AMAZING PAPERS IN NEUROSCIENCE
Unlocking Hidden Awareness: Repurposing fMRI to Detect Levels of Consciousness

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Determining the state of consciousness in patients with disorders of consciousness is a challenging task because for someone to be deemed conscious, both wakefulness and awareness are required. Awareness has traditionally been assessed by examining physical responsiveness but in 2010, Monti et al. explored how using fMRI to measure brain activity in humans could help reclassify the state of consciousness in these patients. The findings, published in *The New England Journal of Medicine*, show that some brain regions are active when patients respond to an imagery or communication task. This is a seminal study because it demonstrates that patients who behaviourally appear to be in a vegetative or minimally conscious state may still have residual brain functions that would not be apparent from a clinical examination alone. Notably, it exemplified how fMRI can be repurposed as a communication tool for this subset of aware, but 'locked in', patients who appear unresponsive. From an educator's perspective, this paper is valuable because it is relevant to a broad audience, both introductory and advanced level undergraduate students. It introduces key concepts in cognitive and clinical neuroscience and encourages students to consider the connections between social issues and technology development in neuroscience. Finally, educators may use this paper to discuss and debate the nature of consciousness and the ethical implications that the use of fMRI for determining consciousness may have on medical ethics.

Key words: Consciousness Disorders, Persistent Vegetative State, Functional Neuroimaging

Disorders of consciousness (DOCs) are among the most challenging consequences of traumatic brain injury, affecting 10-15% of brain-injured patients worldwide (Xie et al., 2017). DOCs reduce patients to vegetative and unresponsive states and there are few reliable ways to assess consciousness in patients with DOCs. The study of brain activity in these patients has gained increasing attention over the past decades, fueled by advancements in neuroimaging techniques such as positron emission tomography (PET), functional magnetic resonance imaging (fMRI), and electroencephalography (EEG) (Demertzi et al., 2017). DOCs broadly encompass varying levels of cognitive dysfunction: from milder delirium and dementia, to coma, vegetative state (VS); absence of responsiveness and awareness), and minimally conscious state (inconsistent, but discernible conscious behaviours) (Calabrò and Naro, 2016). Within DOCs, each subtle, yet distinctive degree of consciousness presents unique diagnostic and prognostic dilemmas. Understanding this spectrum of consciousness and investigating brain activity patterns in patients with DOCs hold immense clinical and scientific relevance, offering insights into the mechanisms underlying consciousness and facilitating accurate and consistent diagnosis, treatment, and ethical decision-making. Given the significance that DOCs pose in clinical practice, it is paramount that neuroscience students understand the nuances of the consciousness spectrum, as well as the ethical considerations and implications that arise in managing such complex conditions. In this paper, we examine the work of Monti et al. (2010), which highlights the potential of neuroimaging techniques to differentiate between levels of consciousness, and we identify key aspects of their research that could be used to supplement the education of undergraduate neuroscience students.

SUMMARY

Monti et al. offer evidence that some clinically diagnosed vegetative patients may be able to control their brain activity, despite an initial presentation of a lack of awareness. This study builds off an earlier case by Owen et al. (2006) which examined an individual who suffered a traumatic brain injury (TBI) and was diagnosed as vegetative. Using fMRI, researchers noted that the patient exhibited clear brain activation in response to language and was able to follow mental commands by picturing spatial and motor imagery-based activities, such as exploring a familiar place for the former or playing tennis for the latter. This patient displayed increased activation in the parahippocampal gyrus and supplementary motor area (SMA) respectively, recapitulating the activation patterns of healthy brains. These results confirm that despite an initial VS diagnosis, the patient clearly understood and demonstrated cognitive responsivity to commands.

Monti et al. decided to examine this phenomenon on a much larger scale with 54 patients diagnosed as either in a minimally conscious or VS. They aimed to determine the

prevalence of this event of consciousness in seemingly unaware individuals as well as to validate fMRI as a communication tool for this population. All participants were tested using the same spatial and motor imagery tasks from Owen et al. (2006).

Monti et al. (2010) identified five of the 54 patients who exhibited significant fMRI brain activation, similar to that of the healthy controls. Four of these participants showed clear increased activation of the parahippocampal gyrus when thinking of the spatial compared to the motor activities, and five showed clear increased activation of the SMA when thinking of the motor compared to the spatial activities.

Additionally, a single patient was given a communication task where they were instructed to answer “yes” or “no” questions by picturing the motor activity for one answer and the spatial activity for another. Notably, this patient was able to answer five out of the six questions presented to them. For example, in response to the question “Do you have any brothers?”, they were directed to imagine themselves playing tennis to indicate a response of “yes” or to envision themselves spatially navigating their house to indicate a “no”. The patient demonstrated activation in the SMA to convey an affirmative response, which was factually correct. This methodology was validated by group of 16 healthy controls.

Overall, these results support the notion that in some previously characterized VS patients there may be a degree of consciousness not evident in a physical exam as well as for the use of fMRI as a communication tool for this subset of aware patients. Importantly, Monti et al. (2010) do identify certain limitations with their research, such as the fact that, upon re-examination, two of the responsive VS patients were found to have some overlooked physical behavioral signs of consciousness, making their original diagnosis incorrect. Despite its limitations, this study offers promising insights into the field of clinical neuroscience and, more specifically, the treatment of DOCs.

TEACHING VALUE

The utility of this paper in teaching undergraduate neuroscience lies primarily in the sheer diversity of topics that it encompasses and thus, modules that it can be tailored to supplement. Broaching concepts from consciousness and neuroimaging all the way to ethics and science communication, this paper is both informative on specific themes in neuroscience, whilst unique in the opportunities it offers to foster thought-provoking discussion amongst budding scholars. By virtue of its significant contributions to the field alone (i.e., the discovery of evidence of awareness in DOC patients and a novel technique that is not contingent on behavioral responsivity), the article serves as an optimal initiator to consciousness research and its translation from the bench to the bedside. In this vein, the paper can also be a valuable resource to present in more specialized topics of clinical neuroscience, for example, introductions into extant assessments of consciousness, and the promise and practicalities of implementing fMRI as a reproducible mode of communication in DOCs. It is additionally worth noting that throughout the text the authors employ precise vocabulary and diagrams that describe the fundamentals of fMRI, without delving deeply into their minutiae. As a result, the paper is highly informative whilst also accessible to all levels of undergraduate students and thus acts as an ideal device to bridge a foundational understanding of fMRI methodology and data interpretation. Moreover, an examination of the paper alongside the case report by Owen et al. (2006) that prompted it can be drawn on to introduce students to a host of research methods and designs that are ubiquitous in cognitive neuroscience, such as the evolution of single case studies into larger investigations.

At more advanced stages of neuroscience education, this paper represents an attractive tool to introduce students to ethical issues surrounding scientific publications. Indeed, this high-profile area of scientific enquiry is exemplary for its conspicuous societal implications**,** offering ample space for engagement in debates. For instance, Monti et al. (2010) leave the reader pondering about the profound impacts of this methodology on legal decisions (i.e., can we use fMRI to ask patients whether they wish to prolong or discontinue their lives?). Such questions may evolve into analytical considerations regarding the reliability of this emerging technology in judging whether a patient is truly responsive. Moreover, because of its substantial press coverage and featuring in the BBC documentary ‘The Mind Reader’, this paper is a powerful means for learning about scientific communication with a lay audience and accurate scientific reporting. Notably, this paper also provides an illustration of how research methodologies are applied to clinical settings and used to solve real world problems. Indeed, in Monti et al. (2010) fMRI acquires a new technical nuance as a brain-machine interface. Thus, this paper encapsulates new avenues for teaching students how existing scientific methodologies can re-emerge as new tools with new applications, and how they can be re-contextualized. Ultimately, this technology has emerged in more recent years as a powerful tool for communication with unresponsive patients, beyond DOCs. For instance, its application to patients affected by Guillain-Barré syndrome has been exceptional for assessing whether these patients retained auditory function and command following abilities as well as for communication (Norton et al., 2023). In another example, fMRI enabled detection of consciousness in epileptic patients during absence seizures, defined as episodes of brain overactivation accompanied by sudden lapses of consciousness (Gotman, 2013). This methodology has also been re-explored via functional near-infrared spectroscopy to detect brain activity, accompanied by a visuo-mental paradigm for communication with late-stage paralyzed amyotrophic lateral sclerosis patients (Borgheai et al., 2020). These publications suggest new directions for the use and adaptations of brain imaging techniques.

Reading Monti et al. (2010) together with follow-up papers in the field highlights the pivotal importance of thinking about research as a circular process rather than a linear one, with generations of researchers returning to ‘drink from the same well’ while also breaking new ground.

AUDIENCE

A unique selling point of this article is that it is relevant and accessible to a wide range of audiences. For students earlier

on in their undergraduate degree, this paper provides a solid introduction to operational definitions of consciousness, DOCs, and how DOCs are assessed clinically. It also provides a platform for understanding the basics of the foundational neuroimaging technique fMRI, which can be quite difficult for students to grasp. Importantly, the authors also consider and discuss limitations to their approach; for example, they point out how DOCs are often more nuanced than traditional diagnoses account for. They also highlight that fMRI information is not as definitive as it might seem (for example, increased neural activity is not necessarily a demonstration of consciousness). It is as important to learn about the limitations of these methodologies as it is to learn about their potential benefits. Thus, this paper can be incorporated into a first- or second- year curriculum as pre-reading for a lecture or as an additional resource for an introductory topics class.

For students later in their academic careers, this paper offers an opportunity for critical discussion and debate. Topics discussed include the validity of this methodology for communication with non-communicative patients, to the flexibility of the research process and whether the unexpected findings from a single case study could be sufficient reason for further research. This paper raises a number of ethical debates. For example, it could be applied to pose questions to the patients regarding their wishes about continuation of life support. Ideally, this paper would be included in third- or fourth- year seminars and workshops where students have space to engage in these important debates and develop skills of critical thinking and analysis. This work serves as an entry point into discussing the development of brain machine interfaces that could improve quality of life and prospects of recovery for 'locked-in' patients.

CONCLUSION

Overall, the pioneering study by Monti et al. (2010) serves as an example of an amazing paper that can be adapted to a variety of teaching situations in neuroscience. It introduces first- or second-year undergraduates to fundamental concepts of consciousness, fMRI, and ethics in decision-making. Additionally, it provides an excellent opportunity to teach upper-level undergraduates about the ethical dimensions of human brain imaging research while fostering the development of their critical thinking skills. The multidisciplinary nature of this paper holds promise of engaging students across various academic fields such as cognitive and clinical neuroscience. Fundamentally, this research impacts the field of neuroscience by demonstrating the use of fMRI to elucidate patient consciousness. Monti et al. (2010) offers a unique opportunity for undergraduate neuroscience education by sparking a thoughtful debate about how we approach DOCs as a society.

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