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President's lecture

40 Years of History as a Psychiatrist

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Abstract

The 117th Annual Meeting of the Japanese Society of Psychiatry and Neurology was held for three days from September 19 to 21 in 2021 at the Kyoto International Conference Hall. It was held three months later than originally planned because of the COVID-19 pandemic. It was the first time in 33 years since Dr. Masami Saito, my predecessor, last hosted the meeting at the Osaka International Exchange Center in 1988. Featuring the themes of "High-quality Psychiatric Medicine Created by Innovation and Tradition," we organized the program consisting of the three pillars of the "Latest Knowledge in Brain Science," "Footsteps of the Giants Who Have Built Psychiatric Medicine," and "Psychiatric Medicine and Arts." We were very pleased that 1,000 members on average per day visited this meeting at that time when the pandemic of COVID-19 was temporarily stabilized at a lower level. Through on-demand streaming, a total of 8,800 members participated in the meeting before it ended at the end of November. In the presidential address, titled "40 Years of History as a Psychiatrist," I gave a talk about my personal history. I was born in Hirano, a historical town in the southern part of Osaka City. Many merchant families in Osaka would squander their fortune to ruin, and my house followed the same fate. Such an environment, I believe, bestowed the affinity for madness in me. During my most impressionable middle-to-late teen years, I was absolutely fascinated with Yukio Mishima, John Coltrane (a jazz super star), Takehiro Honda (a jazz pianist), and the European Catholic arts. What is common

among them, I think, is some sort of madness. This kind of affinity for madness led me to the world of psychiatric medicine. After joining the department of psychiatric medicine, I obtained a degree in the field of electroencephalography, and then studied at the University of Zurich, which made me interested in the electroencephalographic study in patients with schizophrenia and the arts they created, Art Brut.

At the time I joined the department, there was still strongly rooted prejudice against the psychiatric department. However, this department has undergone the most drastic changes in the past 40 years. Psychiatry has become necessary for all generations, both men and women, and must be learned as a part of residency program. While it may be natural to happen, this change cannot help but make me astonished. It has become clear that mental disorders often occur in young people, tend to last for a long period, and cause substantial economic losses, resulting in mental disorders becoming among the top diseases to overcome. In light of this, we are currently conducting research focusing on the discovery of precision medicines for the treatment of mental disorders.

Keywords: EEG, LORETA, Art Brut, precision medicine

Introduction

The 117th Annual Meeting of the Japanese Society of Psychiatry and Neurology was held at the Kyoto International Conference Center for three days from September 19 to 21, 2021, with a change in schedule. The theme of this year's Annual Meeting was "Precious psychiatry bridging between tradition and innovation." The marked impact of the novel coronavirus (COVID-19) has, of course, brought unprecedented changes to all aspects of social life. This pandemic spread around the world rapidly, at a speed that we have never experienced. The impact on society is likely to be no less significant

than the damage caused by war. The impact on psychiatry, which was previously not given much consideration, is also becoming very significant. We would like to have a wide-ranging discussion from a psychiatric perspective not only about the challenges that humanity, which has created a global world, has not experienced to date, but also about how to respond after such a crisis. This annual meeting is divided into three main categories: "The Latest Findings in Neuroscience," "The Footsteps of the Giants Who Built Psychiatry," and "Psychiatry and the Arts" in the 19th and 20th Centuries. We have put

together a wide-ranging program, with the theme of the conference being to weave together tradition with innovation as the warp and weft. This is the first time in 33 years that Kansai Medical University has hosted the conference, since the previous conference held at the Osaka International House Foundation in 1988 by the previous president, Professor Masami Saito. As the President's lecture, I will talk about my career as a psychiatrist over the past 40 years since graduating from university in 1981, with a focus on the relationship with art, and I hope that it will be of some help to young psychiatrists.

I. Upbringing

I was born in 1957 in the town of Hirano in Osaka. My father ran a textile company. My mother helped my father with the company and also brought up the children. I had an older brother and older sister, with 13- and 9-year age differences, respectively, making me the youngest in the family. Given the significant age differences among us, I essentially grew up as an only child.

The town of Hirano has a long history, having existed since the Heian period, but from around the 16th century it became a city surrounded by a moat and run by the self-government of its citizens. From 1592, it became the fief of O-ne (also known as Kita-no-mandokoro,

Kodai-ji), the legal wife of Toyotomi Hideyoshi, and during the Tokugawa period, it was the fief of a retainer of the shogunate (Osaka Castle Governor, Kyoto Governor) from 1713 until the Meiji Restoration.

In his diary entry for January 20th, 1584,⁴⁾ the Jesuit missionary Luis Frois wrote: "There is a beautiful village beyond Sakai, surrounded by bamboo like a castle. It is called Hirano. ... People who were very rich lived here, but Hashiba sent a messenger to ask them to move to Osaka in order to make the town even more prosperous."

My great-grandfather made his fortune in cotton and made a home near the Nagare-machi exit in the Hirano district, as shown in Figure 1, at the end of the Edo period. He did not provide his children (it seems that the girls died young and only the boys grew up) with an education, and may have squandered his fortune (in a kind of madness) to the extent that he lost most of his wealth. He may have had a strong sense that a man's worth was measured by his ability to consume alcohol, engage in gambling, and make purchases. As a characteristic of Osaka merchants, many of them adopted a son-in-law as a son to continue their business. My grandfather was no exception, and he lived his life in accordance with the ideal of a man's worth, but in the end he contracted neurosyphilis and died in a

mental hospital. This was about 10 years before I was born.

The reason why I was drawn to the fascinating world of psychiatry and set foot in it was probably due to the influence of the town of Hirano, which was full of madness. I think there was a predisposition in me, something like an affinity for madness at the genetic level. Then, when I was in the second year of junior high school, there was the seppuku (ritual suicide) of Yukio Mishima, and after that I was drawn into his world of esthetics, and in high school I was captivated by the jazz giant John Coltrane. His famous song “A Love Supreme” is like a hallucinatory experience. After entering university, I was captivated by the extremely powerful and frenetic performances of fellow jazz pianist Honda Takehiro. At the time, the liberal arts program for medical students lasted for two years, so I had a lot of free time. I traveled to Europe during my long summer vacation and became fascinated by Catholic art. The overwhelming presence of churches as places of healing in the history of religious oppression in the Middle Ages was majestic. I was particularly moved by the pensive expression of Filippo Lippi's “Madre Pia (Devout Virgin).” I think that what these four artists had in common was a kind of madness. I feel

that my own affinity for this kind of madness led me to psychiatry.

II. Entering the Department of Psychiatry

I participated in clinical training in psychiatry as a sixth-year university student, and although it is true that there were no other departments that interested me, I decided to enter the Department of Psychiatry without hesitation. This was in 1981, when Dr. Shigekazu Okamoto was the professor. He specialized in epilepsy, and many patients with intractable epilepsy came to the hospital. Of course, EEG testing was essential, so I learned the ABCs of EEG from Dr. Masami Saito, who was a lecturer at the time. He studied under Professor Itil, T. M., who was famous for his work on quantifying EEG (at the University of Missouri), and learned techniques that made full use of the most advanced computer technology. He introduced these techniques to Japan and made quantitative electroencephalography (qEEG), which measures the central effects of psychotropic drugs, his area of specialized research. I also studied quantitative electroencephalography (qEEG) under the guidance of Dr. Saito. At the time, we used a relatively simple method of quantifying spontaneous EEG using Fourier transformation and plotting the power of each EEG band

using t-tests. I submitted a paper, entitled: “A Quantitative Electroencephalographic Study of Nootropics”¹⁴⁾ to the *Psychiatria et Neurologia Japonica* and received my degree. Although I discovered the antidepressant effect of mianserin using qEEG, qEEG did not lead to the discovery of new drugs with unknown effects after that, and I came to understand the limitations of qEEG.

III. Study Abroad

After obtaining my degree, I strongly hoped to study abroad, especially in Europe. My experience of traveling around Europe as a student was the source of my enthusiasm for studying abroad later on. I had a particular longing for France and Italy. I had always liked the novels and essays of French literary scholars such as Tsuji Kunio, Endo Shusaku, and Mori Arimasa, and had been strongly influenced by them since my junior high and high school days. My trip to Europe when I was a first-year university student was also influenced by French literature. I remember how much I enjoyed just walking around the streets of Paris. Unfortunately, however, it was impossible to go to a Latin country for EEG studies. EEG was discovered by the German Berger, H., and developed in German-speaking countries. In 1992, Professor Lehmann, D., of the

University of Zurich's Department of Neurology, who was famous for his EEG mapping, was attending the International College of Neuropsychopharmacology (CINP) held in Nice, France. I expressed my desire to study abroad at that time, and he kindly agreed to facilitate this. With the aim of quantitatively capturing more dynamic EEG changes, I had the opportunity to study abroad at the University of Zurich the following year, in 1993. Zurich is a wonderful city with clean streets and good public safety, and I was able to enjoy living in Europe to the full. Professor Lehmann had developed very unique methods for the analysis of spontaneous EEG, such as the FFT dipole analysis and microstate analysis methods, and he was passionate about elucidating the changes in the central nervous system caused by psychotropic drugs¹⁵⁾²⁹⁾ and the pathophysiology of mental illnesses, particularly schizophrenia. The microstate analysis method used electroencephalograms recorded at a sampling rate of 128 Hz at the time, so it is a method that captures changes in the electroencephalogram every 7.8 msec as a potential map. Global Field Power (GFP), a superior indicator, is used to cluster maps taken every 7.8 msec and summarize the data into 4 or 5 prototype maps. One prototype map represents one brain activity, and it was

possible to reduce it to four or five different brain activities. We compared the duration, frequency of occurrence, and order of transition to other prototype maps of each map with those of healthy people. We found that the duration of activity was shorter in patients with schizophrenia than in healthy people, and that transition patterns were also different. We interpreted this as meaning that the time required for the brain to process information was insufficient and deviated in the case of schizophrenia, and considered that this might be related to the appearance of psychotic symptoms such as delusions and auditory hallucinations.⁵⁾¹⁹⁾ In addition, we have also been actively conducting EEG analysis research using low-resolution brain electro-magnetic tomography (LORETA), a technique developed by Dr. Pascual-Marqui, R.D., a Cuban national who was studying in Zurich at the same time.²⁴⁾ The LORETA method is now recognized as a very famous analysis method. It is a very effective method that has made it possible to solve inverse problems, which are theoretically impossible, by reducing the resolution.

IV. Research at the Department of Psychiatry, Kansai Medical University

Recently, network theory, such as the default mode network, has attracted

attention, and I think that interest in electroencephalography is increasing again. I would like to continue to convey to young doctors the wonderful time analysis capabilities and non-invasive nature of EEG, and continue research on the quantification of EEG using the unique analysis methods described above. I am currently the president of the Japan Pharmaco-EEG Society. I am delighted to see that interest in clinical EEG is increasing, as the incidence of epilepsy in the elderly is increasing markedly in clinical practice.

In addition, with the development of mathematical theory, we are now seeing the use of graph theory and independent component analysis (ICA) as a statistical aid. There is also an increasing amount of research combining findings from functional MRI with studies of brain networks, such as the resting state network²²⁾²³⁾ and research combining genetic factors with studies of state evaluation. With the recent advances in the field of brain science, including neuroimaging techniques, it may be that qEEG itself is also a field with potential for development.

In addition, our department is conducting research on depression and mood disorders, led by Associate Professor Masaki Kato.

This research is aimed at so-called precision medicine, which strives to

provide more appropriate treatment for the different biological backgrounds and clinical characteristics of each case. We started a randomized controlled trial (RCT) based study, and over the past 20 years, we have identified genetic mutations, cytokines, miRNAs, and clinical characteristics that may be used as a basis for selecting drugs in relation to treatment efficacy.²⁾⁽⁸⁾⁽⁹⁾⁽¹²⁾ Using existing data, we have conducted patient-level analysis and proposed new subgroups of depression, and based on this, we have proposed optimal doses of drugs. We are also actively involved in meta-analysis⁷⁾; in particular, our work on the exit strategy for antidepressant treatment, which summarizes the turning points for continuing and discontinuing treatment, has attracted a great deal of attention.¹¹⁾ Furthermore, we are actively involved in the Japanese Society of Clinical Neuropsychopharmacology (JSCNP) and Japanese Society of Mood Disorders (JSMD); in JSCNP, we have been involved in the creation of expert consensus documents (depression, bipolar disorder, and schizophrenia), a large-scale survey of bipolar disorder MUSUBI,¹⁰⁾ and JSMD guidelines (depression, bipolar disorder). As the course of mood disorders is important, we would like to continue our research with the aim of providing precision medicine that will improve long-term

prognosis and factors related to the long-term course, such as one or two years, as well as short- and medium-term evaluation.

Furthermore, we are also conducting research related to schizophrenia, led by Associate Professor Yoshiteru Takekita. In recent years, clinical research related to the treatment of schizophrenia has focused on the following three main areas of interest:

- (i) Efficacy/tolerability of acute-phase treatment
- (ii) Impact of maintenance-phase treatment on relapse/recurrence and cognitive function
- (iii) Establishment of treatment methods for treatment-resistant schizophrenia

For (i), we are continuing research into precision medicine, focusing on patient backgrounds such as genetics; for (ii), we are continuing research into long-acting injection (LAI), which has come to play a leading role in maintenance treatment; and for (iii), we are continuing research into electroconvulsive therapy (ECT), which is the most traditional treatment method and is still an important treatment technique.

Previous studies showed that (i) genetic polymorphisms in 5-HT1A may influence the improvement of negative symptoms,²⁷⁾ (ii) the use of paliperidone-LAI may be beneficial for cognitive and

social functions compared with risperidone-LAI,¹⁷⁾²⁵⁾ and (iii) that the use of general anesthesia in ECT has a significant impact on seizures.¹⁾²⁶⁾

We will continue to actively develop research that contributes to actual clinical practice for patients with schizophrenia.

V. Art Brut

Finally, I would like to introduce a topic related to art. It is Art Brut. It may be an unfamiliar term, but Art Brut refers to art created by people who have not received any formal art education, driven by their inner impulses. It is a concept proposed by the French professional artist Jean Dubuffet. The artists are mainly people with intellectual and mental disabilities, especially schizophrenics. These people create their works in a world that is separate from galleries and museums, and the term “raw art” is often used to translate it. Dubuffet expressed his feelings about Art Brut as follows: “A song sung by a girl brushing a flight of stairs moves me more than a sophisticated song....I also like what is in the embryonic state, underdeveloped, imperfect, and mixed. I prefer unpolished diamonds before their adulteration.”¹⁶⁾ He also established the ‘Art Brut Museum (Collection de l’Art Brut)’ in Lausanne, Switzerland, in

1976 as a facility for collecting and exhibiting works.³⁾²⁸⁾

Let me introduce Adolf Wölfli, one of the most famous figures in the world of Art Brut. Wölfli was born in 1864 in Bern, the capital of Switzerland. His upbringing was poor, and from an early age he suffered physical and sexual abuse. At the age of 10, he became an orphan and was raised in a foster home. From his late teens, he was repeatedly arrested for indecent assault. He was then admitted to the psychiatric department of Bern University Hospital in 1895. When he was first admitted to the hospital, he suffered from violent hallucinations and was so agitated that he was kept in isolation for a long period of time. His diagnosis was paranoid schizophrenia. He began to draw pictures around 1904, nine years later. He started writing his epic autobiographical poem in 1908, and by the time he died in 1930, it had grown to a massive 45-volume, 25,000-page work (Figure 2).²⁰⁾ It is the story of Wölfli's own adventures, from knight Adolf to emperor Adolf and his events. The story is highly exaggerated. His doctor, Morgenthaler, who was very interested in pathology and President of the International Rorschach Society, showed great interest in Wölfli's paintings and contributed significantly to the growing appreciation of Wölfli in recent years. Wölfli's works are now a

treasure in the Kunst House in Bern, attracting art lovers from all over the world.

The following section introduces Yuzo Saeki, who is the author's favorite painter. Saeki was born in 1898 in Nakatsu, Osaka, the fifth son of a family of seven brothers and sisters from a temple. He became interested in art and music from junior high school, and in 1918 he entered the Western Painting Department of the Tokyo School of Fine Arts. While at the art school, he studied under Kuroda Seiki and Fujishima Takeji. He spent a total of three years in Paris, two years from January 1924 to January 1926 and one year from August 1927 to August 1928. During his second stay in Paris, he gradually began to show signs of mental instability, and was even diagnosed with paranoia. Saeki's themes are limited to "facades," "walls," "advertising," and "lettering," and although the color tones are dark, there is a unique beauty to them.¹⁶⁾ In terms of having received an artistic education, they do not fall under the narrow definition of Art Brut, but I think it is safe to consider them as Art Brut in the broad sense of the term.

I think that his 1927 work 'Gas Lamp and Advertisements' (Figure 3)¹³⁾¹⁸⁾ from 1927 represents the pinnacle of Saeki's paintings. The figures drawn like lines are said to be one of the characteristics of the paintings of people

with schizophrenia. The screen is filled with letters, and the mixture of those that make sense and those that don't creates a unique beauty. In June 1928, he was diagnosed with schizophrenia by psychiatrist Dr. Saburo Sakamoto, and he died in Paris in August 1928. 'Brickkiln' (Figure 4) is a masterpiece that led to the Saeki Yuzo Collection, as a wealthy collector in Osaka Yamamoto Hatsujiro fell in love with it at first sight, saying, "I gazed at it for a long time, lost in a strange feeling that made my heart pound." This painting depicts a brick kiln situated in the suburbs of Morin, near Paris. The sky is a deep blue-black that seems to be about to swallow you up, and the red of the bricks looks like the flames of a raging inferno. The contrast between the blue and red is wonderful, and each color is so clear that it is said to have an otherworldly atmosphere. The work entitled "Factory" (Figure 5), which he painted just before his death, shows the beginnings of Cubism, and the fact that he was pursuing new experiments in painting techniques even as he was on the verge of death gives the impression that he was a true seeker of enlightenment through painting. As Jung says, in a great work of art, after a brief rest, it seems as if the energy of creation is gushing out at an unconscious level through divine manipulation.⁶⁾ Van Gogh and others are considered to be

typical examples, but I think that Saeki Yuzo also fits the bill.

Schizophrenia is said to be a disease of creativity from a pathological perspective, but it seems as though creativity can only be realized in such a harsh situation.

Conclusion

I have introduced the current state of the Department of Neuropsychiatry at Kansai Medical University, focusing on my 40-year career. Psychiatry has undergone marked transformation over the past 40 years, but the accumulation of scientific knowledge and objective data is still less than in other medical departments. In the future, I hope to accumulate knowledge and aim for precision medicine. I also hope that young psychiatrists will develop an appreciation for art and a broad range of knowledge.

There is no conflict of interest to disclose in relation to this paper.

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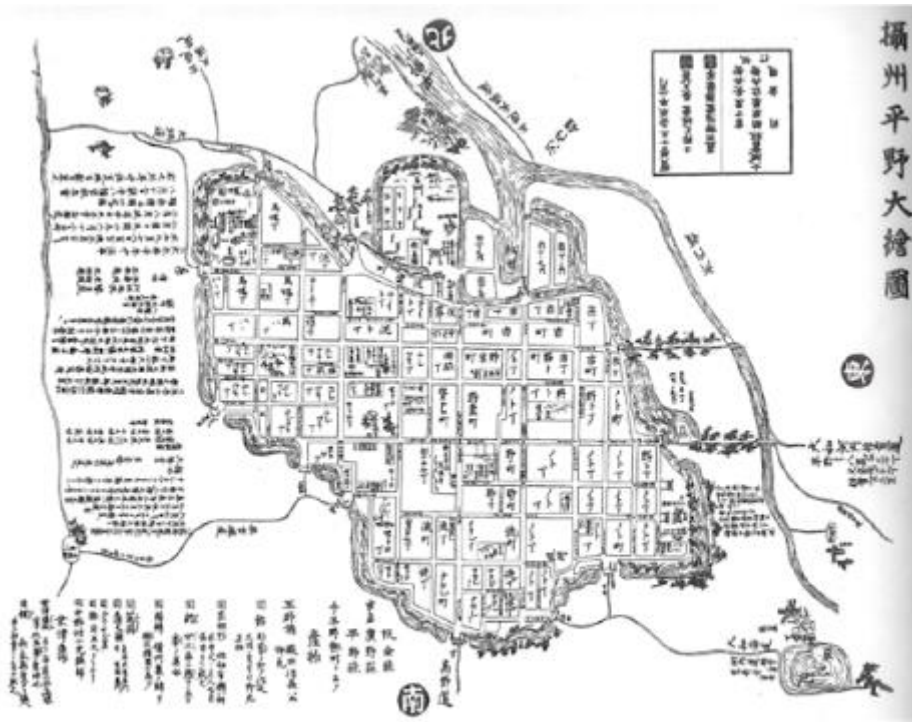


図1 攝州平野大繪圖 (宝暦13年)
(文献4より引用)

Figure 1: Large Map of Settsu Hirano (1738)
(Adapted from Reference 4)



図 2 Adolf Wölfli

St. Adolf-Grave-Source-Castle (Skt. Adolf = Graab = Quellen = Schloss), 1918

From : Books of Songs and Dances,
Book 15, p.1061

Pencil and colored pencil on newsprint
88 × 60.3/61.7 cm

Adolf Wölfli Foundation, Kunstmuseum Bern
A9294-123 (XV/p.1061)

Figure 2: Adolf Wölfli

St. Adolf-Grave-Source-Castle (Skt. Adolf = Graab = Quellen = Schloss), 1918

From: Books of Songs and Dances,
Book 15, p.1061

Pencil and colored pencil on newsprint
88 x 60.3 / 61.7 cm

Adolf Wölfli Foundation, Kunstmuseum Bern
A9294—123 (XV / p.1061)



図3 佐伯祐三『ガス灯と広告』(1927年)

東京国立近代美術館所蔵, 画像提供: MOMAT/DNPartcom
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Figure 3: Yuzo Saeki, “Gas Lamp and Advertisements” (1927)

Collection of the National Museum of Modern Art, Tokyo, Image provided by:
MOMAT / DNPartcom

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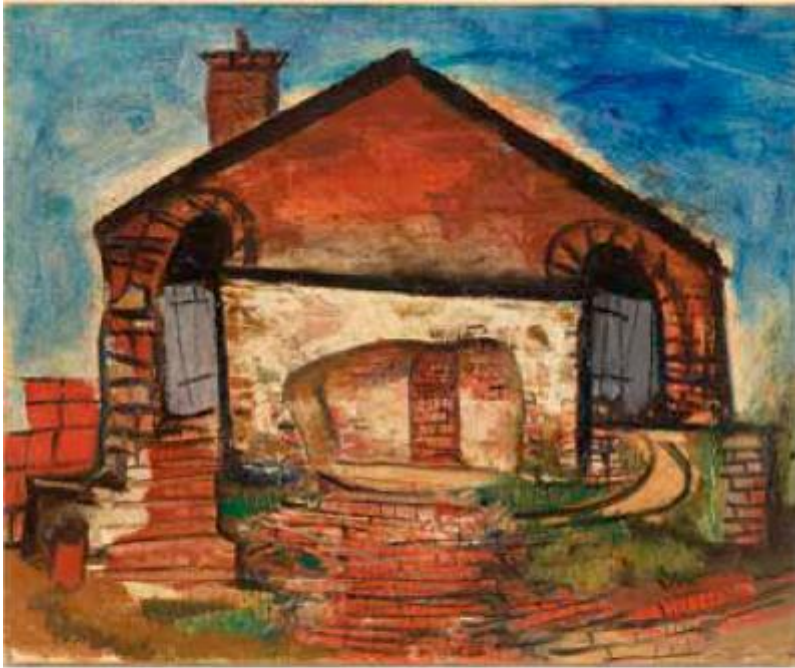


図4 佐伯祐三『煉瓦焼』(1928年)

大阪中之島美術館所蔵, 画像提供: 大阪中之島美術館/
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Figure 4: Saeki Yuzo, “Brickkiln” (1928)

Osaka Nakanoshima Museum of Art Collection, Image provided by Osaka
Nakanoshima Museum of Art / DNPartcom

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図5 佐伯祐三「工場」(1928年)

大阪中之島美術館所蔵, 画像提供: 大阪中之島美術館/
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Figure 5: Saeki Yuzo, "Factory" (1928)

Osaka Nakanoshima Museum of Art Collection, Image provided by Osaka
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