Using Neuroimaging to Detect Covert Awareness and Determine Prognosis of Comatose Patients: Informing Surrogate Decision Makers of Individual Patient Results

Mackenzie Graham, PhD[1] Colin P. Doherty, MD[2] Lorina Naci, PhD[3]

[1] Oxford Uehiro Centre for Practical Ethics, Oxford University, Oxford, United Kingdom
[2] Department of Neurology, St. James's Hospital, Dublin, Ireland
[3] School of Psychology, Trinity College Dublin, Dublin, Ireland

Address for correspondence Lorina Naci, PhD, Department of Psychology, School of Psychology and Global Brain Health Institute, Trinity College Dublin, Dublin D02 PN40, Ireland (e-mail: nacil@tcd.ie).

Semin Neurol 2018;38:555–560.

Abstract

Robust prognostic indicators of neurological recovery are urgently needed for acutely comatose patients. Functional neuroimaging is a highly sensitive tool for uncovering covert cognition and awareness in behaviorally nonresponsive patients with prolonged disorders of consciousness, and may be applicable to acutely comatose patients. Establishing a link between early detection of covert awareness in acutely comatose patients and eventual recovery of function could have significant implications for patient prognosis, treatment, and end-of-life decisions. Because functional neuroimaging of acutely comatose patients is currently limited to the research context, ethical guidelines for disseminating a patient's individual research results to clinical teams and surrogate decision makers are needed. We propose an ethical framework composed of four conditions that can guide ethical disclosure of individual results of neuroimaging research in the acute care context.

Keywords

- neuroimaging
- disorders of consciousness
- brain injury
- disclosure
- research
- ethics

Improvements in intensive care have led to an increased survival rate following coma—the acute state of behavioral nonresponsiveness immediately after a brain injury—during which patients exhibit no evidence of awareness of themselves or of the environment.[1] Long-term patient outcome is highly variable. Some will die, others will go on to make a good recovery, and a third group will progress into a minimally conscious state, or a state of behavioral nonresponsiveness with prolonged disorders of consciousness (PDOC). Patients who remain entirely behaviorally nonresponsive are thought to lack consciousness, and diagnosed as being in a vegetative state.[2] There are currently few tools for assessing brain function during coma, and none offers accurate prognostic indicators of recovery for individual patients. Critically, this prognostic uncertainty during coma frequently biases medical decisions in favor of withdrawing life-sustaining therapies early, typically within the first 72 hours.[3]

Neuroimaging research in behaviorally nonresponsive patients with PDOC[4–11] has established that a lack of behavioral response in severely brain-injured patients does not necessarily imply a lack of consciousness. Studies have found that a proportion of entirely behaviorally nonresponsive patients are not only consciously aware, but critically may have highly preserved levels of mental life.[10,12] Furthermore, recent research shows that some patients who are diagnosed as being unconscious according to internationally agreed upon criteria for the vegetative state (e.g., Coma Recovery Scale-Revised[13]) can go on to have significant recovery of function, including full recovery of consciousness and functional communication.[14]

The functional magnetic resonance imaging (fMRI) assessments used in patients with PDOC involve asking patients to follow specific commands by modulating their brain activity according to the researcher's instructions, or simply to follow along an engaging narrative. In one such neuroimaging paradigm,[4] patients are asked to perform motor (e.g., playing tennis) or spatial navigation (e.g., moving around their house) imagery, or relax, in on–off blocks of 30 seconds. In another kind of paradigm,[9] patients are asked to either

Issue Theme Ethics in Neurology; Guest Editors, Ariane Lewis, MD, and James L. Bernat, MD

DOI https://doi.org/10.1055/s-0038-1667385.
ISSN 0271-8235.

selectively attend to the presentation of a target word while ignoring a nontarget word (either "yes" or "no") or relax, in on–off blocks of 30 seconds. Patients who successfully perform these tasks show task-appropriate (on–off) activity in prespecified brain regions that is statistically similar to that of healthy controls, reproducible, and sustained over long time intervals, allowing researchers to unequivocally conclude that the patient is following commands and, therefore, is consciously aware.

More recently, Naci and colleagues[10] developed a movie-viewing paradigm for the investigation of conscious experiences of behaviorally nonresponsive patients who retain covert awareness, but cannot follow commands due to impaired attention from the brain injury. They focused on the assessment of executive function—a high-level cognitive function that requires conscious awareness—while participants watched a brief (8 minutes) and highly engaging movie by Alfred Hitchcock. Naci and colleagues found that the time course of the activation in frontal and parietal brain regions—known to support executive function—provided a template for decoding whether behaviorally nonresponsive patients exercise similar executive function as healthy individuals in response to the executive demands of the movie. Using this approach, they demonstrated that a PDOC patient who was behaviorally nonresponsive and thought to lack consciousness for 16 years was consciously aware and could continuously engage in complex thoughts about real-world events unfolding over time.[10]

It is worth noting that a negative result in these neuroimaging assessments does not imply a lack of awareness, but rather that no evidence of awareness was detected. This could be due to a genuine lack of awareness, but it could also be due to an inability to perform the task, for example, the patient may not have understood the instructions or may have fallen asleep during the task. Indeed, in some cases, an absence of activation to a specific task can be observed even in healthy individuals. Thus, a negative neuroimaging result provides no additional information beyond the patient's clinical assessment at their bedside. Conversely, if a positive neuroimaging effect is detected, the brain-injured patient's ability to follow commands via brain activity, or closely follow a narrative that develops over time, provides evidence of a complex cognitive repertoire—beyond preserved awareness—including language comprehension, attention, decision making, working memory, and executive function.

This body of research has demonstrated that fMRI is a highly sensitive tool for uncovering covert cognition and awareness in behaviorally nonresponsive patients with PDOC who are clinically diagnosed as being in a vegetative state, and suggests that, similarly, a proportion of comatose patients may retain preserved covert cognition and awareness, despite their apparent nonresponsiveness. In light of these findings, fMRI provides a promising avenue for detecting covert consciousness in the comatose patient population. Indeed, a recent study by Edlow and colleagues[15] found that three patients in the intensive care unit (7–15 days post-injury) who were clinically diagnosed as lacking consciousness demonstrated the ability to follow commands via functional neuroimaging by willfully modulating their brain activity according to instruction. Uncovering covert cognition and consciousness in acutely comatose patients could have important implications for patient prognosis, an area currently poorly understood. Robust prognostic indicators of neurological recovery in this group are desperately needed,[2] and neuroimaging research to ascertain the presence of covert awareness and its relationship to subsequent recovery of function could have profound implications for patient prognosis, treatment, and end-of-life decisions. However, any potential benefit to the patient arising from the acknowledgment of their current covert cognition, awareness, and any prognostic indicators is possible only if researchers can share and discuss the results for individual patients with their surrogate decision makers and medical care team. Therefore, ethical guidelines for the dissemination of research results to surrogate decision makers and medical teams are urgently needed.

To date, the majority of neuroimaging studies that have investigated covert awareness in severely brain-injured patients have been conducted in patients with PDOC; so, disclosure of individual results has pertained to patients who are several years post injury, and whose prognosis is unlikely to change. By contrast, research involving acutely brain-injured patients—within days to a few weeks post initial injury—poses unique challenges because it may impact on end-of-life decisions for those patients. Full acknowledgment of these challenges compels us to ask whether it is ethically permissible to disclose individual results of functional neuroimaging research in the acute patient context. To address this question, we propose an ethical framework composed of four conditions that can guide ethical disclosure of individual research results in the acute care context.

Ethical Principles Supporting the Disclosure of Individual Research Results

Existing ethical guidelines appeal to the principle of beneficence to justify the disclosure of research results to individual research participants.[16–18] These guidelines are based on the presumption that disclosure of individual research results is an exceptional circumstance and should occur only when the results are scientifically valid and have significant implications for the patient's health such that there is a clear clinical benefit to disclosure, such as when results pertain to a condition for which effective treatment is available. Conversely, some critics have argued that guidelines for disclosure grounded in beneficence—that is, sharing only results with clinical utility—are too restrictive, and prevent the disclosure of individual research results that participants may want.[19] They argue that the principle of respect for persons justifies disclosing any individual research results that might have meaning or personal utility for participants, even if they have little to no clinical significance or relate to conditions for which effective treatment does not exist.[19] For example, a genetic test revealing misattributed paternity may have no clinical utility, but can have considerable personal utility for a participant. Disclosing individual research results also shows respect for the

participant's self-determination, by allowing them to incorporate individual research results into their own decision making, and shows gratitude for their participation in research.[19] Lastly, it has been argued that individuals have the right to determine with whom their personal information, such as the information gained through clinical research, should be shared, including themselves.[20]

In previous work,[21] we argued that appropriate guidelines for the disclosure of individual research results must account for both beneficence and respect for persons. Accordingly, we argue that researchers ought to disclose individual research results to the surrogate decision makers of severely brain injured patients when four conditions are met: (1) disclosure does not undermine the scientific validity of the study; (2) results are informative and reliable; (3) the potential benefits of disclosure, including clinical benefits and personal utility or nonclinical benefits, outweigh potential harms; and finally, (4) the participant or surrogate decision maker consents to be informed of the results.

Because acutely comatose patients lack the capacity to consent to participate in research, informed consent to participation is provided by the patient's surrogate decision maker. This individual, typically a close family member, is entrusted with making decisions on behalf of the noncompetent patient. Accordingly, in the present context, it is the patient's surrogate decision maker to whom individual research results would be disclosed. Of note, we refer to a patient's "surrogate decision maker" throughout, while recognizing that surrogate decision making often is a collaborative process between family members and medical staff.

Neuroimaging research in the acute patient context has two aims, and thus, its results have two potential applications. First, this research aims to uncover covert cognition and awareness in comatose patients through functional neuroimaging. A positive result on a given neuroimaging paradigm would provide robust evidence of covert cognition and awareness. This information is available to researchers immediately after the completion of functional neuroimaging. Second, this research aims to inform patient prognosis by illustrating the relationship between covert awareness detected shortly after severe brain injury and a patient's eventual recovery of function or lack thereof. To achieve this aim, results must be collected from a large population of patients over an extended period; so, data generated early in the research program will have minimal prognostic value. In the next sections, we consider how the aforementioned four conditions guide disclosure of research results with regard to both the presence of covert cognition and consciousness and patient prognosis.

Is Disclosure Consistent with Scientific Validity?

A major concern with disclosure of individual research results to a participant's surrogate decision maker is that doing so may compromise the scientific validity of a study. As the primary goal of research is to generate knowledge for the benefit of society, if disclosure compromises scientific validity, it deprives society of the potential benefits of the research.

In the context of patients with PDOC, disclosure of individual research results does not compromise scientific validity, because disclosure of the results obtained from one patient does not affect the results of another. Disclosure occurs after the conclusion of each individual patient's self-contained case study,[4,10] and accordingly does not impact on the researcher's interpretation of the broader, group-level results, nor the research protocol for the next patients.

In the acute context, however, the effect of disclosure on the scientific validity of the study is more complex. As previously mentioned, one of the two goals of this research is to generate information that will improve the accuracy of prognosis for acutely comatose patients. While researchers can gain immediate insight into the presence of covert cognition and awareness on a patient-by-patient basis, each patient remains part of the study after the initial scanning. Their progress over time is assessed against the initial neuroimaging results to evaluate the prognostic value of the neuroimaging findings in the comatose state. Disclosure may impact a patient's natural progression by influencing the end-of-life decision made by the surrogate decision maker and medical team. For example, disclosure that an individual patient has demonstrated, or failed to demonstrate, evidence of covert cognition and awareness may influence a decision to continue, or withdraw, life-sustaining therapy, thereby creating a selection bias for the assessment of the relationship between the results of functional neuroimaging and prognostication.

To avoid this potential bias, it is important that surrogate decision makers clearly understand the nature of neuroimaging research in comatose patients. On the one hand, failure to detect covert awareness offers no new information; thus, disclosure should not influence the surrogate's decision making. On the other hand, disclosure of a positive result in the absence of prognostic utility ought not to be used to inform treatment or end-of life decisions. Nevertheless, disclosure of a positive result may influence surrogate decision making, independent of any prognostic evidence. Given the diversity of values that inform surrogate decision making, we suggest that it is unclear how the presence of covert awareness will influence particular treatment or end-of-life decisions. Therefore, we provisionally argue that disclosure can be consistent with scientific validity, provided suitable conditions are in place for avoiding this potential confounder. For example, surrogate decision makers may need to agree not to withdraw life-sustaining treatment from the participant for the duration of the prognostic study as a condition of enrollment, or make other assurances that disclosure will not impact the withdrawal or continuation of life-sustaining treatment. Alternatively, surrogates may need to agree to delay disclosure of research results until the conclusion of the prognostic study. If these conditions cannot be met, surrogate decision makers would remain free to withdraw from the study at any time.

Are the Individual Research Results Informative and Reliable?

For the disclosure of individual research results to be beneficial to participants or their surrogate decision makers, the

results must be informative and reliable. The neuroimaging paradigms that can be used to detect covert awareness in acutely comatose patients have been validated over numerous studies in healthy participants and PDOC patients.[4,6,9,10] As discussed earlier, a negative neuroimaging result provides no additional information beyond the patient's bedside clinical assessment. By contrast, a positive result provides robust evidence of covert awareness for individual patients and, depending on the nature of the assessment, also provides specific information on preserved cognitive capacities.

In addition to providing reliable information about the presence of covert cognition and awareness, individual results of functional neuroimaging research in the acute context may, in the future, provide reliable prognostic information about patient recovery or lack thereof. Currently, there is insufficient evidence to allow for prognostication based on a patient's functional neuroimaging results. Thus, the disclosure of the patient's neuroimaging research result is both informative and reliable only with respect to the presence of covert cognition and awareness. Until this research matures to enable reliable prognostic inferences for individual patients, researchers must clearly convey to the surrogate decision makers that the patient's individual research results do not provide definitive prognostic information about the recovery of function or lack thereof. This guidance must take place prior to enrolling them in the study, and again prior to disclosure of research results.

Do the Potential Benefits of Disclosure Outweigh the Potential Harms?

In previous work,[21] we argued that disclosure of positive individual research results, such as the presence of covert cognition and awareness, to the surrogate decision makers of patients with PDOC is likely beneficial to the patient. It acknowledges them as persons with subjective interests, and may positively alter the way they are treated and cared for by others, including justifying further attempts at communication with them. Conversely, while the disclosure of negative research results may in some cases result in emotional distress to the patient's family, if they have consented to disclosure, it suggests respect for their contribution to the research endeavor and may be rewarding on this basis. As mentioned earlier, the circumstances of disclosure in the acute patient context are more complex. Individual research results in this context have diagnostic and prognostic relevance and both sets of potential benefits and harms must be weighed to determine whether disclosure is ethically permissible.

Potential Benefits and Harms of Information Pertaining to Covert Cognition and Awareness

We argue that a greater understanding of the patient's condition will, *in general but not always*, help surrogate decision makers act in the best interests of the patient. Disclosure of a positive research result provides the surrogate decision maker information about the patient's preserved awareness and specific cognitive capacities, including language comprehension, attention, decision making, working memory,[4,5,8] and executive function.[10,12,22] Knowledge of a patient's covert awareness and capacity to understand communication validates the family's and medical care staff's attempts to communicate with them and will likely enhance the quality of interactions with the patient.[21] Studies suggest that communicating with patients with disorders of consciousness as if they were aware promotes their well-being by acknowledging their value and demonstrating a sense of genuine care for them.[23] In cases where patients recover consciousness, these interactions are what they remember. Furthermore, the presence of covert awareness suggests that a patient is capable of subjective experiences, such as the experience of pleasure or pain, which may warrant specific interventions, for example, administration of pain medication.

If a patient previously expressed the desire to receive life-sustaining treatment provided they have preserved consciousness, disclosure of a positive individual research result would be beneficial for the patient. Disclosing a negative research result (i.e., that no evidence of covert cognition or awareness was detected) does not add any new information and, as discussed in the previous section, if results are conveyed clearly, should not influence the decision making on behalf of the patient. It is important that researchers collaborate with the patient's clinical team to clearly situate the research results in the context of the patient's other clinical data to ensure that surrogate decision makers do not overestimate, or underestimate, the clinical utility of the research results.

In some cases, disclosure of neuroimaging results may prompt a decision that is not in the best interest of the patient. For example, in the face of a positive neuroimaging result, a surrogate decision maker may choose to maintain life-sustaining treatment even without indication of a positive prognosis, while, unbeknownst to the surrogate, this is not what the patient would have wanted.[24] Some surrogate decision makers may also find it more difficult to withdraw life-sustaining treatment from a patient known to be conscious, even if this is what they believe the patient would want. Surrogate decision makers may feel pressured by clinical staff or others to make certain treatment decisions based on positive or negative research results, independent of what the patient would have wanted. These cases underscore each surrogate decision maker's difficult task. They also demonstrate the important role of researchers and clinical and support staff in helping surrogate decision makers to frame and weigh potential treatment options given a complete picture of the patient's condition and the patient's values, while refraining from biasing their decision. In light of the above scenarios, we argue that information about the patient's condition can enhance the decision-making process of surrogates, but cannot ensure the best outcome with respect to the patient's interests, for all patients.

Potential Benefits and Harms of Prognostic Information

Early in the trajectory of functional neuroimaging research involving comatose patients, individual research results have limited prognostic utility; so, there are no prognostic benefits to the disclosure of a patient's functional neuroimaging results.

Despite this limitation, it is possible that surrogate decision makers will have difficulty understanding the lack of prognostic utility of individual research results and will use them to form their own conclusions about patient prognosis, and ultimately, the decisions they make on behalf of the patient. If this occurs, the potential harm to the patient of disclosure may outweigh its potential benefits. For example, if the disclosure of positive research results for individual comatose patients biases the surrogate decision maker to overestimate the likelihood or extent of possible recovery, this may fail to serve the best interests of the patient. Conversely, if a lack of evidence for covert awareness is mistakenly interpreted as indicating a negative prognosis, this may bias them toward withdrawal of life-sustaining treatment.

For these reasons, it is critical that, until neuroimaging research can provide robust prognostic information for individual patients, researchers work with the clinical team to clearly communicate to surrogate decision makers the gap between preserved cognition and awareness in the comatose state (if present) and future recovery of functions to surrogate decision makers during the consent process, as well as prior to the disclosure of research results. Once this line of research yields prognostic utility, the benefits of disclosure will outweigh its potential harms in as much as surrogates use information about future recovery of function or lack thereof to make decisions that align with the patient's best interests.

Does the Decision Maker Consent to Disclosure?

When disclosure of individual research results satisfies the three aforementioned criteria, researchers ought to make individual research results available to the surrogate decision makers, who may then consent or decline to have the results disclosed to them. The process of disclosure should be discussed with the surrogate decision maker as part of the informed consent process prior to enrolling in the study, and the surrogate should have the opportunity to revise his or her decision prior to the actual disclosure.

A clear plan regarding how disclosure is to occur in the acute setting ought to be a prerequisite of ethical protocols for programs performing functional neuroimaging research on severely brain-injured patients. It may also be necessary for researchers to help correct any misconceptions about this research generated by the popular press.[25] Given the potential implications for decision making on behalf of the patient, it is critical that, when recruited for the study, surrogate decision makers clearly understand the potential outcomes of research with respect to preserved cognitive function and awareness in the comatose state, as well as patient prognosis, and what can and cannot be inferred from them. Current limitations about inferences regarding patient prognosis should be emphasized. As statistically significant information pertaining to prognosis emerges, it should be made available to the surrogate decision makers of those participants who continue to be enrolled in the studies, as well as surrogate decision makers considering participation in the research.

Conclusion

Functional neuroimaging research has the potential to improve our current understanding of preserved cognition and awareness in the comatose state and prognostic accuracy for acutely brain-injured patients. Therefore, it could dramatically impact the practice of medicine for this patient group. However, questions remain about the ethical permissibility of disclosing individual research results to the patients' surrogate decision makers. In prior work, we argued that individual research results may be shared with surrogate decision makers of patients with PDOC when four conditions are met: (1) disclosure is consistent with scientific validity; (2) the results are informative and reliable; (3) the potential benefits of disclosure outweigh the potential harms; and finally (4) the surrogate decision maker consents to disclosure. In our examination of the unique challenges of disclosure of individual research results in the context of comatose patients, we conclude that it is possible for these conditions to be met in some circumstances, and in those cases, individual research results should be made available to surrogate decision makers. We emphasize the importance of clear and transparent communication with surrogate decision makers, to ensure their understanding of the research results so that disclosure is beneficial to the patient.

Conflict of Interest
The authors declare that there is no conflict of interest.

Acknowledgments
This research was supported by the L'Oréal for Women in Science Research Excellence Fellowship and the Wellcome Trust Institutional Strategic Support Fund to L.N. and a Wellcome Centre Grant to the Wellcome Centre for Ethics and Humanities for M.G.

References

1 Young GB. Coma. Ann N Y Acad Sci 2009;1157:32–47
2 Turgeon AF, Lauzier F, Simard JF, et al; Canadian Critical Care Trials Group. Mortality associated with withdrawal of life-sustaining therapy for patients with severe traumatic brain injury: a Canadian multicentre cohort study. CMAJ 2011;183(14):1581–1588
3 Multi-Society Task Force on PVS. Medical aspects of the persistent vegetative state (1). N Engl J Med 1994;330(21):1499–1508
4 Owen AM, Coleman MR, Boly M, Davis MH, Laureys S, Pickard JD. Detecting awareness in the vegetative state. Science 2006;313 (5792):1402
5 Monti MM, Vanhaudenhuyse A, Coleman MR, et al. Willful modulation of brain activity in disorders of consciousness. N Engl J Med 2010;362(07):579–589
6 Cruse D, Chennu S, Chatelle C, et al. Bedside detection of awareness in the vegetative state: a cohort study. Lancet 2011;378 (9809):2088–2094
7 Bardin JC, Fins JJ, Katz DI, et al. Dissociations between behavioural and functional magnetic resonance imaging-based evaluations of cognitive function after brain injury. Brain 2011;134(Pt 3):769–782
8 Fernández-Espejo D, Owen AM. Detecting awareness after severe brain injury. Nat Rev Neurosci 2013;14(11):801–809
9 Naci L, Owen AM. Making every word count for nonresponsive patients. JAMA Neurol 2013;70(10):1235–1241

10 Naci L, Cusack R, Anello M, Owen AM. A common neural code for similar conscious experiences in different individuals. Proc Natl Acad Sci U S A 2014;111(39):14277–14282
11 Stender J, Gosseries O, Bruno MA, et al. Diagnostic precision of PET imaging and functional MRI in disorders of consciousness: a clinical validation study. Lancet 2014;384(9942):514–522
12 Naci L, Graham M, Owen AM, Weijer C. Covert narrative capacity: mental life in patients thought to lack consciousness. Ann Clin Transl Neurol 2017;4(01):61–70
13 Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. Arch Phys Med Rehabil 2004;85(12):2020–2029
14 Naro A, Calabrò RS, Pollicino P, Lombardo C, Bramanti P. Unexpected recovery from a vegetative state or misdiagnosis? Lesson learned from a case report. NeuroRehabilitation 2017;41(04): 735–738
15 Edlow BL, Chatelle C, Spencer CA, et al. Early detection of consciousness in patients with acute severe traumatic brain injury. Brain 2017;140(09):2399–2414
16 National Bioethics Advisory Commission. Research involving human biological materials: ethical issues and policy guidance. Rockville, MD: National Bioethics Advisory Commission; 1999. Available at: https://bioethicsarchive.georgetown.edu/nbac/hbm_exec.pdf. Accessed May 25, 2018
17 Medical Research Council. Human tissue and biological samples for use in research. Operational and ethical guidelines. London: Medical Research Council; 2001. Available at: http://www.mrc.ac.uk/news-events/publications/human-tissue-and-biological-samples-for-use-in-research/. Accessed May 25, 2018
18 Canadian Institutes of Health Research. CIHR best practices for protecting privacy in health research. Canada: CIHR; 2005. Available at: http://www.cihr-irsc.gc.ca/e/29072.html. Accessed May 25, 2018
19 Shalowitz DI, Miller FG. Disclosing individual results of clinical research: implications of respect for participants. JAMA 2005;294 (06):737–740
20 Laurie GT. In defence of ignorance: genetic information and the right not to know. Eur J Health Law 1999;6(02):119–132
21 Graham M, Weijer C, Peterson A, et al. Acknowledging awareness: informing families of individual research results for patients in the vegetative state. J Med Ethics 2015;41(07):534–538
22 Naci L, Sinai L, Owen AM. Detecting and interpreting conscious experiences in behaviorally non-responsive patients. Neuroimage 2017;145(Pt B):304–313
23 Puggina ACG, Paes da Silva MJ, Schnakers C, Laureys S. Nursing care of patients with disorders of consciousness. J Neurosci Nurs 2012;44(05):260–270
24 Kitzinger J, Kitzinger C. The 'window of opportunity' for death after severe brain injury: family experiences. Sociol Health Illn 2013;35(07):1095–1112
25 Samuel G, Kitzinger J. Reporting consciousness in coma: media framing of neuro-scientific research, hope, and the response of families with relatives in vegetative and minimally conscious states. JOMEC Journal 2013;3(01):1–15