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## **President's lecture**

### **Psychiatry to Bridge Human, Mind, and Brain: Beyond Time and Current Matters**

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## **Abstract**

There are more than a hundred psychiatric societies due to the wide range of psychiatry and the variety of subjects and problem-solving approaches. At the 115th Annual Meeting, I focused on the fact that the Society plays an important role as a core academic society, and sought to find a way for experts in a wide range of fields to participate with a "mind of proactive involvement."

The theme of this meeting is "Psychiatry to bridge human, mind, and brain: Beyond time and current matters." In Japanese "toki" of the "toki-wo koete" (beyond time) has multiple meanings, such as time, unlocking secrets, and the name of the Japanese crested ibis. It is infused with a message that signifies an unraveling of the mysteries of the functions and afflictions of the heart and mind, moving beyond the crested ibis, the symbol of Niigata. We take it for granted that people exist in a biopsychosocial realm. In addition to people's existence as biological entities, we also have a psychological presence complete with a complex mind, our greatest features that differentiate us from other creatures. We form an extremely complex society, where we can share "meaning" and "information" by acquiring the ability to shift from a "sense of recognizing differences" to "recognizing similarities by closing our eyes to differences(assimilation)" and where we emphasize the importance of this pursuit. As social beings, people influence society, while also simultaneously being greatly

affected by society. As experts, we develop responses to medical issues that appear in the "mind". However, in order for us to properly deal with problems of the "mind", we must understand this phenomenon well and enrich our understanding of the functions of the "brain", which forms this base. It is extraordinarily difficult to shed light on this phenomenon, but we must move beyond. I wish psychiatry focused more on each "person" as a whole and not as a reductive understanding and connected the "mind" and "brain" with the "person" playing a leading role, trying to aim at medical care with an understanding of that person's life experiences and value.

Based on this feeling, in the Chairman's lecture, I first outlined the progress of psychiatry and the transition of psychiatric diagnostics over the past two centuries. The introduction of the international diagnostic system is said to have improved reliability and promoted the progress of treatment and biological research. On the other hand, there is an increasing lack of recognition that the current system is only a tentative one in the process of development. I discussed the problem of poor understanding of symptoms and diseases and proposed measures to improve them.

Various findings that elucidate the etiology and pathology of mental illnesses have been reported to deepen its understanding. However, the understanding of the connection between all the levels starting from the genetic level to the functions of the mind is not sufficient. I believe that the understanding of such a multi-layered system that forms the "mind" is most important in 21st-century psychiatry.

Next, advances in psychiatric treatment have brought about standardization and optimization of drugs and psychosocial treatments, enabling many patients to live in society, while the QOL reduction and physical risk due to side effects of drug therapy have drawn attention. I introduced the increasing related evidence regarding this issue.

The progress in medical treatment has also brought about changes in medical needs. The importance of considering the future psychiatric medical care system based on accurate prediction and the importance of developing psychiatry in connection with society were pointed out.

**Keywords** : transition of psychiatric diagnostics, etiology and pathology, advances in psychiatric treatment, changes in medical needs, connection with society

## Introduction.

Psychiatry has a broad base, and its many related professional societies are active because of the diversity of its subjects and approaches to solving problems. In preparing for the 115th Annual Meeting of the Japanese Society of Psychiatry and Neurology, we emphasized the fact that this society plays an important role as the backbone of these societies, and sought to create a society in which specialists working on various problems in a wide range of fields can participate with a "spirit of proactive involvement". The term "professional autonomy" was used by Dr. Matsuda, the vice president, in his article 11) in this journal. Dr. Hosoda, the vice president, wrote "Let's talk about our experiences" 5), and this author believes that such a place is the true form of society.

In addition to the conventional general abstracts, this year's meeting has newly established special "review" sections that outline the current status and issues of each organization and theme. We hope that you will make use of this as a place to learn about the themes and results that universities, professional societies, and related organizations are working on, a place to share and exchange opinions about the appeal and problems of each training program, and a place to

provide information to residents.

The theme of the conference was "Psychiatry to bridge human, mind, and brain: Beyond time and current matters." In Japanese "toki" of the "toki-wo koete" (beyond time) has multiple meanings, such as time, unlocking secrets, and the name of the Japanese crested ibis. It is infused with a message that signifies an unraveling of the mysteries of the functions and afflictions of the heart and mind, moving beyond the crested ibis, the symbol of Niigata. In order to respond appropriately to mental problems, it is important to understand the phenomena and to do so, we must deepen our understanding of the underlying brain functions. Even if the path is difficult, we must overcome it. On the other hand, it is not a reductive understanding, but a holistic understanding of the human being, with each individual person playing a leading role.

The 34<sup>th</sup> Annual Meeting of the Japanese Society of Psychiatry and Neurology was held in Niigata in 1935 (it was the 7<sup>th</sup> venue in Japan), as well as the 53rd. This year's meeting will be the third in 63 years. At the 34th Annual Meeting, the name of the society was changed from "Japan Neurological Society" to "Japanese Neuropsychiatric Society" and the

journal was changed from "Journal of Neurology" to "Journal of Neuropsychiatry", a change that is referred to as the "Niigata Revolution". Dr. Ryuji Nakamura, who served as the president of the 53rd Annual Meeting, founded "Folia", the predecessor of the English-language journal "Psychiatry and Clinical Neurosciences (PCN)" with Dr. Michinori Hayashi of Okayama Medical University. Dr. Tadao Kamimura, the president of the 53rd Annual Meeting, made great efforts to reprint "Folia" which had stopped publication after the war and contributed greatly to internationalization.

### **I. Trends in Modern Psychiatry**

In 1910 (Meiji 43), when Japan's modern medical education had just begun, the government-run Niigata Medical College was established here in Niigata and was upgraded to Niigata Medical College in 1922, which became the sixth national university medical school.

At that time, Kraepelin, E. summarized Dementia praecox (premature dementia) in the 6th edition of the Textbook of Psychiatry in 1899 and presented the framework of endogenous psychosis in contrast to manic-depressive psychosis. Additionally, Bleuler, E. proposed the

concept of schizophrenia in 1911, incorporating psychoanalysis and focusing on its cross-sectional symptoms, especially Spaltung (Table). One hundred years back then, in the 19th century, psychiatry in Europe gradually became what it is today. In France, Pinel, P., Esquirol, J. E. D., Morel, B. A., Lasegue, C., and Magnan, V. J. J. appeared, and in Germany, Griesinger, W., Kahlbaum, K. L., Hecker, E, and others emerged to examine the characteristics of various forms of psychosis and clarify the contours of the disease. It is noteworthy that there was no concept corresponding to the current schizophrenia, and that its fragments were viewed in different frameworks. Melancholy described a variety of chronic mental illnesses, different from its meaning used today, and mania meant an acute onset delusional illness. Morel, who was the first to use the term premature dementia, saw it as a process of premature devastation, but he did not see it as a single disease unit as Kraepelin did.

In the beginning, France was the leading country in psychiatry, but gradually it moved to Germany, where the concept of what is now called biological psychiatry took center stage: "Mental disorders are diseases of the brain and should be classified according to their etiology", "but since

that is not yet known, let us classify them symptomatically (Griesinger) or pathologically (Wernicke, K.), or by assumed etiology, symptoms, and course (Kahlbaum and Kraepelin)". Kraepelin's concept of disease dominated the 20th century, and it is not an exaggeration to say that we are still challenging this assumed concept of endogenous disease. In recent years, evidence has emerged to contradict this assumption, and it is time to take a hard look at the problems associated with this assumption.

Definitions of psychiatric disorders that have not yet clarified etiology and pathogenesis are taxonomies of psychological and behavioral phenomena, and few of them describe structural pathology, etiology, biases from physiological norms, or anatomical and physiological symptom presentation that are used in medical disease definitions. Or perhaps it is more accurate to say that although we can detect masses of structural pathology and biases from physiological norms, we do not yet have enough of them to define individual disease states. In essence, we must first challenge this problem. On the other hand, the acquisition of biological and brain science indicators does not undermine the importance of understanding individual psychological and behavioral phenomena.

In the first half of the 20th century, the ideas of Freud, S., Kraepelin, Bleuler, and Meyer, A. were widely accepted in clinical practice, and each of them made their own diagnosis based on their own theories. On the other hand, the need for a common language among psychiatrists arose from the practical necessity of sharing information in clinical practice, medical education, administration, law, and epidemiological, etiological, and therapeutic research. The International Classification of Diseases (ICD) first included psychiatric disorders in ICD-5 in 1938, but only six categories were adopted: alcoholism, mental retardation, premature dementia, manic-depressive illness, psychogenic psychosis, and epilepsy. Later, ICD-6, 7, 8, and 9 were created, and in response, the American Psychiatric Association created the DSM-I and DSM-II, but there were no significant changes here, and it can be considered that they were almost similar.

However, a problem arose here. The diagnostic reliability of ICD-6 and 7, which were supposed to be developed as a common language, was found to be extremely low. As a result, in the 1960s and 1970s, there was a great deal of interest in devising diagnostic categories and evaluating them through empirical studies. A

comparison of diagnoses between the U.K. and the U.S. using patient videos was shocking, revealing a large discrepancy in diagnoses between the two countries, even when the same patient was examined. The PSE/CATEGO, St. Louis diagnostic criteria, RDC, etc. were developed, but the most notable was a series of studies called the IOWA500 by a group at the University of Iowa. In this study, the reliability and validity of diagnoses, family history, suicide, and outcomes for each disease were examined and clarified one after another. The results themselves were new, but the impact of the ability to collect useful information on mental illness in this way must have been even stronger.

The creation of the DSM-III in 1980 led to the widespread use of operative diagnostic criteria, but, due to space limitations, I will not go into the basic philosophy of the DSM, the history of the DSM, or the misconception that "what the diagnostic criteria define is the disease", and suggestions for dealing with this misconception. For more details, please refer to 6)13)17) in my book. In addition to "assuming the ideological type of the disease encompassed in the diagnostic criteria", it is important to emphasize the viewpoint of "human understanding": even if a diagnosis is given by correctly applying the DSM, it

does not mean that the true reality of the patient is understood. We must not forget that psychiatric diagnostics is not only about diagnostic names for disorders or understanding the pathology of the brain, but also about understanding people from multiple perspectives, taking into account the personality and social and environmental background of each patient. This is the reason why we have chosen "people" as the first word in the theme of this year's Annual Meeting.

## **II. Development of Biological Psychiatry Research: An Example of Schizophrenia Research at Niigata University**

I would like to consider recent developments in psychiatric diagnostics, using the activities of Niigata University as an example.

Three research approaches have been taken for schizophrenia (Fig. 1).

In genome research, genome-wide association studies have been conducted to identify risk single nucleotide polymorphisms (SNPs) with common allele frequencies but small effect sizes, while whole-exome sequencing studies have been performed to detect risk variants with rare allele frequencies but large effect sizes. In a Japanese collaborative study 7), we conducted a genome-wide

association study that comprehensively analyzed SNPs and demonstrated a genome-wide significant association between an SNP in the *NOTCH4* gene and schizophrenia. In addition to innovations in genome analysis technology, the development of diagnostics has been the primary reason for the ability to conduct large-scale collaborative studies involving approximately 6,600 patients. The problem is that the degree of risk is small and whether this is due to the nature of the risk itself, or rather the clinical phenotype defined in the current diagnostics, needs to be further examined.

Similarly, the identification of risk variants that are rare but have a high relative risk is also an important issue. We performed whole-exome sequencing of a multiplex schizophrenia family 2) and showed that a rare missense mutation in the *UNC13B* gene was found in 5 of 6 affected individuals, but not in 8 unaffected individuals and one individual with unknown disease status.

We have also conducted postmortem brain studies and animal model studies in collaboration with Brain Research Institute, Niigata University. In postmortem brain studies, we found abnormalities in the expression of neurotrophic factors and cytokines, including increased brain-derived

neurotrophic factor (BDNF) in the anterior cingulate cortex and hippocampus 24) and increased interleukin (IL)-1 $\beta$  to IL-1RA (receptor antagonist) ratio in the prefrontal cortex 26). In addition, we have reported that animals treated with cytokines during the neonatal period exhibit schizophrenia-like behavioral characteristics after sexual maturation. Based on the results of these postmortem brain studies and animal model studies, we proposed the "cytokine hypothesis of schizophrenia" in Psychiatry and Clinical Neurosciences, which postulates that abnormalities in cytokine signaling are involved in the pathogenesis of schizophrenia 29). In 2018, the Niigata University School of Medicine and the iPS Portal signed a collaboration agreement and planned to conduct research using iPS cells for elucidating pathogenesis and developing treatments.

In addition, we have been engaged in clinical research to link the results obtained from basic research to the development of new diagnostic and therapeutic methods. In order to develop a blood test kit for schizophrenia, we conducted gene expression analysis using a DNA microarray with approximately 55,000 probes 25). By using neural network analysis, we extracted 14 probes for the



classification prediction model and showed that the prediction model could discriminate with high accuracy of 82.4% sensitivity and 93.8% specificity. If such a blood test kit is put to practical use, it will be useful in supporting the early diagnosis.

### III. Toward Multilayered and Comprehensive Pathophysiological Research: The Case of Neurodevelopmental Disorders

In order to elucidate the pathogenesis of neurodevelopmental disorders, we have aimed for a more multilayered and comprehensive research strategy (Fig. 2). In other words, we are trying to understand the various layers that make up symptoms and brain functions in a multilayered manner. Here, we introduce the results of studies on brain regions, genes, and brain circuits.

First, in a study of brain region exploration 3), the ratios of N-acetylaspartate to creatine (NAA/Cr), an index of neurodevelopmental maturity, were measured using magnetic resonance spectroscopy (MRS) and compared between the typical and impaired neurodevelopmental groups for each disease type. The correlation between symptom intensity and NAA/Cr values indicated that autism spectrum disorder (ASD) is associated with impaired neurodevelopment in the

amygdala and that the more severe the disease type and symptoms, the worse the neurodevelopment.

At the genetic level, we analyzed the entire exome of families with three ASD patients and identified a missense mutation in the gene CLN8 1). We focused on this gene and resequenced the exonic region of CLN8 in approximately 300 ASD DNA samples from our laboratory, and identified several mutations that are more frequent in patients than in typically developing individuals.

Using Japanese macaques, we experimented to investigate the "theory of mind", a function to infer the state of mind of others that is different from the facts, which is considered to be a core symptom of ASD 4). We measured the direction in which the monkeys first looked when shown a video of a non-verbal task, and whether they could correctly infer the mind of the character in the video.

The results showed that the monkeys significantly looked in the direction of the video when they could correctly infer the mind of the character in the video, which was different from the factual situation. We also found that the tendency to infer the mind of a character in a movie was abolished when a ligand was injected to activate hM4Di receptors, an inhibitory DREADD (designer receptors



exclusively activated by designer drugs), that had been virally expressed in Brodmann's area 9 of the medial prefrontal cortex. This suggests that Japanese macaques have a theory of mind and that the medial prefrontal cortex may be part of this brain circuit.

In the future, it will be necessary to develop a multilayered understanding of what genetic abnormalities give rise to abnormalities at the protein and synapse levels, and how these form abnormalities in brain regions, brain circuits, and cognition and behavior, as well as a structural understanding of pathogenesis. This is the most important issue for psychiatry and brain science in the 21st century.

#### **IV. Importance of therapeutic research**

I would like to introduce a section of Dr. Shigenobu Kanba's article 8) in this journal.

Although problems such as small effect size and large variance still need to be overcome, there has been recognition that "mental illness is a medical illness and psychiatry is a branch of medicine".

The creation of innovative technologies will lead to a breakthrough in our understanding of the neural basis of mental illness.

There is no guarantee that schizophrenia, bipolar disorder, obsessive-compulsive disorder, panic

disorder, PTSD, etc. will not be classified in the chapter on neurological disorders. We may encounter claims that schizophrenia can be treated by non-psychiatrists. The only thing that determines the validity of such a claim is the judgment of who can provide the best treatment.

The ability to properly diagnose and properly treat patients is the most important and the greatest strength of psychiatrists, and that is why we must also promote research that is useful for clinical practice. This is discussed below.

In Niigata Prefecture, we predicted that the number of inpatients with schizophrenia, which was 4,337 in 1990, would decrease to 2,355 over the next 40 years (Fig. 3) 14). This corresponds to a nationwide decrease from 210,000-220,000 people to 120,000 people. This estimate was made between 2000-2003, but 16 years have passed since then, and the number of schizophrenic patients has actually decreased almost as much as or more than the estimate. This means that we have reached the eighth stage of the change, where the number of schizophrenic inpatients will decrease to more than 50% over about 40 years.

From the national data (Fig. 4) 16), we can see that the ratio of 20,000 schizophrenics (right axis) to 7,000 hospitalized patients (left axis)

continued to overlap nicely. In other words, there was a generation and an era in which 35% of people with schizophrenia were hospitalized across the board; the gap began to widen after 1953, and by the time we were born in 1958, only 20% of people with schizophrenia were hospitalized, and the second baby boomers, who were 15 years younger than us, were hospitalized only about 10% of the time.

The driving force behind this was the discovery of chlorpromazine in 1952, which led to the development of antipsychotic treatment, psychiatric drug therapy, and a growing awareness of community support. More than 60 years have passed since the development of antipsychotics, and many patients are now able to live in the community. While this is a major contribution of psychiatric drug treatments, a new problem has emerged in the past decade or so: the shortening of life expectancy of patients with schizophrenia. The analysis of survival at age 15 (Fig. 5) 10) shows that the survival curve for both males and females is quite steep for schizophrenia from a young age, compared to the survival curve for the general population, which is gradual until age 60. Since bipolar disorder is shown as the curve between green and orange, it means that schizophrenics

lost a total life span of the combined space shown in green and orange, which was 18 years for men and 16 years for women.

This was found to be due to an increase in cardiovascular disease, and one of the reasons for this disease is the effects of psychotropic medications on the heart, causing prolongation of the QT interval and, in some cases, fatal arrhythmias. In our study 27), we examined the diurnal variation of the QT interval between risperidone and olanzapine groups and a control group and found that there was an inter-drug difference in the QT interval prolongation depending on the drug. Attention to this problem of drug-induced QT prolongation may reduce the risk of death.

Another route of cardiovascular mortality risk is metabolic syndrome (MetS), in which obesity and abnormalities in glucose and lipid metabolism lead to atherosclerosis and death from ischemic heart disease such as myocardial infarction. The relationship between fasting blood glucose and 2-hour blood glucose in patients with schizophrenia undergoing treatment was investigated 12). The results showed that 3 out of approximately 250 patients, or 1%, showed borderline values in fasting, while 3.1% were diabetic and 18.4% borderline, for a total of 21%, of 100

patients with 2-hour blood glucose intolerance. Of the 100 patients, 21% were found to have impaired glucose tolerance. Comparing the glucose tolerance of the antipsychotic group with that of the control group, which was limited to patients with no abnormalities in fasting blood glucose, it was clear that the glucose levels in the group taking antipsychotic medication remained high, resulting in excessive insulin secretion 19). We psychiatrists should pay more attention to these abnormalities in glucose metabolism.

On the other hand, the phenomenon of reactive hypoglycemia induced by second-generation antipsychotics (SGAs) in non-diabetic schizophrenic patients was discovered and published in the BMJ, sounding the alarm 23). They also published the finding that the HDL cholesterol level, which is considered to be good cholesterol, was significantly lower in the group taking SGA than in the control group, indicating the importance of properly monitoring these levels 28).

## **V. Joint Project on Antipsychotic Treatment and Physical Risk**

In cooperation with the Japanese Association of Psychiatric Hospitals and the Japanese Society of Clinical Psychopharmacology, we launched a joint project to conduct a nationwide

survey on antipsychotic treatment and somatic risk to raise awareness among medical staff. In this project, we received a large number of case data, and an analysis of the data revealed that the risk of MetS was high in outpatients according to all MetS criteria 21). However, even in hospitalized patients, we found that the risk of MetS was low in the elderly, but high in young men, and it is important to accumulate these characteristics and findings and apply them to clinical practice.

In addition, an intervention study was conducted with 265 patients from hospitals across the country, including physicians and dietitians, in which patients were divided into groups based on their physical risks for obesity and MetS 22). These three groups were then again divided into three groups: a group that received feedback after weight measurement by writing it in a notebook, a group that received weight measurement and nutritional guidance, and a group that received nothing.

Intervention and evaluation were conducted and more than 70% completed the follow-up. The results showed that the intervention was effective, with significant weight loss and BMI reductions in the weight measurement and nutritional guidance group, and a clear reduction in MetS

incidence only in the weight measurement and nutritional guidance group. Only the group with a 7% weight loss and the group with a 5% weight loss, which are considered clinically significant weight loss, showed a clear improvement.

On the other hand, there is another serious physical risk among hospitalized patients: being underweight 20). The problem is that as many as 8% of hospitalized patients meet the weight criteria for neuroleptic emaciation. Further research is needed to elucidate the pathogenesis of this problem and to find effective treatments.

The results of these joint projects were summarized, and recommendations were made 18). In the future, it will be important for psychiatric staff to address this issue, and this series of physical risk studies can be summarized as follows.

The advent of first-generation antipsychotics (FGAs) has led to dramatic advances in the treatment of schizophrenia, and the change in model to SGAs is said to have led to further advances. However, the life expectancy of patients with schizophrenia is about 15 years shorter, cardiovascular mortality is about twice as high as in the general population, and the risk of sudden cardiac death is higher in patients taking SGA than in those

taking FGA, suggesting that the high prevalence of MetS is one of the reasons for the high cardiovascular mortality in patients with schizophrenia. How to protect patients from such life- and health-threatening risks is a major concern in clinical psychiatry.

## VI. Through Disaster Psychiatry in Niigata

Finally, I would like to mention disaster psychiatry. Niigata has experienced major disasters over the past century. In the 1964 Niigata earthquake, the number of cases hospitalized due to the shock increased, and the hospital rooms were overcrowded. In the 2004 Niigata-Fukushima torrential rain disaster, the Department of Psychiatry at Niigata University conducted organized activities for the first time. Since then, whenever there is a disaster in Niigata, the university, public hospitals, private hospitals, and nursing, psychology, and social work organizations unite to respond to the disaster, and a system called the "Council for Mental Health Care in Disasters" 15) has been established and is functioning very well. In the same year, the Chuetsu Earthquake occurred, and by utilizing the experience of the torrential rain disaster, the department and related hospitals were able to work together to

respond to the disaster. The know-how of the mental health care team at that time has since been utilized in disaster relief activities nationwide. In addition, the assistance style of the Niigata Mental Health Care Center, which was set up to provide support to the community during the recovery period, was used mainly in Miyagi Prefecture after the Great East Japan Earthquake.

After experiencing the Chuetsu-Oki Earthquake in 2007 and establishing the Niigata University Research Institute for Natural Hazards and Disaster Recovery Science in 2011, I realized the need for efficient identification and intensive support of subpopulations vulnerable to disaster stress while engaging in disaster psychiatry and research. In addition to direct support, I have recognized the importance of disaster relief logistics, and am currently working on its implementation in the Niigata University Disaster Medical Education Center.

There is a possibility that various disasters will occur in various places in the future, but the most important thing is to establish a system that can provide necessary support in a timely manner and build cooperative relationships with related organizations. This kind of connection with society is important not only for

disaster psychiatry but also for psychiatry in general.

### **Conclusion.**

This society plays an extremely important role as a core society representing the field of neuropsychiatry. In addition to contributing to the development of psychiatry as an academic discipline, we hope that the society will continue to develop in cooperation with related societies and organizations. The society aims for further internationalization, which will enable participants in the Annual Meeting to learn about the current status and issues in fields other than their specialty, and to disseminate the image of psychiatry and psychiatric care as a benefit to society.

The 115th Annual Meeting of the Japanese Society of Psychiatry and Neurology = session: June 20-22, 2019, Venue: Toki Messe

Basic Theme of the General Assembly: Psychiatry to Bridge Human, Mind, and Brain: Beyond Time and Current Matters

President's lecture: Psychiatry to Bridge Human, Mind, and Brain: Beyond Time and Current Matters  
Chairperson: Shigenobu Kamba (Department of Psychiatry, Kyushu University Graduate School of Medicine)

## Opposite interests

Companies with COI relationships that should be disclosed in relation to this paper

Asahi Kasei Pharma, Astellas Pharma, AbbVie LLC, Abbott Japan, Eisai Co. Ltd., Taisho Pharmaceutical Co., Ltd., Dainippon Sumitomo Pharma Co., Ltd., Takeda Pharmaceutical Company Limited, Mitsubishi Tanabe Pharma Corporation, Tsumura Corporation, Eli Lilly Japan K.K., Novartis Pharma K.K., Pfizer K.K., Mylan EPD G.K., Meiji Seika Pharma K.K., Mochida Pharmaceutical Co. Ltd., Mochida Pharmaceutical Co.

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表 精神医学の歴史的背景

ドイツ	Kraepelin, E. (1856~1926) : 1899 年 早発性痴呆と躁うつ病 Bleuler, E. (1857~1939) : 1911 年 精神分裂病 (統合失調症)
フランス	Pinel, P. (1745~1826) 「鎖からの解放」 la manie, la melancolie, la demence, l' idiotisme Esquirol, J. E. D. (1772~1840) melancolie を lypemanie と monomanie に分けた 後天性のものを demence, 先天性のものを idiotisme とした Morel, B. A. (1809~1873) demence precoce (早発痴呆) Lasegue, C. (1816~1883) 被害妄想病 Magnan, V. J. J. (1836~1916) 系統的に発展する慢性妄想病
ドイツ	Griesinger, W. (1817~1868) 「精神病は脳の病気である」 Kahlbaum, K. L. (1828~1899) 緊張病 Hecker, E. (1843~1909) 破瓜病

Table 1. Historical background of psychiatry

#### Germany

Kraepelin, E. (1856-1926): 1899 Premature dementia and manic depression

Bleuler, E. (1857-1939): 1911 Schizophrenia (schizophrenia)

#### France

Pinel, P. (1745-1826): "Freedom from chains"

La manie, la melancolie, la demence, l'idiotisme

Esquirol, J. E. D. (1772-1840).

Divided melancolie into lypemanie and monomanie

The acquired type are called demence and the congenital type idiotisme.

Morel, B. A. (1809-1873) Demence precoce (early onset dementia)  
 Lasague, C. (1816-1883) Paranoia  
 Magnan, V. J. J. (1836-1916) Chronic delusional disease with systematic development  
 Germany  
 Griesinger, W. (1817-1868) "Mental illness is a disease of the brain"  
 Kahlbaum, K. L. (1828-1899) Catatonia  
 Hecker, E. (1843-1909) Breakthrough disease

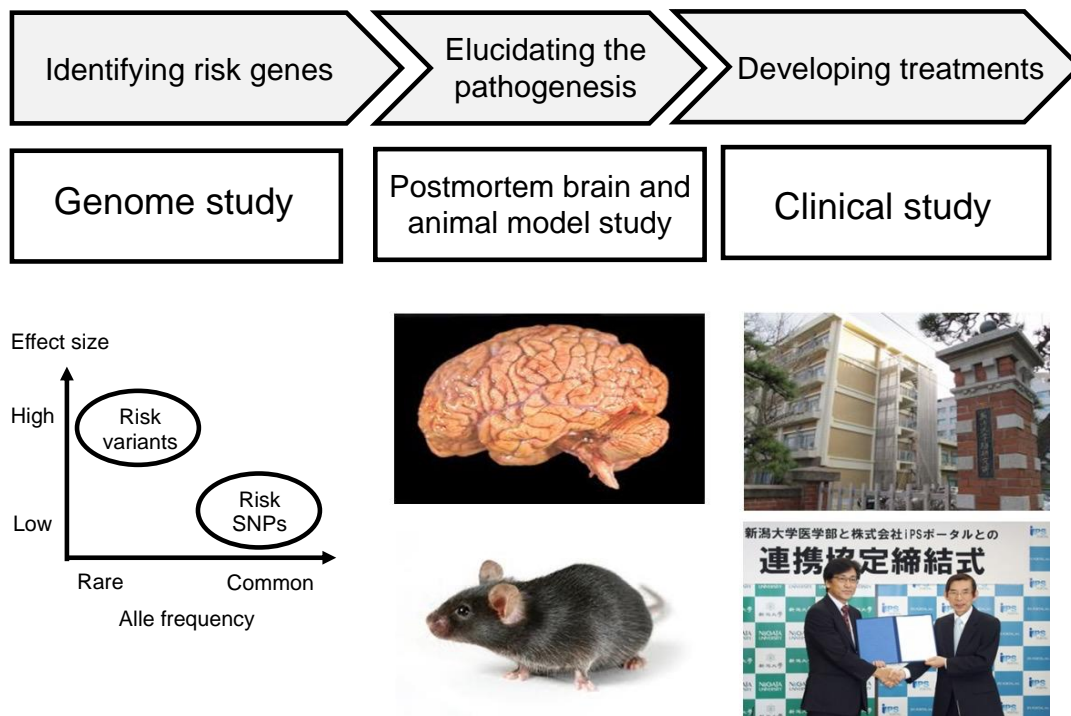


Figure 1. Schizophrenia research approaches

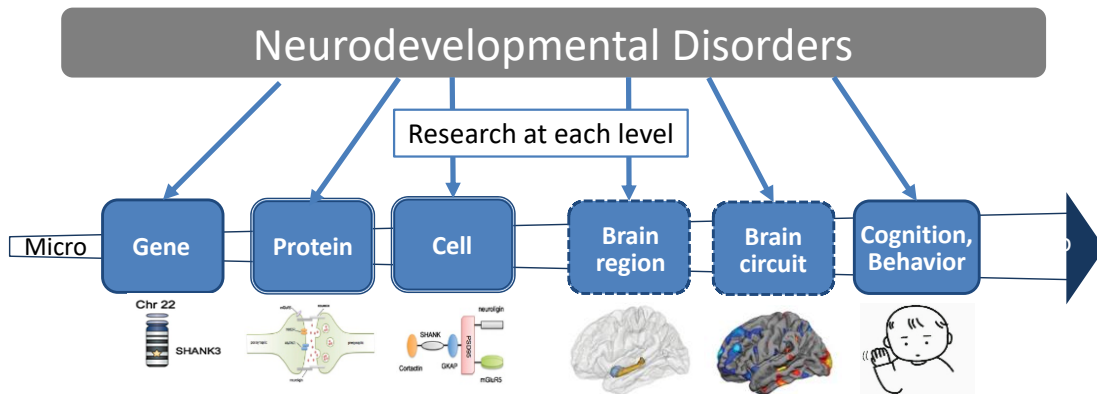


Figure 2. Strategies for understanding the pathogenesis of neurodevelopmental disorders

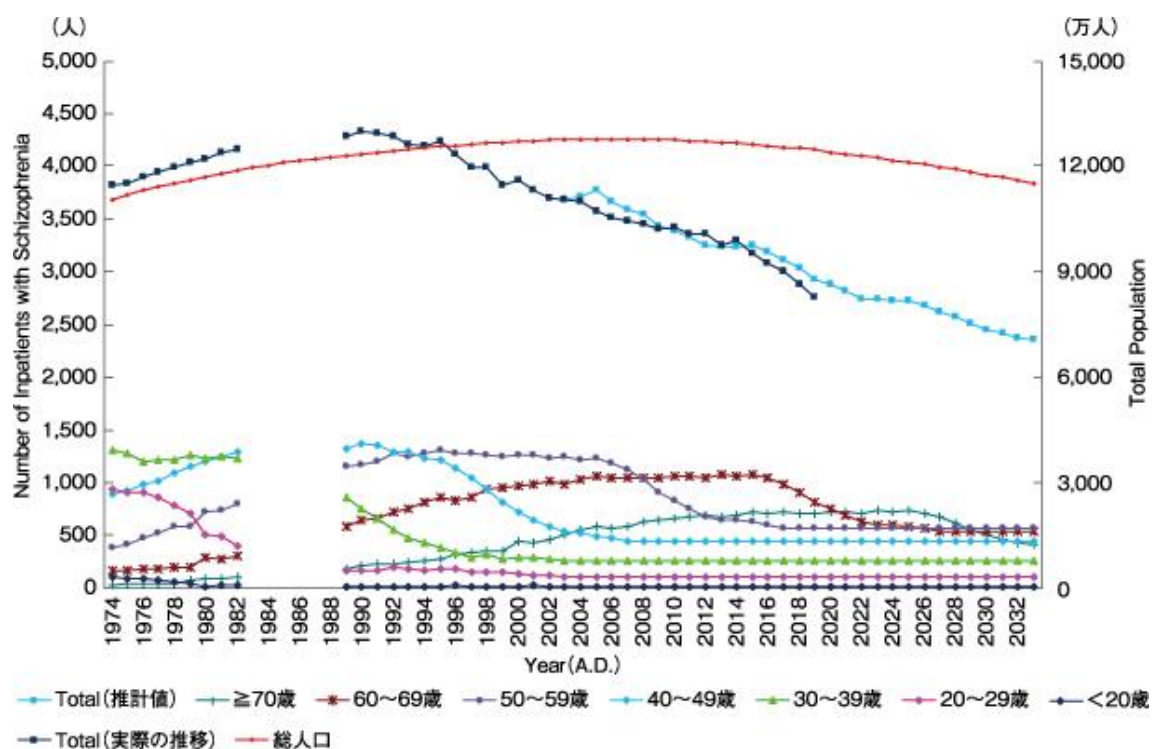


図3 統合失調症による在院患者数の上方予測

1974年から2003年までの年代別統合失調症在院患者数推移をもとに、2004年以降の在院患者数を推計した。水色が2004年以降の合計患者数推計値、濃い青色が実際の推移を示す。1983年から1988年は調査が行われなかった。(文献14より引用)

Figure 3. Upward projection of the number of patients hospitalized for schizophrenia

The number of patients with schizophrenia in hospitals after 2004 was estimated based on the change in the number of patients with schizophrenia by age from 1974 to 2003. The light blue color indicates the estimated total number of patients after 2004, and the dark blue color indicates the actual trend. (Adapted from Reference 14)

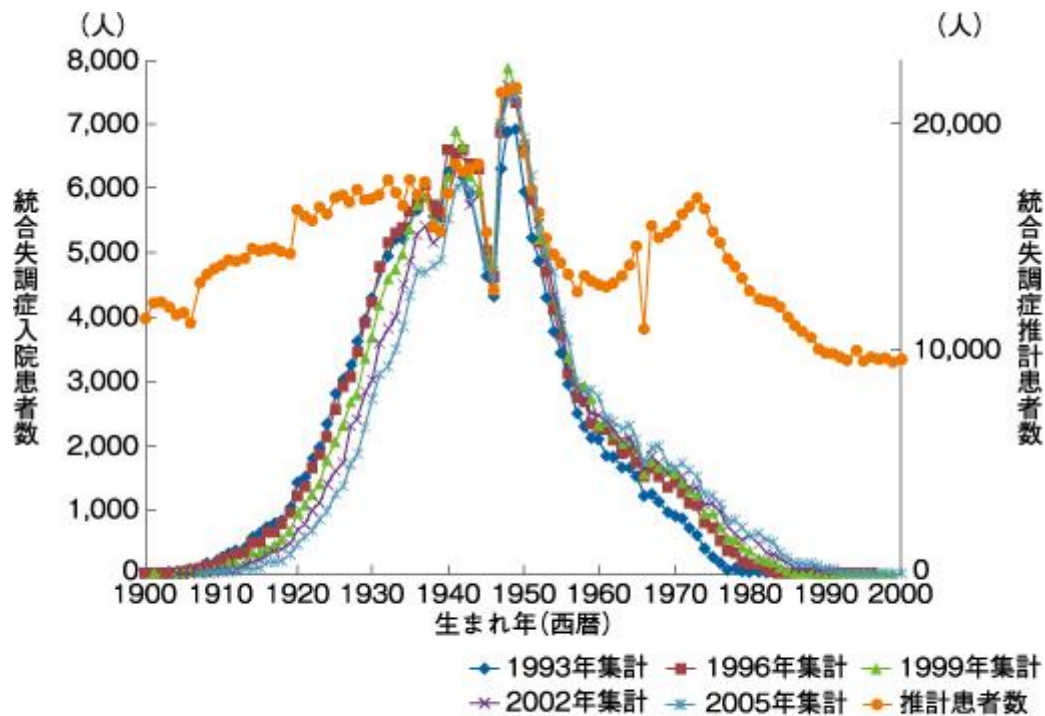


図4 統合失調症入院患者の生まれ年分布  
各集計年度の統合失調症入院患者数と統合失調症推計患者数  
(文献16より引用)

Figure 4. Year of birth distribution of schizophrenia inpatients  
Number of inpatients with schizophrenia and estimated number of patients with schizophrenia in each year of aggregation.  
(Taken from Reference 16)

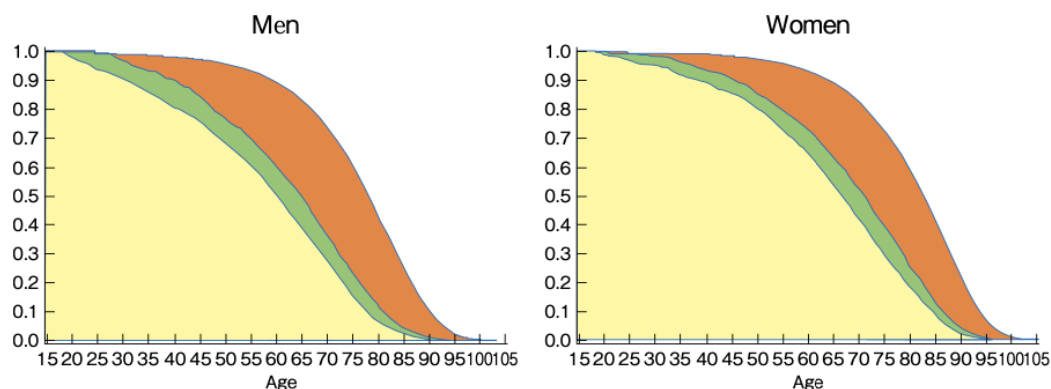


図 5 Life expectancy among persons with schizophrenia or bipolar affective disorder

The yellow area is the expected age at death for persons with schizophrenia, the green and yellow area is the expected age at death for a bipolar cohort member. Total area (yellow, green, orange) under the survival curve is the expected age at death for the psychiatric disease free cohort members. (文献 10 より引用)

Figure 5. Life expectancy among patients with schizophrenia or bipolar affective disorder

(Taken from Reference 10)