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Minimizing the Harm of Accidental Awareness Under General Anesthesia: New Perspectives From Patients Misdiagnosed as Being in a Vegetative State

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An estimated 20,000 to 40,000 patients experience accidental awareness during general anesthesia (AAGA) yearly in the United States alone.[1] AAGA can be accompanied by intraoperative distress and lead to posttraumatic stress disorder (PTSD) in as many as 70% of those who experience it, as well as clinical depression or phobias.[2,3] Yet, because its risk factors are not yet fully understood, as well as the lack of sensitive depth-of-anesthesia monitoring devices, prevention and detection of AAGA is extremely challenging.[3]

Similarly, in the United States, there are an estimated 13,000 to 53,000 patients in a "vegetative state" (VS), also known as a disorder of consciousness (DoC), although precise numbers are difficult to determine.[4] Patients clinically diagnosed as VS show no signs of awareness of themselves or the environment and are entirely behaviorally nonresponsive. However, recent studies show that a minority of patients (19%)[5] clinically diagnosed as VS can, nevertheless, demonstrate covert awareness through cognitive responsivity in neuroimaging tasks, a phenomenon captured by the recently coined term "cognitive motor dissociation" (CMD).[6] This, however, may not capture patients who do not respond for other, yet-to-be-determined causes.

In recent years, increased understanding of covert consciousness in patients diagnosed as vegetative has highlighted the importance of safeguarding and promoting their well-being.[7] Similarly, there have been significant efforts to enhance awareness about AAGA among anesthesiologists.[2,3,8] In this article, we present a novel perspective on this issue, by drawing parallels between these 2 patient groups. Like CMD patients, AAGA patients appear to lack consciousness but, nevertheless, are aware of themselves and of their environment, and thus can experience harm. We discuss how best practices applicable to brain-injured, behaviorally nonresponsive patients could be extended to AAGA patients, to minimize the potential harm of intraoperative awareness.

AAGA: BACKGROUND

The incidence of intraoperative awareness with explicit postoperative recall ranges from 0.005%,[2] when based on spontaneous patient reports, to 0.1% to 0.2%, when based on structured postoperative interviews, such as the Brice Questionaire.[3,9] The incidence of AAGA without explicit recall is harder to determine, although studies suggest it may be up to 25 times higher than with explicit recall.[2,10] The discrepancy may be due to the fact that anesthetic agents like propofol are powerful anterograde amnesiacs and, moreover, the dose of anesthetics required for unconsciousness are higher than those required for amnesia.[3] A recent international and multicenter study of 260 patients that used the isolated forearm technique—wherein an inflatable cuff placed at the forearm prevents paralysis of one hand from neuromuscular blockade—found that, immediately after induction of general anesthesia, 4.6% of patients responded to verbal commands by squeezing the researcher's hand, including to questions about pain experience.[10] However, these patients did not exhibit postoperative recall, likely due to the anterograde amnesic effects of anesthetics, which may explain the discrepancy between this rate and the one established with postoperative interviews. It is important to note, however, that this study investigated intraoperative awareness shortly after (typically within 1 minute) securing the endotracheal tube and may not be reflective of the likelihood of AAGA across the time course of the surgical procedure.

Common experiences associated with intraoperative awareness include hearing voices or equipment noise, the sensation of paralysis or pain, and awareness of tracheal intubation and the inability to breathe.[2,11] These sensations may also be accompanied by feelings of anxiety, panic, or that one is permanently paralyzed or dying.[11] Between 28% and 46% of patients experience pain, and 36% to 65% of patients experience an acute emotional reaction, such as distress.[2,11] However, it is worth noting that some patients who experience AAGA are relatively unconcerned by it.[2]

Critically, negative experiences of AAGA can also result in postoperative, long-term harm to patients.[2,11] A recent, large-scale study[2] found that 41% of patients who had

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experienced AAGA suffered moderate to severe long-term harm, including flashbacks or nightmares, hyperarousal, avoidance of situations relating to the experience (eg, lying flat, future anesthetics), and PTSD. In fact, 79% of patients who experienced distress reported moderate to severe long-term symptoms, compared with only 3% of patients without distress during AAGA.[2]

CMD: BACKGROUND

A proportion of patients who survive serious brain injury are rendered behaviorally nonresponsive and exhibit no responsivity to commands administered at the bedside by clinical staff. At the most extreme end of this spectrum, a patient appears to be awake but shows no evidence of voluntary response to visual, auditory, tactile, or noxious stimulation in repeated behavioral examinations with standardized assessment scales (eg, the Coma Recovery Scale-Revised).[12] Patients with this behavioral profile, particularly signs of wakefulness—that is, periodic eye opening and closing—in the absence of signs of awareness of themselves, or of the environment, rather than any particular neural pathology, are clinically diagnosed as being in the VS.[13] Mirroring the situation of AAGA patients, the clinical detection of awareness in brain-injured behaviorally nonresponsive patients is particularly difficult because of its reliance on the subjective interpretation of inconsistent behaviors, which are often limited by motor constraints.[14] Up to 43% of patients who are initially diagnosed as VS demonstrate evidence of awareness on more specialized behavioral examinations.[15]

Some patients, who show no signs of behavioral responsivity on repeated and specialized assessments, may yet show preserved basic sensory functions[16] and higher cognitive processes, such as emotional[17] and semantic processing,[18] when their brain responses are measured with electroencephalography or functional magnetic resonance imaging. A proportion of these patients (19%) are even able to follow commands by modulating their brain activity in different kinds of neuroimaging paradigms, thereby indicating that they are consciously aware despite their clinical diagnosis of VS.[19,20] In one such neuroimaging paradigm,[19] patients are asked to perform motor (eg, playing tennis) or spatial navigation (eg, moving around their house) imagery, or relax, in on-off blocks of 30 seconds. In another kind of paradigm,[20] patients are asked to either 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. Efforts to translate these neuroimaging techniques for use in clinical practice are ongoing.[18] Beyond preserved awareness, the brain-injured patient's ability to follow commands via brain activity provides evidence of a complex cognitive repertoire, including language comprehension, decision making, working memory, and executive function.

SIMILARITIES BETWEEN CMD AND AAGA PATIENTS

Similar to brain-injured patients mistakenly thought to be unconscious, patients under general anesthesia, including those who follow commands or communicate intraoperatively by squeezing the researcher's hand, or recall events postoperatively, demonstrate preserved awareness and high levels of intact cognition, in spite of a presumed lack of consciousness. Critically, for both groups, the presence of consciousness is not known a priori (with rare exceptions, eg, when they are part of a research study) and may be mistakenly ruled out, while they remain susceptible to harms like pain[21] or emotional distress, which may indeed be caused or exacerbated by this misperception.[7] Thus, the similarity between these patient populations is based in part on an intrinsic property of the patient (ie, preserved consciousness) and also on a property others have with respect to them (ie, the mistaken belief that these patients are unconscious). Although a smaller proportion of intraoperative patients may retain awareness and high-level cognition than brain-injured patients diagnosed as VS (0.1%–0.2% of patients under general anesthesia versus 19% of VS patients via neuroimaging), the ethical obligation to protect the patients' well-being applies similarly to both groups. While these patient populations may differ in other ways, including the structural and functional integrity of their brains and the means by which consciousness is presumed to be extinguished, these differences are extraneous to our discussion.

Pain Management

One of the most important aspects of promoting patient well-being is minimizing their pain.[21] Assessing pain experience in both patient groups is challenging because they cannot provide self-report. Potential "pain behaviors" in DoC patients—grimacing, vocalizations, or body movements—can occur in the absence of consciousness[21] and their presence does not clearly indicate a patient's conscious experience of pain.[22] Similarly, autonomic signs such as increased blood pressure and heart rate, lacrimation, sweating, or pupillary dilation—traditional signs of inadequate depth of anesthesia—are variable and may be affected by patient medications, making them unreliable indicators of awareness in many circumstances.[22] Conversely, a patient may have a conscious experience of pain and be unable to demonstrate it behaviorally.[22]

It is difficult to differentiate between a patient's reflex movements and his or her attempts to alert the medical team to awareness or pain experience.[11]

In contrast to the context of brain-injured patients, where pain management aims to minimize excessive discomfort in the provision of normal care, for intraoperative patients, pain directly results from the medical intervention and could have severe long-term effects. Therefore, more proactive management is required for the intraoperative group. Nevertheless, the therapeutic goal of minimizing pain is consistent across both populations and can be complicated by the mistaken presumption of unawareness. Although patients under general anesthesia are presumed incapable of pain experience due to the presence of analgesics, the aforementioned prospective and multicenter study of 260 patients found that of the 12 patients who responded to the verbal commands of researchers, 5 individuals (42% of isolated forearm technique responders or 1.9% of the study cohort) also reported pain experience.[10] However, the authors suggest that these results may be a conservative estimate of intraoperative awareness.[10] This finding calls for proactive pain management wherever possible to ensure patient comfort, irrespective of the potential absence of postoperative recall due to the memory-suppressing effect of anesthetics.[10] Critically, adequate management of pain can reduce the potential for long-term harm in AAGA patients. The combination of paralysis and pain has been shown to be the most common reason for distress (77% of patients), which, in turn, is the most predictive factor of PTSD in AAGA patients.[2] Therefore, it has been suggested that when intraoperative awareness is suspected, prompt deepening of anesthesia ought to be accompanied by the administration of analgesics.[3] However, caution should be exercised when responding to patient movement, and the administration of neuromuscular blockade alone in these cases has been discouraged.[3,8]

Patient Communication

Communication is another important aspect of promoting the well-being of covertly aware patients, whether CMD or AAGA. Studies suggest that communicating with DoC patients promotes their well-being by acknowledging their value and demonstrating a sense of genuine care for them.[23] Patients who recover consciousness report that, while they are presumed unconscious, communication and its content has a profound effect on them.[24] Adequate communication requires a concerted effort on the part of care providers, including referring to the patient by name, verbally guiding and informing them, and maintaining a professional demeanor that reinforces their dignity, all of which is challenging in the absence of patient feedback. Studies show that nurses in the intensive care unit spend, on average, only 4 to 12 minutes communicating verbally with brain-injured patients thought to be unconscious during a 4-hour observational period.[23] Another study conducted in coma patients found that 90% of care procedures were carried out in complete silence.[23]

Similarly, the demands of clinical care make it unfeasible for physicians and nurses to take the time to speak to all intraoperative patients. The high incidence of misdiagnosis in CMD patients motivates routine patient communication, whereas the low incidence of AAGA established with postoperative interviews (0.1%–0.2%) may discourage it. However, recent findings suggesting that the incidence of AAGA, particularly without explicit recall,[3] may be higher than the previously established rate—especially when anesthesia is "light," such as during cardiac surgery or cesarean delivery, or shortly after induction or before emergence—provides an impetus for patient-centered communication. Moreover, research suggests that communication is not only highly sought by patients during AAGA but that support of this nature is a significant factor in protecting patients from PTSD.[25] Indeed, evidence suggests that communication-oriented care strategies can promote the well-being of patients who may experience AAGA, irrespective of postoperative recall. A meta-analysis of 32 randomized controlled trials including 2010 patients found that positive or therapeutic messages given to patients under general anesthesia (who did not experience AAGA) had a significant positive effect on postoperative outcome measures including medication and recovery.[26]

In special cases of intentionally "light" anesthesia, or when the nature of the patient or the procedure increases the risk of AAGA, or when awareness is suspected, the provision of verbal reassurance acknowledging a possible problem and efforts to resolve it can benefit the patient. For example, one patient, who was mistakenly given suxamethonium chloride to induce paralysis before induction[2] and, consequently, experienced paralysis and fear of dying, reported being very reassured by the anesthetist's immediate explanation and had minimal long-term sequelae. Although this case presents a clinical mistake and is not a typical representation of AAGA patients, the patient's experiences were similar to those of AAGA patients, and his reaction illustrates the positive value of patient-oriented intraoperative communication.

Further, studies show that intraoperative patients more readily recall information that has emotional significance compared to neutral information,[8] suggesting that comments of medical staff may influence the likelihood of postoperative recall. If recalled, negative comments can lead to greater unhappiness than other aspects of the AAGA experience.[2] Conversely, reassuring explanations provided by the clinical staff may reduce the negative impact of AAGA.[2]

CONCLUSIONS

In this article, we draw parallels between brain-injured patients clinically diagnosed as being in a VS, who, in fact, retain covert awareness, and patients who become accidentally aware during general anesthesia. We argue that strategies for promoting the well-being of the former group may be extended to intraoperative patients and can help minimize the harms of accidental awareness.

DISCLOSURES

Name: Mackenzie Graham, PhD.
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Contribution: This author helped provide feedback.
Name: Kaman Çipi, MD.
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REFERENCES

1. Avidan MS, Zhang L, Burnside BA, et al. Anesthesia awareness and the bispectral index. *N Engl J Med*. 2008;358:1097–1108.
2. Pandit JJ, Cook TM; The NAP5 Steering Panel. *NAP5. Accidental Awareness During General Anesthesia in the United Kingdom and Ireland: Report and Findings*. London: The Royal College of Anesthetists and Association of Anesthetists of Great Britain and Ireland; 2014. Available at: http://www.nationalauditprojects.org.uk/NAP5_home. Accessed on May 3, 2017.
3. Mashour GA, Avidan MS. Intraoperative awareness: controversies and non-controversies. *Br J Anaesth*. 2015;115(suppl 1):i20–i26.

4. Beaumont JG, Kenealy PM. Incidence and prevalence of the vegetative and minimally conscious states. *Neuropsychol Rehabil*. 2005;15:184–189.
5. Cruse D, Chennu S, Chatelle C, et al. Bedside detection of awareness in the vegetative state: a cohort study. *Lancet*. 2011;378:2088–2094.
6. Schiff, ND. Altered consciousness. In: Winn R, ed. *Youmans and Winn's Neurological Surgery*. 7th ed. New York, NY: Elsevier Saunders; 2016
7. Naci L, Graham M, Owen AM, Weijer C. Covert narrative capacity: mental life in patients thought to lack consciousness. *Ann Clin Transl Neurol*. 2017;4:61–70.
8. Kent CD, Domino KB. Update on unintended intraoperative awareness. *Adv Anesth*. 2006;24:109–125.
9. Sandin RH, Enlund G, Samuelsson P, Lennmarken C. Awareness during anaesthesia: a prospective case study. *Lancet*. 2000;355:707–711.
10. Sanders RD, Gaskell A, Raz A, et al. Incidence of connected consciousness after tracheal intubation: a prospective, international, multicenter cohort study of the isolated forearm technique. *Anesthesiology*. 2017;126:214–222.
11. Bruchas RR, Kent CD, Wilson HD, Domino KB. Anesthesia awareness: narrative review of psychological sequelae, treatment, and incidence. *J Clin Psychol Med Settings*. 2011;18:257–267.
12. Giacino JT, Kalmar K, Whyte J. The JFK Coma Recovery Scale-Revised: measurement characteristics and diagnostic utility. *Arch Phys Med Rehabil*. 2004;85:2020–2029.
13. The Multi Society Task Force on PVS. Medical aspects of the persistent vegetative state. *N Engl J Med*. 1994;330:1499–1508.
14. Owen AM, Coleman MR. Using neuroimaging to detect awareness in disorders of consciousness. *Funct Neurol*. 2008;23:189–194.
15. Schnakers C, Vanhaudenhuyse A, Giacino J, et al. Diagnostic accuracy of the vegetative and minimally conscious state: clinical consensus versus standardized neurobehavioral assessment. *BMC Neurol*. 2009;9:35.
16. Menon DK, Owen AM, Williams EJ, et al. Cortical processing in persistent vegetative state. Wolfson Brain Imaging Centre Team. *Lancet*. 1998;352:200.
17. Kotchoubey B, Kaiser J, Bostanov V, Lutzenberger W, Birbaumer N. Recognition of affective prosody in brain-damaged patients and healthy controls: a neurophysiological study using EEG and whole-head MEG. *Cogn Affect Behav Neurosci*. 2009;9:153–167.
18. Coleman MR, Davis MH, Rodd JM, et al. Towards the routine use of brain imaging to aid the clinical diagnosis of disorders of consciousness. *Brain*. 2009;132:2541–2552.
19. Owen AM, Coleman MR, Boly M, Davis MH, Laureys S, Pickard JD. Detecting awareness in the vegetative state. *Science*. 2006;313:1402.
20. Naci L, Owen AM. Making every word count for vegetative patients. *JAMA Neurol*. 2013;70:1235–1241.
21. Chatelle C, Thibaut A, Whyte J, De Val MD, Laureys S, Schnakers C. Pain issues in disorders of consciousness. *Brain Inj*. 2014;28:1202–1208.
22. Palanca BJ, Searleman A, Avidan MS. Current controversies in intraoperative awareness: II. In: Mashour GA, ed. *Consciousness, Awareness, and Anesthesia*. New York, NY: Cambridge University Press; 2010:148–171
23. Puggina AC, Paes da Silva MJ, Schnakers C, Laureys S. Nursing care of patients with disorders of consciousness. *J Neurosci Nurs*. 2012;44:260–270.
24. Pistorius M. *Ghost Boy: The Miraculous Escape of a Misdiagnosed Boy Trapped Inside His Own Body*. Nashville, TN: Nelson Books; 2013.
25. Osterman JE, van der Kolk BA. Awareness during anesthesia and posttraumatic stress disorder. *Gen Hosp Psychiatry*. 1998;20:274–281.
26. Rosendahl J, Koranyi S, Jacob D, Zech N, Hansen E. Efficacy of therapeutic suggestions under general anesthesia: a systematic review and meta-analysis of randomized controlled trials. *BMC Anesthesiol*. 2016;16:125.