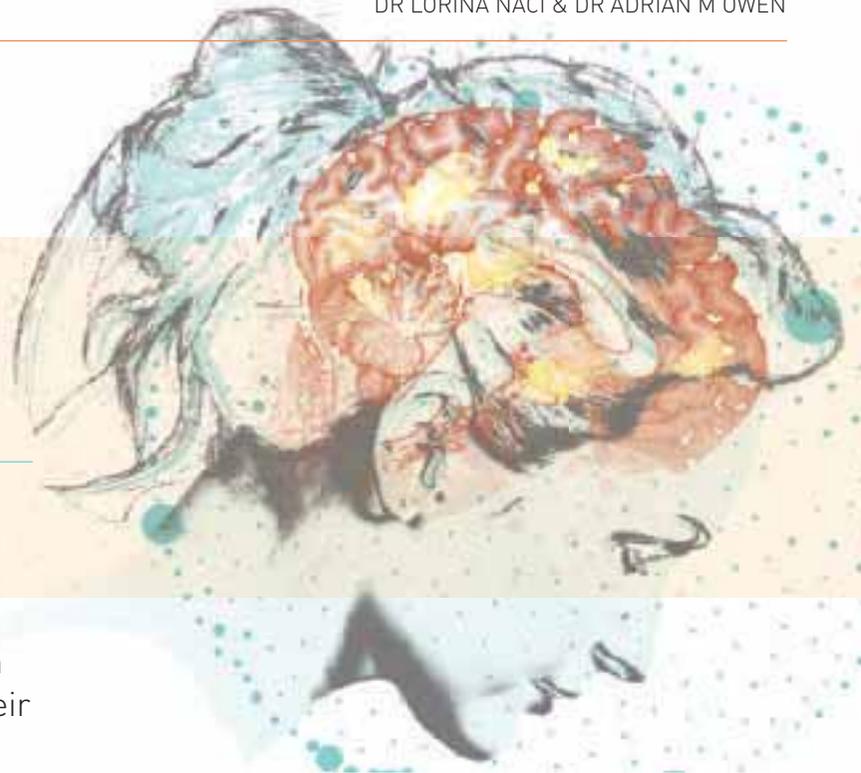


Decoding human thought

Drs Lorina Naci and **Adrian M Owen** discuss their work at the cutting edge of neuroscience, using imaging of the brain to decode the thoughts of patients in a vegetative state. They explain how a Hitchcock film helped their team to understand executive function, and detail their ambitious future objectives



Could you begin by providing the context of your current research?

LN&AO: Improvements in intensive care have led to an increased survival rate following serious brain injury. After a period of coma, some patients progress into a vegetative or minimally conscious state, characterised by the absence of purposeful behaviour. A significant proportion of these patients are conscious, but remain unable to speak or exhibit wilful behaviour, leading to a high rate (up to 43 per cent) of clinical misdiagnosis. Our research uses neuroimaging to detect covert awareness, establish communication and understand the mental life of such patients. One objective is to improve on current tests for detecting consciousness.

How does this work build on your past findings?

LN&AO: In previous work, we asked behaviourally non-responsive patients to follow commands, and therefore demonstrate conscious awareness, via their brain activity. Although this was an important step in the right direction, previous neuroimaging tests were effortful and cohort studies have shown that only one in five patients responds to these methods. We suspect that the number of patients who are aware might be higher. To address this discrepancy, we are presently working on approaches that are unconstrained by any task commands but rather capture attention naturally, and therefore might be more effective for detecting conscious awareness. Another more ambitious objective is to find out what it is like for patients to be in a vegetative or minimally conscious state, especially with respect to whether such individuals can experience the world similarly to healthy individuals.

What first sparked your interest in neuroscience?

LN: My background is in artificial intelligence and experimental psychology. I've always been intrigued by human consciousness; questions such as 'What makes human consciousness special?', or 'Can we build intelligent machines that are indistinguishable from humans?' have informed my previous work. However, how consciousness emerges from the workings of the human brain, I find the most fascinating puzzle of all, and this has led to my work in neuroscience.

Can you explain how your group utilised 'Alfred Hitchcock Presents – Bang! You're Dead' to decode vegetative state experiences? What was the rationale behind this experiment?

LN&AO: We wanted to use executive function as an empirical window for quantifying human conscious experience. However, prior to our work, laboratory tests of executive function had not been related to the open-ended nature of conscious experiences. Our solution was to investigate executive function during movie viewing. By their very nature, movies are designed to give viewers a shared conscious experience, driven in part by the recruitment of similar executive processes, as each viewer continuously integrates their observations, analyses and predictions, while filtering out any distractions – leading to an ongoing involvement in the movie's plot.

What did your findings reveal about executive function in the brain?

LN&AO: We found that when a group of healthy participants viewed this engaging short movie in the functional MRI scanner, they displayed

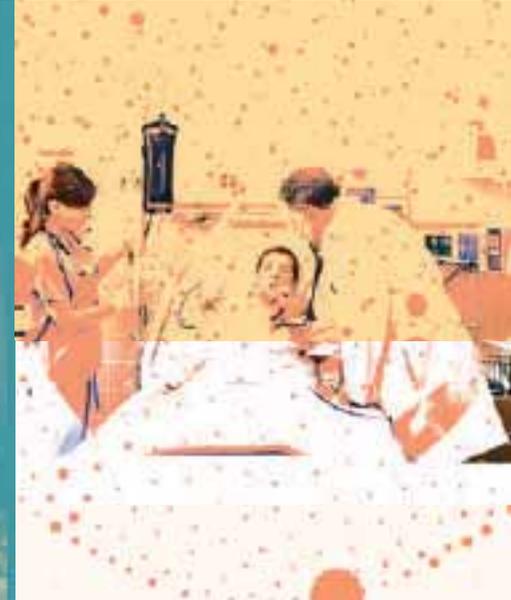
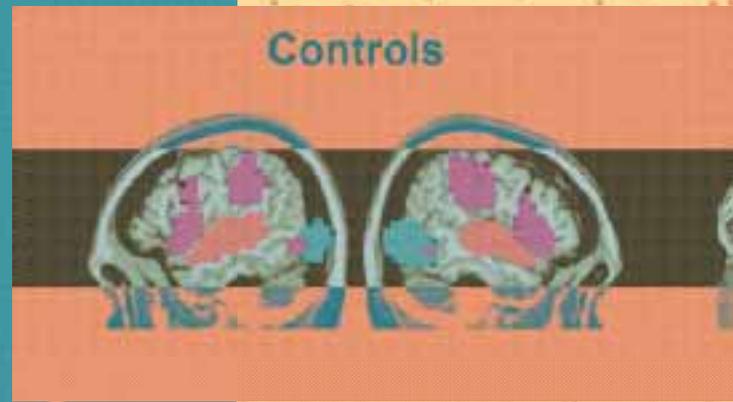
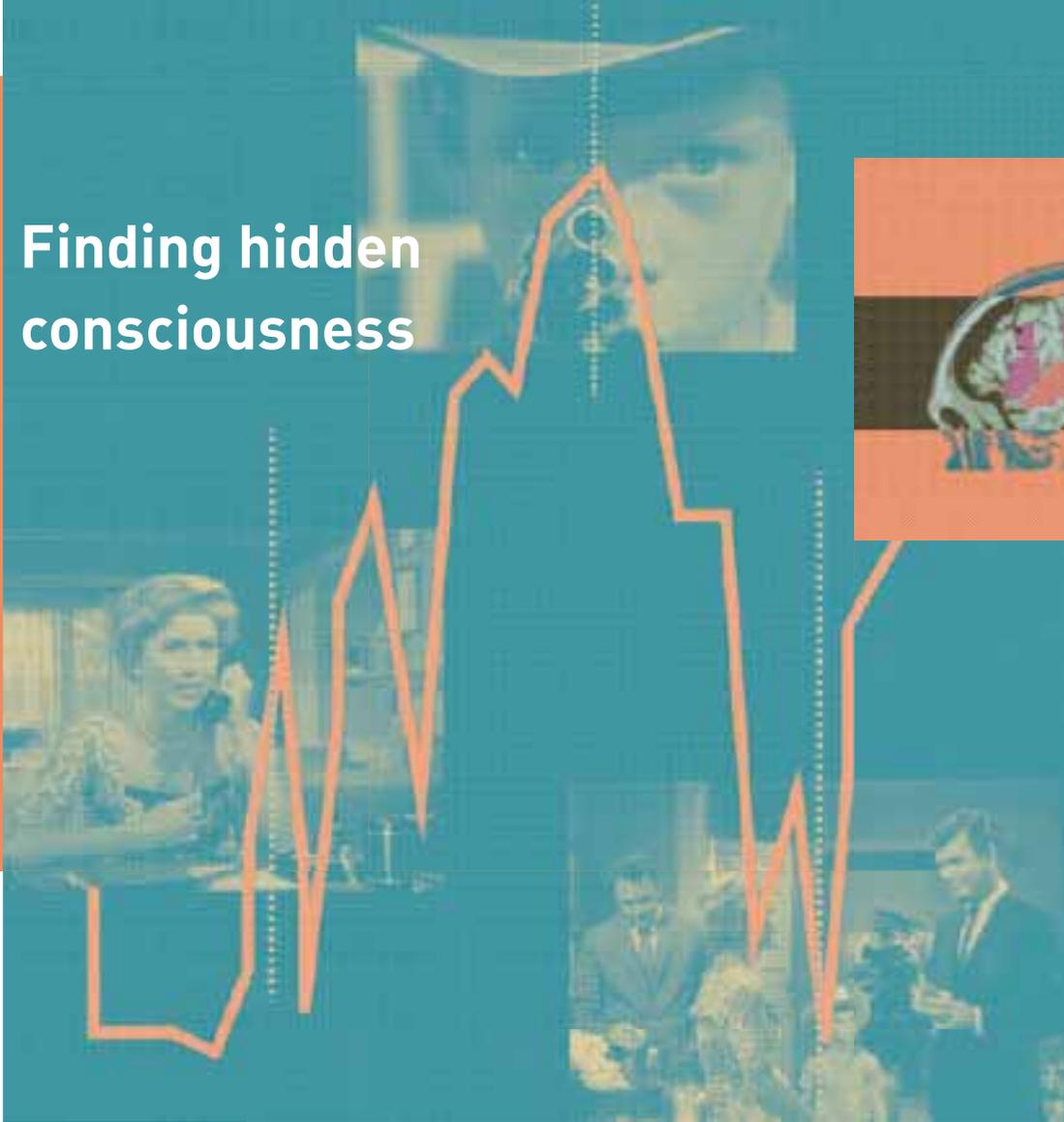
highly synchronised brain activity in the frontal and parietal regions, known to support executive function. In the context of the film, such function is essential. When the child is about to fire, to follow the plot and predict what might happen, viewers need to remember it's a real gun, appreciate that a gun is dangerous, and even think back to how many bullets were loaded in a previous scene.

The movie's executive demands, assessed quantitatively with a dual-task procedure, predicted activity in these frontal and parietal regions. Importantly, suspense ratings throughout the movie showed significant inter-subject correlation, confirming the common conscious experience of individuals watching it. Together, these results suggested that the movie's executive demands drove brain activity in frontal and parietal regions, and, further, that the synchronisation of this activity across individuals underpinned their similar experience. The degree to which each individual's frontoparietal brain activity could be predicted from the rest of the group's represented a reliable neural index of how similar his or her cognitive experience was to that of the others.

Were these findings consistent with your hypothesis?

LN&AO: Yes, as predicted, our findings suggest that a common neural code underpins similar conscious experiences, which could be used to decode these experiences in the absence of behaviour. In support of this, the same approach has recently generated strong evidence for intact consciousness in several brain injured patients.

Finding hidden consciousness



Researchers in the Brain and Mind Institute at **Western University**, Canada, have used short films and brain scanning to detect consciousness in patients in vegetative states. This approach could represent a new way of identifying individuals who are aware, but have no way of expressing it

IMAGINE BEING LOCKED in a body – fully able to think, feel and experience the world around, but entirely unable to communicate. It would be impossible to express pain, contribute to decisions about medical treatment or even decide what to eat for dinner. Sadly, this may be the status quo for many more people than is realised. For individuals who have suffered a serious brain injury, there is a risk of being left in such a vegetative state where, unlike a coma, affected individuals wake, sleep and have basic reflexes, but are unable to communicate in any way. While long believed to lack consciousness, many such patients are now known to be fully alert and simply unable to show this through movement or speech.

Indeed, because there is no simple test to identify conscious thought, many patients could be misdiagnosed as 'vegetative'. However, scientists are working on developing methods to identify thought without relying on speech or action, but instead by measuring brain activity. By decoding brain activity, researchers at Western University's

Brain and Mind Institute aim to defeat one of neuroscience's greatest challenges: interpreting human consciousness.

The group, led by Canada Excellence Research Chair in Cognitive Neuroscience Dr Adrian Owen, and including postdoctoral fellow Dr Lorina Naci, is using neuroimaging to examine the brains of non-responsive patients. In doing so, they aim to better understand brain injury, contribute to more accurate diagnoses and, ultimately, allow non-responsive patients to communicate once again.

THE SUSPENSE RESPONSE

In previous work, Naci and her colleagues, Drs Rhodri Cusack and Owen, devised a study to establish whether selective attention – the ability to selectively respond to certain stimuli – could be used as a method of brain-based communication [Naci et al. *J Neurosci* 2013; 33(22), 9385–9393]. This study, along with several others, suggested that perhaps one in five patients who appear to be vegetative is actually fully conscious.

Spurred on by the belief that this may be an underestimation, Naci recently pioneered a more sensitive technique to detect consciousness. The team – Naci, Cusack, Anello and Owen – asked participants to watch a highly engaging film while their brains were analysed by a functional magnetic resonance imaging (fMRI) scanner – a neuroimaging method that measures activity in the brain via blood flow. As brain injured patients tire easily, they needed a film that packed a complete plot into a very short period of time. They decided to use the work of Alfred Hitchcock who, in the 1950s, directed a series of TV shows called 'Alfred Hitchcock Presents'. The original short film of 30 minutes was edited by Cusack, packing the suspenseful plot into just eight minutes.

A master of suspense, Hitchcock was the ideal film maker for this experiment. His creations are layered with inference and deduction, complexities which require executive processing – the brain functions that necessitate conscious thought to coordinate basic cognitive processes.

Patient



"Executive function is integral to our conscious experience of the world, as prior knowledge is integrated into the current 'state of play' to make predictions about likely future events," Naci explains.

SIGNS OF CONSCIOUS LIFE

In order to understand the 'normal' conscious response to the film, the researchers first ran the experiment with a series of healthy participants, plotting the activity of different regions of their brain throughout the film. All 12 individuals showed similar brain patterns, with particularly intense activity in the frontal and parietal regions (linked to higher cognition) and the auditory and visual cortices (responsible for processing sensory information). They then conducted the same experiment with long-term non-responsive patients. Comparing their activity levels, the researchers made an astounding finding. The results, published last year (Naci L et al.; *PNAS*; 2014; 111(39):14277-82), showed that one of these patients had exactly the same brain activity, in the same regions and at the same time, as the healthy individuals – in fact, his brain activity was virtually indistinguishable from that of the controls.

This 35-year-old man, who became non-responsive after a tragic accident at the age of 19, had shown no signs of movement or communication, and no signs that he could hear, or even recognise objects in his environment – including his loved ones. Yet, how his brain responded to the film indicated that he was fully aware of what was happening around him. "His response suggested that he could maintain much more complex mental processes than could ever be inferred based on his behaviour," Naci articulates.

A METHOD OF COMMUNICATION

As well as showing – for the first time – that a patient with unknown levels of consciousness was able to monitor and analyse information from the environment, the study suggested that enriching experiences, such as going to the cinema or listening to music, could improve quality of life – and perhaps even facilitate

By decoding brain activity, researchers at Western University's Brain and Mind Institute aim to defeat one of neuroscience's greatest challenges: interpreting human consciousness

recovery. The father of this patient had taken his son to the cinema every week for over 15 years – previously acting on faith. Naci believes it may be possible that these experiences helped him to stay mentally active: "Exposing non-responsive patients to enriching events may not only provide fulfilling experiences, but also increase the likelihood of positive outcomes, and maybe even lead to recovery of function".

This work offers indisputable evidence that it is possible to identify consciousness in vegetative patients, and could provide a route to allowing nuanced communication – beyond answering simple yes/no questions – with these patients. It brings the team one step closer to meeting the urgent clinical need for reliable tools to detect neural signs of consciousness. While such tools may not be able to take patients out of a life of dependency, they could return some element of control to their lives, allowing them to play a role in deciding their own future.

A BETTER QUALITY OF LIFE

Looking ahead, Naci has exciting plans to develop this research further. "We would like to piece together the puzzle of residual cognitive function, to create a full picture of a patient's abilities," she describes. The researchers' aim is that by performing meaningful tests such as these, it will be possible to characterise multiple levels of cognition, from image processing to executive function. As a result, they will be able to estimate what proportion of brain function remains intact. One day, it may even be possible for a patient who is cognitively able, despite appearing unaware, to take part in their own medical decisions. "This work has profound implications for clinical care, diagnosis, medical ethics and decision making relating to the prolongation of life after severe brain injury," Naci concludes.

INTELLIGENCE

A COMMON NEURAL CODE FOR SIMILAR CONSCIOUS EXPERIENCES IN DIFFERENT INDIVIDUALS

Naci L et al.; *PNAS*; 2014; 111(39):14277-82

OBJECTIVES

To understand the effects of brain injury in order to improve diagnosis and early detection and find possible new treatments.

KEY COLLABORATORS

Dr Rhodri Cusack, The Brain and Mind Institute, Western University, Canada, www.cusacklab.org

PARTNERS

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DR LORINA NACI obtained her PhD as a Cooke Scholar from the University of Cambridge, UK, and is presently a postdoctoral fellow at Western University, Canada. She

uses neuroimaging to understand how consciousness emerges from the human brain. Naci's work has been published in high-impact scientific journals and covered widely in the international media.



DR ADRIAN M OWEN gained his BSc in Experimental Biology from University College London, before completing his PhD at the University of London, both in the

UK. Following a postdoctoral position at the Montreal Neurological Institute in Canada, Owen relocated to the University of Cambridge, UK. In 2011, Owen returned to Canada to take up the prestigious position of Canada Excellence Research Chair in Cognitive Neuroscience and Imaging at Western University.

