

Psychiatric Dysfunction Model Animals in Relation to Gene and Stress

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Schizophrenia (SZ) is a chronic and severely debilitating mental illness that affects about 1% of the population worldwide. SZ is characterized by positive symptoms of hallucination and delusion, by persistent negative symptoms of social withdrawal, flattened affect and decreased motivation, and by profound cognitive deficits in attention, working memory and executive functioning. Current antipsychotics and psychosocial therapy have limited efficacy. In fact the inveterate cases that enough curative effect is not provided, reach 2/3. Therefore, we should urgently elucidate the pathogenic mechanism of SZ, make model animals which accorded with the pathological condition of the patient and develop effective treatment / prevention.

Although mice treated with psychomimetic compounds, such as phencyclidine and methamphetamine, are used as models for SZ, they may not reflect any disease etiology. It has been suggested that susceptibility genes for SZ may be advantageous in producing more etiology-relevant models. Disrupted-in-Schizophrenia-1 (DISC1) has been identified as a genetic susceptibility factor for schizophrenia and other mental disorders. It plays roles during neurodevelopment and influences adult high brain functions including cognition and information processing. "Neurodevelopmental disability hypothesis" has been advocated based on susceptibility to mental disorders in the patients who have impaired neuronal maturation. In addition, the development of the brain is affected not only by the genetic, but also environmental factors in the prenatal / perinatal periods (1 hit), and afterwards the mental diseases are developed by mental stress and/or abused drugs in the adolescence (2 hit), namely "two-hit hypothesis". Therefore, we investigated to develop new model animals for mental disorders which have neurodevelopmental impairment in relation to genetic and environmental factors. We focused on DISC1 as a genetic factor and viral infection or social isolation as environmental factors based on clinical backgrounds. In this presentation, I would like to introduce our model animals which show face, construct and predictive validities.

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