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RESEARCH NEWS STORY

February 5, 2026

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Clinical Relevance of Brain Functional Connectome Uniqueness in Major Depressive Disorder

Study highlights the uniqueness of individual brain functional connectomes as a promising approach to identify biomarkers for major depressive disorder

A team of researchers, through a collaborative study, now points to functional connectome uniqueness (an individual-level measure from brain fingerprinting that captures how distinctive a person's intrinsic connectivity patterns are) as a reliable framework for discovering neurobiological biomarkers of major depressive disorder (MDD). This approach of individual connectivity profiles may cut through study heterogeneity and enhance reproducibility in biomarker research for MDD.

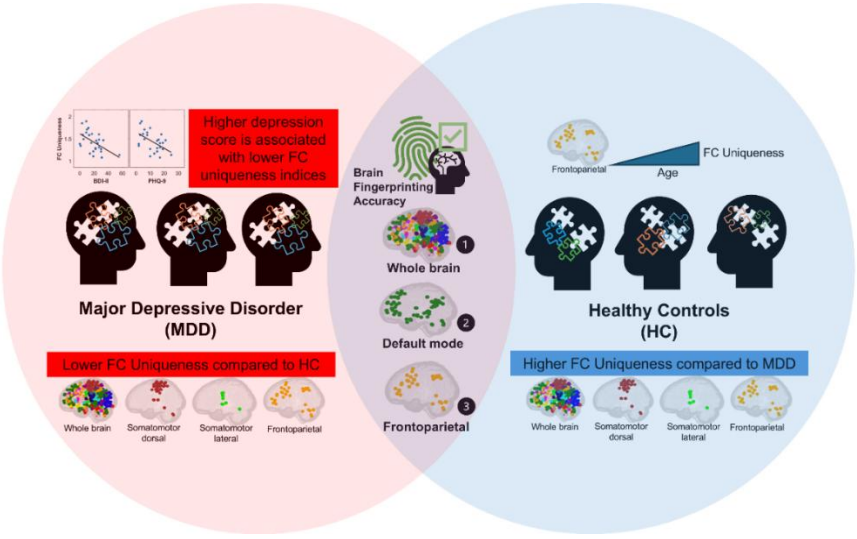

Image title: Comparative analysis of the brain functional connectome (FC) uniqueness
Image caption: Brain FC uniqueness is lower in patients with major depressive disorder (MDD) at the whole-brain level, frontoparietal, and sensorimotor networks. Furthermore, FC uniqueness correlated negatively with depression assessment scores.
Image credit: Research Fellow Siti Nurul Zhahara and Professor Yoshiyuki Hirano, Chiba University, Japan

Major depressive disorder (MDD) is a debilitating condition that affects more than 246 million people worldwide, yet scientists have struggled to identify consistent brain markers that could improve diagnosis and treatment. Finding reliable neurobiological markers for MDD has been hampered by the methodological differences observed across neuroimaging studies. Traditional brain imaging studies have produced conflicting results, often due to differences in methods and analysis pipelines. This inconsistency has made it difficult to pinpoint reliable neurobiological signatures of depression.

Against this backdrop, a new study led by Research Fellow Siti Nurul Zhahara and Professor Yoshiyuki Hirano from the Research Center for Child Mental Development, Chiba University, Japan, and the United Graduate School of Child Mental Development, Osaka University, Japan, highlights a promising approach to investigate the uniqueness of each individual's brain connectivity, known as functional connectome (FC) uniqueness. This approach, when applied to patients with MDD, can aid in finding potential biomarkers. The study was co-authored by Professor Eiji Shimizu of the Department of Cognitive Behavioral Physiology, Graduate School of Medicine, Chiba University, and Professor Go Okada of the Department of Psychiatry and Neurosciences, Graduate School of Biomedical and Health Sciences, Hiroshima University, Japan. Their findings were made available online on January 4, 2026, and will be published in Volume 399 of the *Journal of Affective Disorders* on April 15, 2026, bringing fresh evidence to the study of mood and emotional regulation.

"MDD has an extensive effect with impaired daily functioning, reduced quality of life, and productivity losses, along with an economic burden. This severe impact highlights the need for research to improve diagnosis and treatment strategies. Our study aids in understanding the neurobiological basis and core mechanisms of MDD," says Prof. Hirano.

FC uniqueness, sometimes called "brain fingerprinting," captures how distinctive an individual's brain connectivity patterns are. Previous research has shown that these patterns remain stable across time and conditions, suggesting they could serve as a reproducible measure of mental health.

The study examined resting-state functional magnetic resonance imaging (fMRI) data of young adults with and without MDD across multiple sites. It confirmed that healthy brains could be reliably identified by their unique connectivity signatures. In contrast, patients with MDD displayed reduced FC uniqueness, especially in frontoparietal and sensorimotor networks.

Researchers applied a standardized FC uniqueness analysis to patients with MDD and healthy controls. They found that FC uniqueness correlated negatively with depression severity. Significantly, lower uniqueness was associated with higher scores on standard depression assessment tools (PHQ-9 and BDI-II), suggesting an association between brain connectivity patterns and symptom severity.

Prof. Hirano shares, *"The significant reduction in whole-brain FC uniqueness among patients with MDD supports our hypothesis that depression pathology is associated with less distinctive functional brain organization."*

These findings highlight FC uniqueness as a reproducible and clinically meaningful marker, offering new potential for improving diagnosis and tailoring treatment in depression.

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About Professor Yoshiyuki Hirano from Chiba University, Japan

Dr. Yoshiyuki Hirano serves as a Professor in the Research Center for Child Mental Development, Chiba University, Japan. His research interests include cognitive behavioral therapy, eating disorders, anxiety disorders, and obsessive-compulsive disorder. Prof. Hirano has been actively involved in investigating the brain characteristics of individuals prone to these disorders and examining the corresponding treatment strategies. He has published more than 100 articles and has been awarded multiple times for his remarkable contributions, including awards for his work in functional imaging from the International Society for Magnetic Resonance in Medicine.

Funding:

This work was supported by the AMED Brain/MINDS Beyond Program (Elucidation of Neural Circuits of Mood Disorders in Adults and Related Disorders Based on Longitudinal MRI Data [JP18dm0307002] and Elucidating Cortico–Subcortical Brain Dynamics Underlying Depressive Symptoms and Cognitive Impairment Using Multidimensional Longitudinal Human Data, with Validation in a Primate Model [JP24wm0625204]) and JSPS KAKENHI (Grant Numbers: JP19K03309, JP21K03084, JP23K22361, JP24K21493, JP25K00879, JP25K06842, and JP25H01085).

Reference:

Title of original paper: Reduced functional connectome uniqueness on the whole brain and network levels as a clinically relevant and reproducible neuroimaging marker in major depressive disorder

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Journal: *Journal of Affective Disorders*
DOI: 10.1016/j.jad.2025.121073

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