PRESS RELEASE

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Novel Accurate Approach Improves Understanding of Brain Structure in Children with ADHD

Researchers demonstrate that the traveling-subject method reduces measurement bias, increasing the reliability of brain imaging studies on ADHD

Magnetic resonance imaging often yields inconsistent results when assessing the brain's structural characteristics in children with attention deficit/hyperactivity disorder (ADHD). To address this, scientists from Japan have used a harmonization method called traveling-subject (TS) to reduce measurement bias in brain imaging datasets from multiple sites. The TS harmonized datasets showed significant reductions in measurement bias and revealed apparent volumetric changes in specific brain regions, indicating promise for developing a more robust diagnosis for ADHD.

Over five percent of children and adolescents are diagnosed with attention deficit/hyperactivity disorder (ADHD) globally. This condition is characterized by a short attention span, hyperactivity or impulsive behavior that is age-inappropriate, making it difficult for patients to navigate interpersonal relationships, the formal education system, and social life. Researchers have used brain imaging analyses such as magnetic resonance imaging (MRI) to understand the neurological basis of ADHD. Understanding brain structure abnormalities that lead to ADHD-related pathologies is crucial for designing early assessment and intervention systems, especially for children.

Although multiple studies have used MRI to understand ADHD in children, the results have been inconclusive. While some brain imaging studies have shown decreased gray matter volume (GMV) in children with ADHD, others have either reported no change or an increase in GMV compared to subjects without ADHD. These conflicting results are mostly due to small sample sizes, differences in MRI machines used, or the variation among the subjects recruited. Previous studies have accounted for the bias caused by different MRI machines using a method called ComBat harmonization, which controls for site and MRI differences in large samples. However, ComBat overcorrects sampling bias, which may include biological characteristics of the sample; therefore, it may not be able to accurately correct the MRI differences.

The traveling-subject (TS) method is a new correction approach to account for variations in measurements across MRI machines for the same subject. In this method, measurement biases can be controlled for the same participants using MRI scans from multiple institutions, facilitating the collection of more accurate datasets. In this collaborative study, Assistant Professor Qiulu Shou and Associate Professor Yoshifumi Mizuno from the University of Fukui, Japan, Professor Yoshiyuki Hirano from Chiba University, Japan, and Professor Kuriko Kagitani-Shimono at The University of Osaka, Japan, validated the TS method in an independent dataset. Their findings were published in *Molecular Psychiatry* on August 8, 2025.

Dr. Shou introduces the methodological framework of the study: *"MRI data of 14 TS, 178 typically developing (TD) children, and 116 children with ADHD were collected from multiple sites, and the TS method and ComBat were used to correct for measurement bias."* Fourteen healthy subjects underwent MRI scans on four different machines over a three-month period to extract measurement biases across these machines. This was then applied to an independent dataset of children from the Child Developmental MRI (CDM) database. The CDM database was jointly established by the University of Fukui, The University of Osaka, and Chiba University, with the goal of collecting brain imaging data from over 1,000 child participants for research on neurodevelopmental disorders such as ADHD. GMV was then estimated and compared between the two groups of children in the study. The research team calculated measurement and sampling biases among TS-corrected, ComBat-corrected, and raw data. The results showed that compared to raw data, the TS method significantly reduced measurement bias while maintaining sampling bias. In contrast, ComBat effectively reduced measurement bias and significantly decreased sampling bias.
"TS-corrected data showed decreased brain volumes in the frontotemporal regions in the ADHD group compared to the TD group," explains Dr. Mizuno while discussing their findings. *"Patients with ADHD displayed smaller volumes in those regions of the brain that are crucial for cognitive functions, such as information processing and emotional control, which are often affected in these patients,"* adds Dr. Shou.

Furthermore, if TS-harmonized multi-site MRI data on specific brain structure patterns can be associated with ADHD, they can then be used as neuroimaging biomarkers for accurate and early ADHD diagnosis, treatment, and treatment outcome monitoring, leading to effective personalized therapeutic strategies.

"*By applying the TS harmonization method to correct for site-related biases in multi-site MRI data, this study aims to identify brain structure characteristics in children with ADHD. These identified characteristics could facilitate earlier diagnosis and more precise, individualized interventions. In the long term, this approach may improve the quality of life for affected children and reduce the risk of secondary psychiatric disorders,"* concludes Dr. Shou.

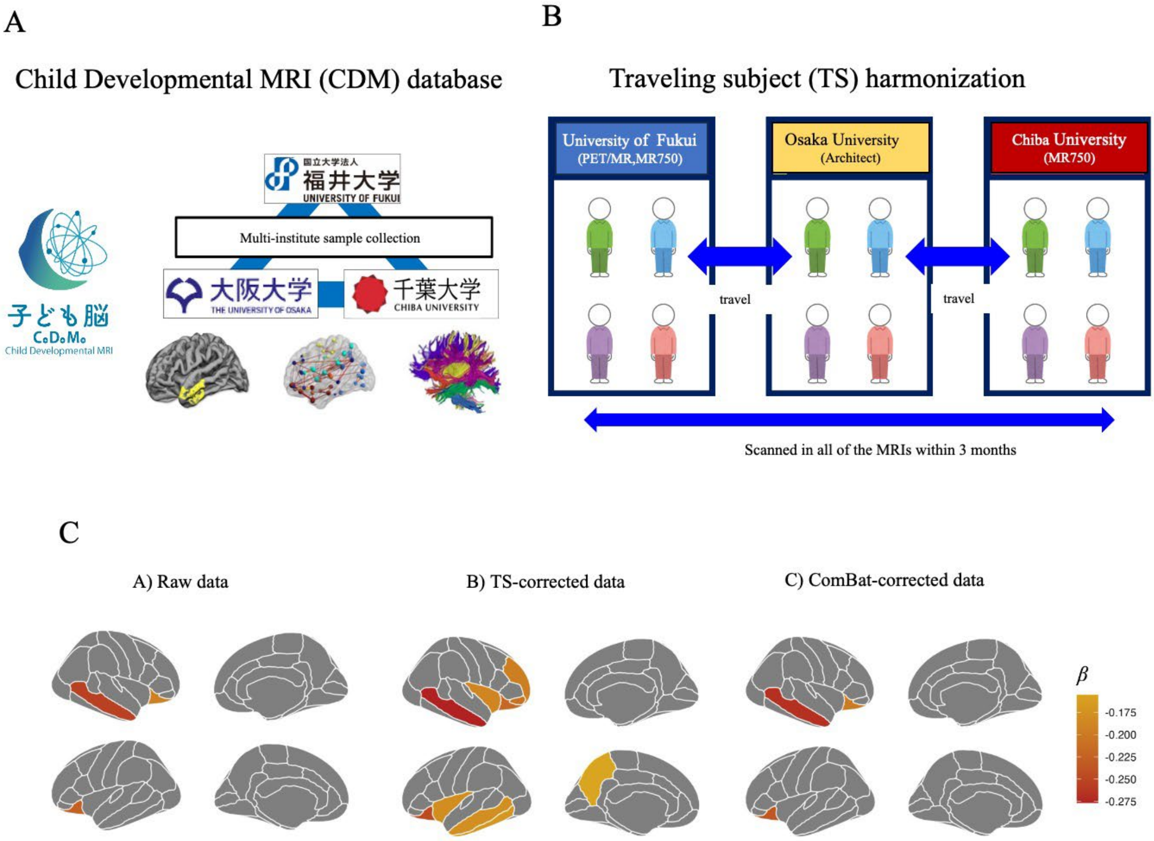

Image title: Traveling-subject (TS) harmonized brain imaging data shows reduced measurement bias
Image caption: Brain imaging methods like magnetic resonance imaging (MRI) are used to characterize structural differences in the brains of children with attention-deficit/hyperactivity disorder (ADHD). However, these results are often inconsistent, revealing different results across machines and hospitals. Researchers from Japan employed an approach called the TS method to reduce measurement bias in brain imaging datasets sourced from multiple locations. Their results reveal that, compared to the raw data, TS-corrected data significantly reduced measurement bias and revealed volumetric changes in brain regions in children with ADHD.
Image credit: Associate Professor Yoshifumi Mizuno from the University of Fukui, Japan
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About Assistant Professor Qiulu Shou from the University of Fukui, Japan
Dr. Qiulu Shou serves as an Assistant Professor at the Research Centre for Child Mental Development, University of Fukui, Japan. Additionally, Assistant Professor Shou also works at the United Graduate School of Child Development, The University of Osaka, Kanazawa University, Hamamatsu University School of Medicine, and Chiba University, in Japan. Her areas of expertise include pediatric brain development, neurodevelopment, and developmental disorders of the brain.

About Associate Professor Yoshifumi Mizuno from the University of Fukui, Japan
Dr. Yoshifumi Mizuno, MD, PhD, is an Associate Professor who specializes in MRI-based neuroimaging research on attention-deficit/hyperactivity disorder (ADHD). From 2019 to 2021, he served as a JSPS Overseas Research Fellow at the Department of Psychiatry and Behavioral Sciences, Stanford University, USA, where he contributed to advancing the understanding of ADHD's neural mechanisms. Currently, Dr. Mizuno leads groundbreaking research as the Principal Investigator of the Division of Affective and Cognitive Development at the Research Center for Child Mental Development, University of Fukui, Japan.

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