How the brain's wiring leads to cognitive control

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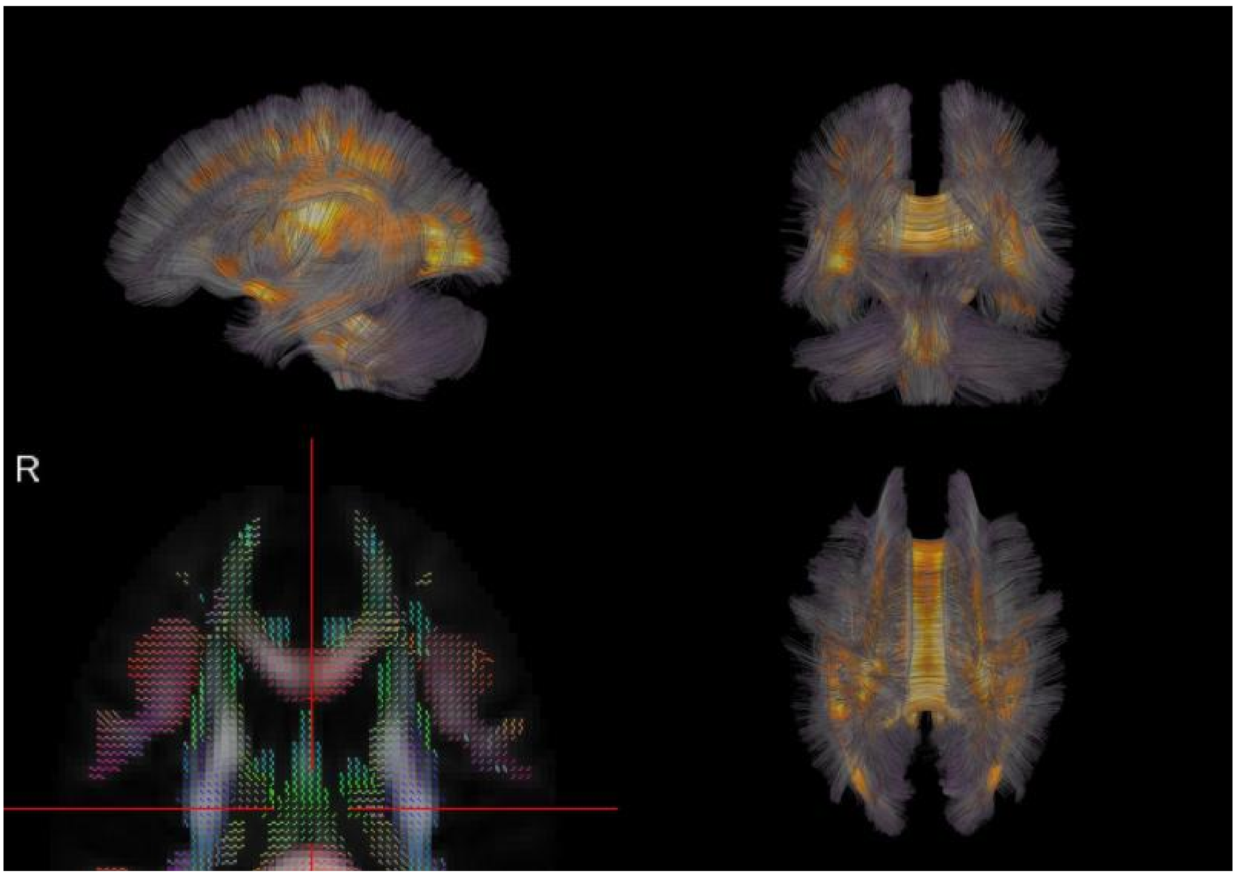


Captured through diffusion imaging, 'wiring diagrams' of the brain show how information transmission and communication is constrained between different regions. Credit: University of Pennsylvania

How does the brain determine which direction to let its thoughts fly?

Looking for the mechanisms behind cognitive control of thought, researchers at the University of Pennsylvania, University of California and United States Army Research Laboratory have used brain scans to shed new light on this question.

By using structural imaging techniques to convert brain scans into "wiring diagrams" of connections between brain regions, the researchers used the structure of these neural networks to reveal the fundamental rules that govern which parts of the brain are most able to exert "cognitive control" over thoughts and actions.

Earlier research has long placed the frontal cortex as the core of this cognitive control network, which allows people to stay focused on one task or switch to a radically different one. This study is the first to provide a mechanistic explanation for how the frontal cortex accomplishes this feat, exerting control over trillions of individual neurons.

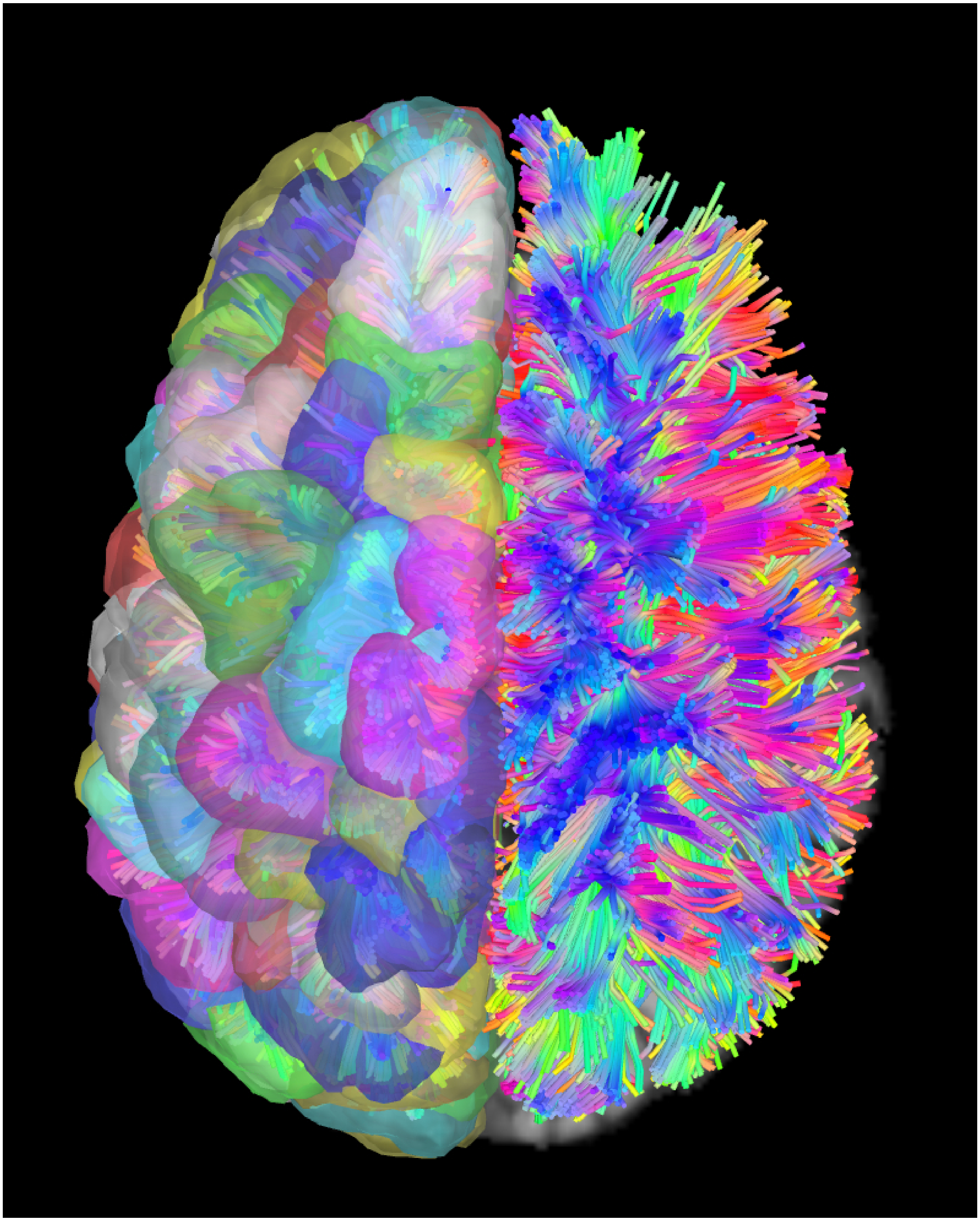
The work, published in *Nature Communications*, weds cutting-edge neuroscience with the emerging field of network science, which is often used to study social systems. It applies control theory, a field traditionally used to study electrical and mechanical systems, to show that being on the "outskirts" of the brain is necessary for the frontal cortex to dynamically control the direction of thoughts and goal-directed behavior.

This fundamental understanding of how the brain controls its activity could help lead to better interventions for medical conditions associated with reduced cognitive control, such as autism, schizophrenia or dementia.

Danielle Bassett, the Skirkanich Assistant Professor of Innovation in Penn's School of Engineering and Applied Science, is senior author on the study. Shi Gu, a graduate student in the School of Arts & Sciences' Applied Mathematics and Computational Science program, was the lead author.

They collaborated with Fabio Pasqualetti, a control theorist at the University of California, Riverside. The research also featured work from the Scott Grafton, Matthew Cieslak and Michael Miller of the University of California, Santa Barbara, along with researchers at the Army Research Laboratory, including Jean Vettel, Alfred Yu and joint ARL-Penn scientists Qawi Telesford and Ari Kahn, and a researcher at the Moss Rehabilitation Research Institute, John Medaglia.

"Surprisingly," Bassett said, "our results suggest that the human brain resembles a flock of birds. The flock comes to a consensus about which way to fly based on how close the birds are to one another and in what formation. Birds that fly at specific places in the flock can drive changes in the flock's direction, being leaders in a so-called multi-agent system.



Researchers applied control theory, normally used in engineered systems, to predict which regions could exert the most influence. Credit: University of

"Similarly, particular regions of your brain are predisposed to control your thoughts based on where they lie in relation to other regions."

Cognitive psychologists and neuroscientists have long known that the frontal cortex is heavily involved in cognitive control. It is most active in experimental subjects asked to do tasks that require executive function, and damage to that region of the brain, through disease or injury, often results in loss of that function.

The researchers were interested in developing a more fundamental understanding of how that region of the brain interacts with others to allow for executive function.

Starting with detailed brain scans that show how neurons are physically connected to one another with one-millimeter precision, the scientists used a mathematical technique drawn from control theory in engineering.

"We need a basic theory of how the brain controls itself, and to get there we suggest treating the brain as an engineering system," Bassett said. "Cognitive control is a lot like engineering control: you model the system's dynamics by identifying key points. If I push on that one piece or pull this lever, I can offer a prediction of how it's going to affect other parts of the network."

By applying control theory equations to the "wiring diagrams" generated from brain scans, the researchers showed that the geographical and functional differences between regions of the brain are linked.

"In fact," Pasqualetti said, "we believe that the human brain responds to internal and external stimuli with principles akin to large-scale dynamical network systems, such as power systems and robotic networks, and that a few carefully selected locations may be preferentially located to optimally guide complex functions."

While the analysis cannot say whether the frontal cortex's location or its role evolved first, it suggests that part of the frontal cortex's ability to control executive function depends on its distance from other parts of the brain network.

"The regions on the outskirts can perform a very specific kind of control," Bassett said. "They can move the system to distant states, like switching from working at your job to playing with your kids.

Regions that are most interconnected, and therefore more internal to the network, are very good at moving the brain into nearby states, like from writing someone an email to talking to them on the phone. What's particularly interesting is, if we look at where those inner nodes are, they're all in 'default mode' regions, which are the regions that are active when you are resting. This makes sense, because if you were engineering an optimal system, you would want to put its baseline somewhere where it can get to most of the places it has to go pretty easily."

This type of holistic understanding of the relationship between brain regions' location and their roles is necessary for tailoring better treatments for people who have lost executive function due to disease or injury.

"We're very interested in controlling brain networks with techniques like optogenetics, transcranial magnetic or direct-current stimulation, deep brain stimulation or even neurofeedback," Bassett said, "but the problem has been that there is little theoretical basis to determine how these stimulations affect the dynamics of the whole brain. In most cases, stimulation is applied via trial and error. This research helps to build up an understanding of the impact of stimulation in one region on cognition as a whole."

Future research will test whether "wiring" differences between people predict their performance on cognitive tasks. It will also underpin work on therapeutic and adaptive technologies that capitalize on brain networks' unique advantages over their computerized counterparts.

"Humans can recognize millions of objects in milliseconds," said ARL's Jean Vettel, "but computer vision research has limited success after decades of research on autonomous agents. Our focus on brain networks aims to capture the time-evolving nature of global brain dynamics so we can predict fluctuations in human performance. We can then build neurotechnologies that can image the brain and allow us to gain access to covert mental events and build systems that can adapt to us humans, helping us more when we are tired and less when we are alert."

More information: *Nature Communications*, dx.doi.org/10.1038/ncomms9414

Provided by University of Pennsylvania