「統合失調症の分子異常に対する発達神経科学的解析法の構築と評価技術の開発」

Development of Neurodevelopmental Analyses and Molecular Markers for the Pathogenesis and Pathophysiology of Schizophrenia

西川　徹

東京医科歯科大学大学院医歯学総合研究科精神行動医科学分野
教授，医学博士

1977 年東京医科歯科大学医学部卒業。1985 年同大学院医学研究科修了（医学博士）。国立精神・神経センター神経研究所室長（1987 年）・部長（1994 年）を経て，1999 年より現職。

NISHIKAWA, Toru, MD, PhD

Professor, Division of Psychiatry and Behavioral Sciences, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University

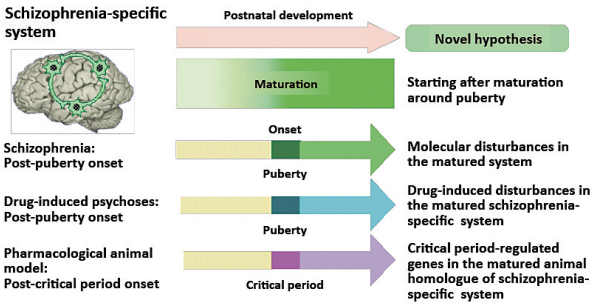
1977 Graduated from Tokyo Medical and Dental University, Faculty of Medicine. 1985 Completed the Doctoral Course in Medical Sciences in Tokyo Medical and Dental University. 1987 Section Chief, National Institute of Neuroscience, NCNP. 1994 Director, National Institute of Neuroscience, NCNP. 1999- Professor, Tokyo Medical and Dental University.

■ 研究内容

統合失調症と，そのモデルである特定の薬物による精神症状や動物の行動異常は，一定の発達段階（ヒトでは思春期）以降に出現するため，この時期を，本症で特異的に障害される神経回路および動物の相同回路が機能的に成熟する臨界期と捉えることができます。本研究では，この臨界期前後で基礎的発現や統合失調症様症状発現薬への応答が変化する遺伝子を同定することにより，本疾患の分子機構の理解と分子マーカー開発を目指します。

■ Research works

In this mission, to get further insights into the molecular basis of the novel diagnosis and treatments for schizophrenia, our research team will intend to explore “the social brain markers” associated with maturation of the specific social behavior that is disturbed in schizophrenia from the pharmacological and developmental views. The schizophrenomimetic actions of dopamine agonists and NMDA type glutamate receptor antagonists may be explained by the possibility that these drugs disturb the molecular and cellular equipment in an information processing system or neuron circuit that specifically malfunctions in schizophrenia. Although the exact causative mechanism for schizophrenia remains unclear, the pathophysiological changes in the information processing system might be associated with the development-dependent nature of schizophrenia and a schizophrenomimetic-induced mental symptoms. Thus, the onset of schizophrenia typically occurs after adolescence. It has been consistently reported that schizophrenomimetic drugs often induce psychotic symptoms in adults, but not in children. In experimental animals, the psychotomimetic effects of dopamine agonists and NMDA receptor antagonists have also been observed after the critical period around postnatal week three. The late-developing features of schizophrenia and its pharmacological models indicate that maturation of the specific neuronal systems could be required for their onsets. The hypothetical human system and its animal homologue should contain molecules that are responsive to the schizophrenomimetic drugs only after the adolescence and the critical period for the animal model of schizophrenia. We therefore will focus our efforts on seeking such critical period-regulated genes and on clarifying their expressional and/or genomic features to obtain candidates for “the social brain markers”



図：統合失調症の発達神経薬理学的仮説

Fig. The new developmental and pharmacological hypothesis of schizophrenia for the present mission