

Mark D'Esposito, MD

Scientia

LEVERAGING NEW TECHNOLOGIES TO TREAT BRAIN INJURY

The brain is the most mysterious organ in the human body – despite decades of research, we have just begun to scratch the surface in understanding how the brain works and how we can help it to heal following an injury. **Professor Mark D'Esposito** of the University of California, Berkeley, uses advanced imaging technology to illuminate how the connections in our brain function in order to find new ways to aid brain healing after injury.

The human brain is the most advanced and complex information processing instrument on earth. Despite decades of trying, we have not been able to create a computer that performs complex operations with the speed and nuance of the brain. The brain is composed of a vast network of neurons, the number of which is greater than the connections between every electronic device on earth, and their constant communication creates what you and I experience as consciousness.

Professor Mark D'Esposito of the University of California, at Berkeley, is a neurologist seeking to understand how the networks of neurons within our brain function together, and how we can leverage this understanding to treat people with traumatic brain injuries and other neurological disorders. Using advances in functional magnetic resonance imaging (fMRI) he is mapping neuronal networks to illuminate how the brain works.

Thinking in Modules

While we are still working to understand how the brain works as a whole, we have some ideas about how it works in general. We know that some areas of the brain perform specific functions, such as processing sounds. This is because the brain cells or neurons in these areas share similar purposes and must communicate rapidly to produce efficient responses. Professor D'Esposito refers to these areas as modules. He explains: 'Facebook is a helpful metaphor: think of your closest friends on the social network as being in your module, the people closest to you and with whom you are most likely to communicate.'

While these brain modules may perform fairly specific functions, they must also share information with other areas to create the full human experience – for example, processing a sound, interpreting it as speech, and then understanding the message requires the tight coordination of multiple modules, but happens so seamlessly in a healthy brain that our perception of a sound and its message seems instantaneous.



In order to understand how the brain works, it is critical to understand how the brain functions as a whole. Professor D'Esposito explains that, 'it is presumed that each brain module performs a discrete function, such as producing language or seeing the world around us. However, brain modules must also communicate with each other to accomplish more complex behavior – such as multitasking or solving a mathematical problem.'

A primary focus of Professor D'Esposito and his team's research has been understanding how different modules of the brain work together in a network to create goal-directed behaviour, and what those connections imply for the treatment of traumatic brain injuries and other neurological disorders. 'My take-home message is simple,' he says,

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Historically, it has been assumed that damage to a specific area of the brain only impacts processes that that area manages – for example, damage to the visual cortex would only affect a person's ability to see. However, Professor D'Esposito and his colleagues have found that this is not always the case and that may actually be good news for patients with brain injuries.

The Pieces That Form the Whole

Executive control refers to a collection of mental processes that are necessary to identify, plan, and execute the behaviours needed to complete a goal. These processes, including selective attention, working memory, task switching, sequencing, and planning, are essential to navigating everyday life. A common effect of brain injury is the loss of executive control – patients struggle to pay attention, organise, and develop strategies that help them get things done. This is particularly true of injuries to the prefrontal cortex, the area of the brain where many executive control processes are localised, that gives us the experience of conscious control and abstract thought. The prefrontal cortex is believed to be one of the most critical connector areas of the human brain, having extensive reciprocal connections to virtually all cortical and subcortical structures. This places the prefrontal cortex in a unique and privileged position to monitor and manipulate diverse cognitive processes. Thus, dysregulation of the prefrontal cortex, whether through direct injury or indirect effects of damage to other modules of the brain, leads to symptoms that strongly impact the lives of those afflicted.

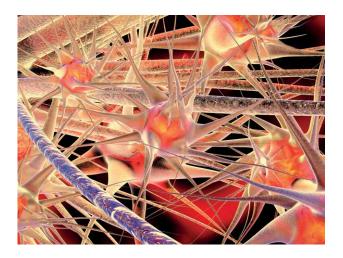
A critical finding that has shaped the work of Professor D'Esposito's team, is the discovery that localised brain damage impacts the large-scale function of the brain as a whole, particularly when the damage impacts an area of the brain that had served as a connector for multiple modules across the brain. Using fMRI scans to observe the brain activity of a group of patients with damage to a specific area of the brain, they were able to demonstrate that undamaged regions were also dysregulated following the injury.

These findings explain many of the unpredictable symptoms experienced by patients that have suffered a brain injury that are often seemingly unrelated to the function of the area that was injured.

The more modules that are connected to a damaged area, the more widespread the dysregulation will be. While at the surface this may seem like an undesirable finding for patients with brain injuries, Professor D'Esposito sees these network connections in a different light – by understanding how the network is connected, we can look for ways to reconnect it following trauma.

Reprograming the Networks of the Brain

Professor D'Esposito and his team took note of clinical studies that were helping patients improve attention and problem-solving skills through training programs and suspected that these



strategies could be used to improve executive control functions in patients with brain injuries. Specifically, they predicted that attention would serve as a keystone process that could improve cognitive function in these individuals.

Attention training activities included mindfulness-based regulation practices and goal-management strategy making. They piloted training sessions with two groups. One group was given educational seminars and another underwent attention training over five weeks. They found that while participation in the educational seminars had no effect, the training sessions created lasting behavioural changes that not only improved the patients' performance on executive function tests, but more importantly, improved their ability to complete tasks in real life scenarios.

When Professor D'Esposito and colleagues took this experiment a step further and took fMRI scans of the brains of patients in the training study, they made an even more exciting discovery. The training sessions weren't just helping patients learn new tricks, they were actually changing the neural pathways being used during attention tasks.

In the extrastriate cortex, one of the brain modules associated with the training task, all patients showed increased neural connections. Interestingly, training had different impacts on each patient's prefrontal cortex, depending on how they had processed information prior to training. Those who had been more goal-oriented prior to training shifted towards processing more irrelevant information after training. In contrast, those who had been more focused on irrelevant information prior to training shifted to toward more goal-relevant information after training. In both cases, training improved overall executive control, regardless of the shift made. This suggests that different people with different predispositions will use different strategies to cope with forming new neural networks.

Taken together, these results indicate that not only is it possible to use training programs to improve the experience of people with brain injuries, but these training sessions create tangible and lasting change in the brain's structure that benefit the longterm health of patients that receive them. Professor D'Esposito notes that, 'understanding brain connectivity in this way helps us develop rehabilitation therapies that stimulate the brain to reconfigure itself with new functional connections that bypass damaged brain regions that serve as connector hubs.'

Understanding Individual Responses

Though cognitive training and rehabilitation benefits can benefit patients with brain injuries, the degree to which each patient sees results varies drastically. Professor D'Esposito and his colleagues wanted to understand why some patients experienced transformative results, while others were showing only minor improvements, even when their brain injuries were similar in size and location. They again turned to fMRI, comparing the baseline scans taken prior to the training interventions, and the results each patient experienced following rehabilitation.

Patients with highly modular brains, that is, more connections within modules than between modules, prior to training were most likely to see great improvements with training. Professor D'Esposito has repeated these studies with aging adults and found that older adults with more modular brains are also more responsive to both cognitive training and the neurological benefits of physical exercise. These findings suggest that the brain has an easier time rerouting the connections between modules than it does trying to recreate more broad, undefined networks.

These findings have enabled Professor D'Esposito and his team to use fMRI to predict which patients will respond best to treatment and are spurring them to identify ways to enable similar responses in patients whose brains are less optimally wired to benefit from treatment. For now, these discoveries are helping neurologists to tailor treatment plans with the highest likelihood of success.

Professor D'Esposito notes: 'We still have much to learn about optimal brain states, such as whether we can alter or optimise them or why brain states differ from one person to the next. But our findings nevertheless highlight the tremendous power of brain imaging and its potential impact on medical treatments.'

The Future of Brain Health

Through advances in imaging technology, Professor D'Esposito and other neurologists are making powerful discoveries about how the brain works that have major implications for how we approach the treatment of brain damage in the future. He concludes that, 'recent scientific advances have given us basic knowledge of the functional architecture of the human brain. We are now in an excellent position to develop effective treatments for the millions of individuals who suffer from brain disorders.'



Meet the researcher

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Professor Mark D'Esposito earned his medical degree at the SUNY Health Science Center at Syracuse and completed clinical training in Neurology at Boston University Medical Center. After prestigious appointments at the Memory Disorders Research Center at Boston University and Braintree Rehabilitation Hospital and the University of Pennsylvania School of Medicine, he was recruited to the Helen Wills Neuroscience Institute at the University of California, Berkeley to become Professor of Neuroscience, and the Director of the newly created Henry H Wheeler, Jr Brain Imaging Center. He is also practicing neurologist at the Northern California VA Health Care System. His research investigates how the structure of the brain impacts how it recovers from injury and potential treatments for the injured brain. Over the course of his career, Professor D'Esposito has published over 375 academic articles as well editing books about cognitive neuroscience and neurology. He is currently Editor-In-Chief of the Journal of Cognitive Neuroscience, and past President of the Society for Behavioral and Cognitive Neurology and Chair of the Organization for Human Brain Mapping. Professor D'Esposito has received numerous awards and honors including the Norman Geschwind Prize in Behavioral Neurology from the American Academy of Neurology and election to the American Association for the Advancement of Science.

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FURTHER READING

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