3D brain mapping opens a window to the aging brain

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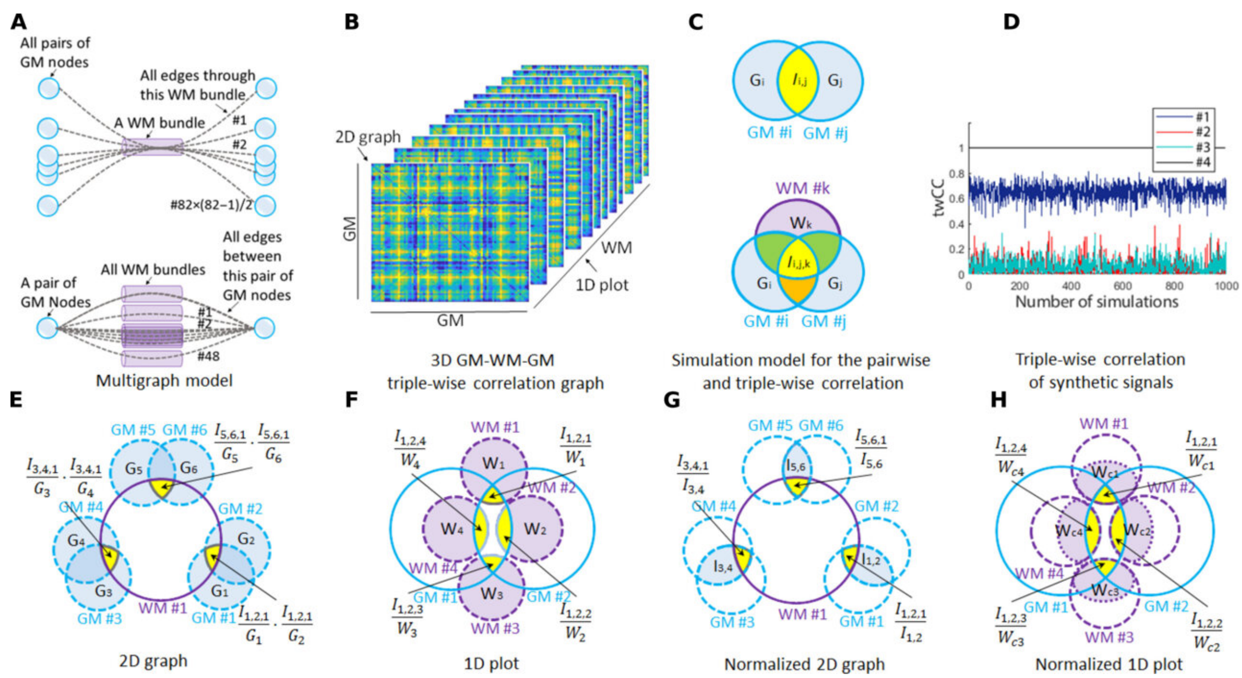


Illustration of the triple-wise correlation network model. Credit: *Science Advances* (2024). DOI: 10.1126/sciadv.adi0616

By mapping brain activity in three dimensions, researchers at Vanderbilt University Medical Center have achieved a more detailed picture of how the brain changes with age.

Their [findings](), described in the Jan. 26 issue of the journal *Science*

Advances, may help advance the understanding, early diagnosis and treatment of Alzheimer's disease, bipolar disorder and other disruptions of normal brain function.

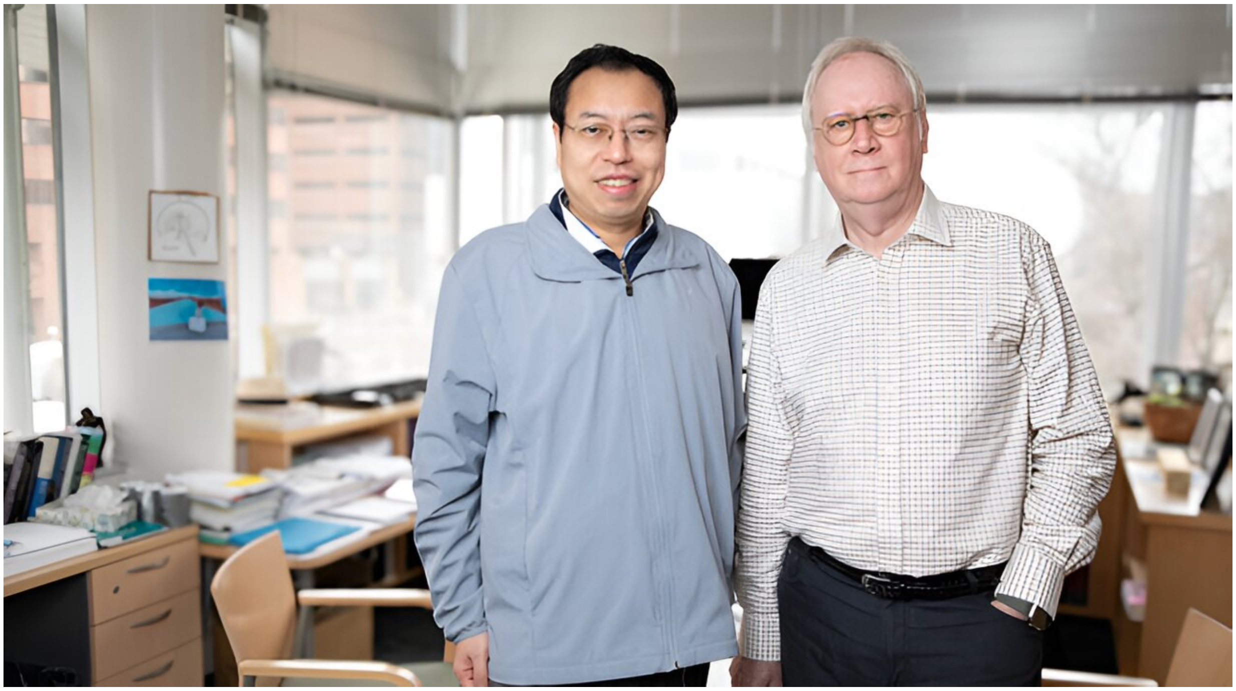
Half of the human brain is made up of gray matter, nerve cells that process sensation, control voluntary movement, and enable speech, learning and cognition. The other half is white matter, the axons that connect areas of gray matter to each other and project to the rest of the body.

Within the field of functional magnetic resonance imaging (fMRI) of the brain, white matter historically has been understudied, in part because it is easier to detect functional signals from gray matter.

Recently VUMC scientists found they can reliably separate and detect white matter signals, opening the door to better understanding of the other, previously neglected half of the brain.

Now they've taken the research to the next level. Through a complicated series of mathematical formulas, the paper's first author, Zhongliang Zu, Ph.D., has proposed a method for simultaneously mapping how areas of gray matter "talk to each other" through connections of white matter.

"It's a major extension of using brain imaging to study brain networks, but bringing in, for the first time, white matter," said John Gore, Ph.D., director of the Vanderbilt University Institute for Imaging Science and the paper's corresponding author.



Zhongliang Zu, PhD, left, and John Gore, PhD, are leading an effort to map brain networks in three dimensions. Credit: Erin O. Smith

A major technique for studying brain activity, fMRI measures changes in blood oxygenation-level dependent (BOLD) signals that, in gray matter, reflect a rise in blood flow (and oxygen) in response to increased neuronal activity.

While BOLD signals in white matter are less well understood, it is becoming clear that white matter is not passive tissue that merely connects areas of gray matter.

White matter "plays a pivotal role in human learning processes," the VUMC scientists state in their paper. Changes in the microstructure of white matter "alter the fidelity of neural signal transmissions and consequently brain function."

Prior research has determined the functional connectivity between two areas of gray matter by correlating their BOLD signals.

As described in the current paper, Zu, research associate professor of Radiology and Radiological Sciences and of Biomedical Engineering, conceived a "triple-wise correlational framework" that incorporates signals from white matter into the study of functional connectivity pathways.

Using fMRI images of the brains of 490 individuals from publicly accessible databases and by applying multivariant statistical methods, Zu, Gore and their colleagues were able to determine that white matter fibers form multiple and complex gray matter connections.

"A white matter fiber may carry signals from multiple potential inputs to different gray matter areas," Gore explained. "At the same time, any pair of gray matter areas might communicate through many different (white matter) pathways."

Zu's mathematical equations have worked out how much each pair of gray matter contributes to signal transmission through a single white matter fiber and, at the same time, how much each pair uses different fibers. "That's really a major step," Gore said.

Incorporating white matter signals provides, as the paper's title suggests, the "missing third dimension" to understanding functional connectivity between different brain regions.

By studying the brain scans of different age groups, the researchers discovered that overall connectivity in parts of the brain declined with age, while brain activation increased in the frontal cortex, which is involved in higher cognitive function.

This shift is possibly to compensate for the decline in other areas, they noted.

The researchers are now investigating what the functional consequences might be of vascular changes in white matter that have been associated with brain disorders such as Alzheimer's disease.

In the future, measuring changes in functional connectivity between brain regions could serve as a biomarker—a way to monitor the progression of diseases that affect white matter and response to treatment, Gore said.

More information: Zhongliang Zu et al, The missing third dimension—Functional correlations of BOLD signals incorporating white matter, *Science Advances* (2024). DOI: 10.1126/sciadv.adi0616

Provided by Vanderbilt University