Abstract
It was reported the unconjugated bilirubin may be associated with neurotoxicity in the developing nervous system. And it is also reported that neonatal hyperbilirubinemia might be a vulnerability factor for the development of mental disorders.

Individuals with schizophrenia show a significantly higher frequency of hyperbilirubinemia relative to patients with other psychiatric disorders and the general healthy population. We have also observed that patients with schizophrenia frequently have an elevated bilirubin plasma concentration on admission to the hospital.

There has been a report of a positive relationship between schizophrenia and hyperbilirubinemia. We assume that a high serum unconjugated bilirubin concentration has a pathogenic effect on the development of the brain and consequently the behavioral abnormalities of schizophrenia.

The Gunn rat, a mutant of the Wistar strain, has been used in several previous studies as an animal model of bilirubin encephalopathy. The Gunn rat has a genetic deficiency in glucuronyltransferase and thus is hyperbilirubinemic. It has been reported that the neural damage in Gunn rats almost always occurs in the first month after birth.

We assumed Gunn rats as one of the schizophrenia animal models. To validate as the schizophrenia model, we examined the acute behavioral abnormalities of Gunn rats and Wistar rats, after injection of NMDA-antagonist ketamine. The locomotor stimulatory effect of ketamine was significantly greater in Gunn rats compared with Wistar rats, and furthermore interfered PPI after ketamine injection was observed in Gunn rats.

Gunn rats were more vulnerable to ketamine than Wistar rats. The results related to the face, predictive and construct validities.

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Early risperidone exposure affects serotonin, dopamine and cannabinoid receptors binding density differently in male and female juvenile rats
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Abstract
Background: Antipsychotic drugs were developed to treat schizophrenia in adults, however they have been increasingly prescribed in children and adolescents without understanding the underlying mechanisms. The serotonin, dopamine and cannabinoid pathways are involved in antipsychotic efficacy and neurodevelopment, as well as the pathophysiology of schizophrenia. This study investigated the effects of early risperidone exposure on binding densities of serotonin 5-HT₂A receptors (5-HT₂A), 5-HT₂C receptors (5-HT₂C), dopamine D₁ receptor (D₁R), D₂ receptor (D₂R) and cannabinoids CB₁ and CB₂ receptors (CB₁ and CB₂) in the prefrontal cortex (PFC), cingulate cortex (Cg) and nucleus accumbens (NAc) and caudate putamen (CPu) of juvenile rats.

Methods: Male and female Sprague Dawley rats treated orally three times per day with risperidone (0.3 mg/kg) or vehicle (control) starting from postnatal day (PD) 23 (±1 day) for 3 weeks (a period corresponding to the childhood-adolescent period in humans). Quantitative autoradiographic methods were used to detect binding density of [³H]ketanserin (for 5-HT₂A), [³H]mesulergine (for 5-HT₂C), [³H]SCH23390 (for D₁R), [³H]raclopride (for D₂R), and [³H]CP55940 (binding to CB₁ and CB₂) and [³H]SR141716A (for CB₁).

Results: Risperidone decreased [³H]ketanserin binding in the PFC of female rats (p<0.05), while it significantly attenuated the [³H]SCH23390 binding in the PFC and Cg of male rats (p<0.05). However, risperidone had no effect on [³H]mesulergine binding in both genders. Risperidone significantly increased the [³H]CP55940 bindings in the PFC, NAc (p<0.01), and Cg, CPu of male rats (p<0.05), but not in female rats. Risperidone tended to increase [³H]SR141716A binding in the PFC (p=0.055), NAc (p=0.055) and significantly enhanced it in the CPu of male rats only (p<0.05).

Discussion: These results suggested that early risperidone exposure affected serotonin, dopamine and cannabinoid neurotransmission differentially in male and female rats. Further studies are necessary to investigate whether risperidone treatment has differential long-term effects between males and females.

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Effects of sulforaphane in the maternal immune activation model of schizophrenia
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Abstract
Objective: Accumulating evidence suggests the role of inflammation and oxidative stress in the pathophysiology of schizophrenia. Keap1-Nrf2 signaling plays an important role in the anti-inflammatory and anti-oxidant effects. Sulforaphane (SFN), a potent Nrf2 activator, has a potent anti-inflammatory and anti-oxidant activity. It is reported that SFN could attenuate behavioral abnormalities in mice after administration of methamphetamine or phencyclidine. The objective of this study was undertaken to examine whether glucoraphanin (a glucosinolate precursor of SFN) can prevent the onset of schizophrenia-like behavioral abnormalities in the offspring after maternal immune activation.

Methods: The synthetic double strand RNA polyriboinosinic-polycytidylic acid (poly I:C; 5.0 mg/kg) or saline were injected into pregnant ddY mice (E12 – E17). The offspring were separated from their mothers after 3 weeks, and male mice were used in the subsequent experiments. Mice (4-weeks old) were divided into a normal food pellet group and a 0.1% glucoraphanin containing pellet group for 4-weeks. Then, normal food pellet was given to the all groups for 2-weeks, and behavioral tests (locomotion, novel object recognition test) were performed at 10-weeks old.

Results: In the novel object recognition test, the offspring from poly I:C-treated group showed cognitive deficits at adulthood. Interestingly, the dietary intake of 0.1% glucoraphanin during 4 – 8 week old could prevent the onset of cognitive deficits at adulthood.

Conclusion: This study suggests that SFN can prevent the onset of behavioral abnormalities at adulthood in the immune activation model of schizophrenia. Therefore, the dietary intake of