

## News Release

### Title

The development of an artificial intelligence (AI) method for the estimation of a brain network relating to the onset of disease.

— An estimation of brain networks associated with autism spectrum disorder and schizophrenia by analyzing the human genome —

### Key Points

○ We developed an artificial intelligence (AI) method for analyzing how the influence of genome mutation associated with the onset of disease propagates in the brain.

○ We estimated brain networks relating to the onset of autism spectrum disorder and schizophrenia, respectively.

○ Our research is expected to be the basis for the development of diagnostic methods and therapies for personalized medicine based on individual genetic information.

### Summary

Designated Assistant Professor Hideko Kawakubo and Designated Associate Professor Teppei Shimamura (Department of Systems Biology), Professor Norio Ozaki (Department of Psychiatry - Department of Psychotherapy for parents and children) at Nagoya University Graduate School of Medicine (Dean: Kenji Kadomatsu), Itaru Kushima at the Institute for Advanced Research (Director: Yoshiyuki Suto), and collaborators developed a machine learning method tied to artificial intelligence (AI) technology to analyze how the influence of genomic mutation associated with the onset of disease propagates in the brain, and used this method to estimate brain networks relating to the onset of autism spectrum disorder (ASD), and schizophrenia.

ASD and schizophrenia are psychiatric disorders caused by brain dysfunction due to multiple factors such as genome and environment. Unfortunately, the mechanisms that make up the foundation of these psychiatric disorders has not been fully elucidated yet at the molecular, cell, and circuit level. To clarify the mechanisms, it has become increasingly important to investigate the questions of if and how each region of the brain has functional interaction, that is, to examine the relationship (network) between brain regions.

In this research, we applied our machine learning method to gene networks composed of disease related genes in order to investigate how the influence of the genomic mutations associated with ASD and schizophrenia propagate across the brain, and then estimated the structure of the brain network relating to each disease.

As a result of our analysis, we can observe how the influence of the genomic mutation propagates to various brain regions (e.g. the temporal lobe, the hippocampus, the thalamus,

etc.) centering on the regions known to have strong relationships with ASD and schizophrenia (the amygdala, and the frontal lobe). In addition, we compared the resulting brain networks and confirmed that there is a network similarity of about 80% between ASD and schizophrenia.

In the future, it is expected that our research will be the foundation for new diagnostic methods and therapies based on individual genetic information in personalized medicine. This research is supported by the Strategic Research Program for Brain Sciences of the Japan Agency for Medical Research and Development (AMED). Our paper was published online in the British science journal, "Bioinformatics," on January 15, 2019.

## **Research Background**

ASD and schizophrenia are psychiatric disorders caused by brain dysfunction due to multiple factors such as genome and environment. Unfortunately, the mechanism related to the onset of these psychiatric diseases has not yet been fully determined. So far, the relationships between specific brain regions and disease have been well studied. However, there is no research that clarifies the whole picture of the relation between the brain regions associated with disease. In order to clarify the mechanism of the onset of disease, it has become increasingly important to comprehensively investigate the relationship (network) between the brain regions associated with disease.

## **Research Results**

We developed a machine learning method for analyzing how the influence of the genomic mutation associated with the onset of disease propagates in the brain, and estimated brain networks relating to the onset of autism spectrum disorder (ASD), and schizophrenia. In our method, we use gene networks for each brain region composed of disease related genes as input. Then we set a certain region's gene network as the target, and estimate which other regions' gene networks are relevant to the target gene network. This estimation is performed on all the brain regions. Finally, the results obtained in each brain region are integrated, and a brain network model relating to disease is constructed (Figure 1)

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## **Research Summary and Future Perspective**

In the future, it is expected that our research will be the foundation for new diagnostic methods and therapies based on individual genetic information in personalized medicine.

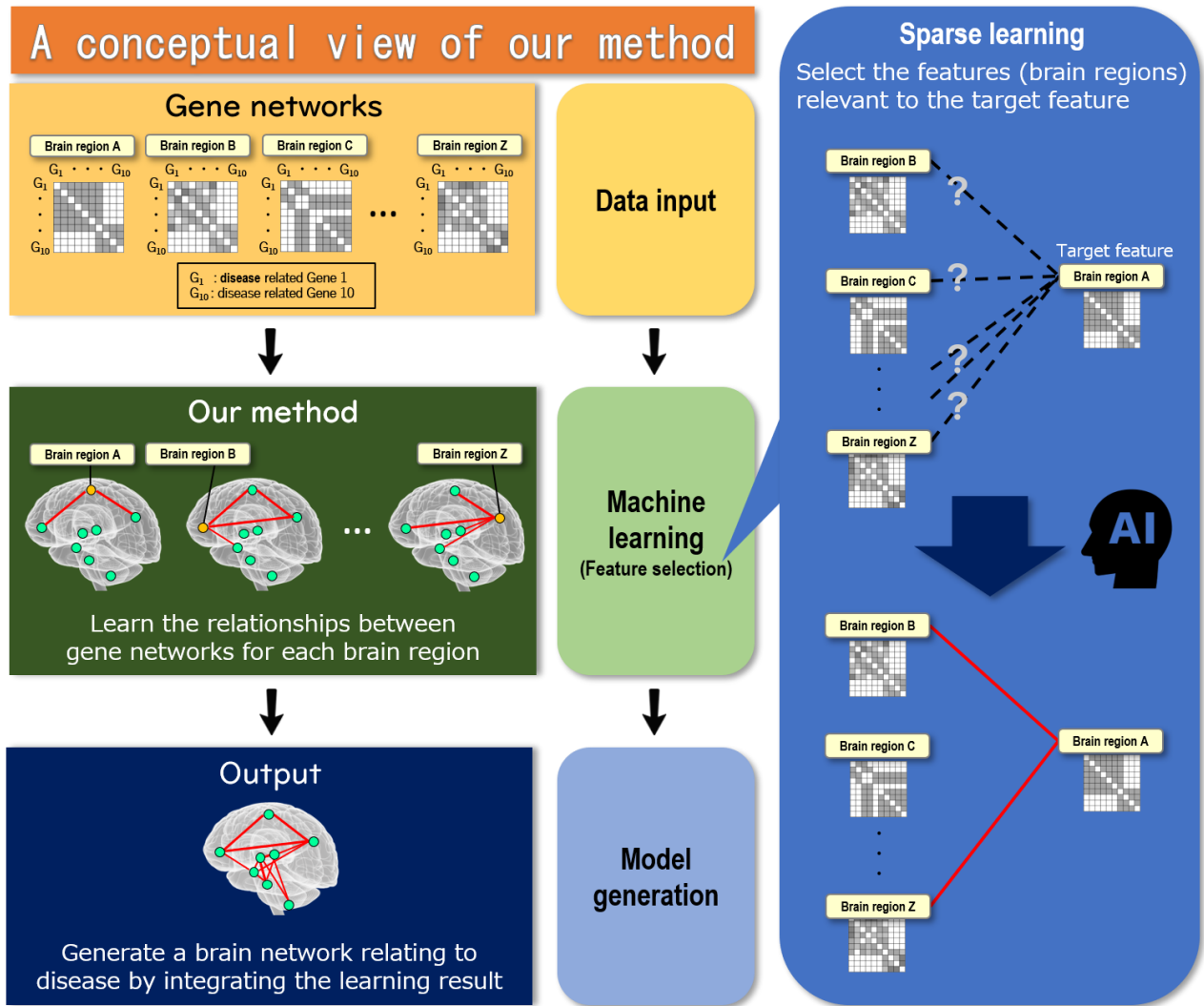
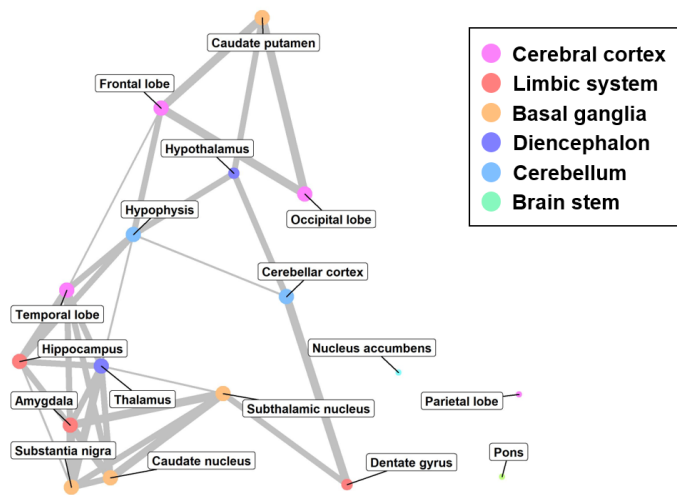


Figure 1: A conceptual view of the developed AI method. Using gene networks for each brain region composed of disease related genes as input, our method learns the relationships between gene networks for each brain region. This essential work of our method is called feature selection in machine learning. In this research, we adopt sparse learning for feature selection. Feature selection is performed on each brain region; relevant features (brain regions) to the target feature (brain region) are selected in each region and irrelevant features (brain regions) are eliminated. Our method eventually generates a brain network relating to disease by integrating the learning result.

Brain network relating to autism spectrum disorder



Brain network relating to schizophrenia

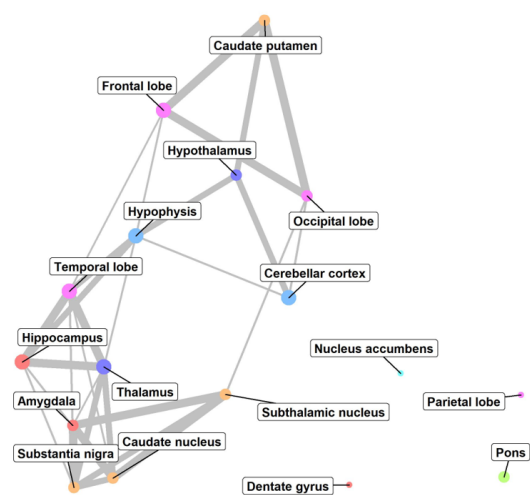


Figure 2: The resulting estimation of the influence of genomic mutation associated with the onset of autism spectrum disorder and schizophrenia and their propagation across the brain.

## Publication

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