction and impaired immune system contribute to the pathophysiology of schizophrenia. Prefrontal cortex (PFC) undergoes maturation and development during adolescence as a critical time window, during which brain is vulnerable to environmental adversities and is prone to the development of psychiatric disorders such as schizophrenia.

**Methods:** Applying eight weeks of post weaning social isolation stress (PWSI) to rats, as an animal model of schizophrenia, we evaluated the effects of PWSI on the mitochondrial function and expression of immune-inflammatory genes in the PFC of normal and stressed rats and then, each group were divided into treatment (clozapine; CLZ, 2.5 mg/kg/day for 28 days) and non-treatment groups.

**Results:** Our data showed that PWSI provoked schizophrenic-like behaviors in rats and induced mitochondrial dysfunction and upregulation of genes associated with innate immunity in the PFC. Chronic treatment with CLZ attenuated the effects of PWSI on behavioral abnormalities, mitochondrial dysfunction as well as immune-inflammatory responses in the PFC of rats.

**Conclusions:** These results may advance our understanding about the mechanism of action of CLZ that targets mitochondrial dysfunction and immune-inflammatory responses as factors involved in the pathophysiology of schizophrenia.

**Key words:** Schizophrenia; Clozapine; Mitochondria; inflammation ; Social isolation stress, Adolescence

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