Isolated Forearm Test: Replicated, Relevant, and Unexplained

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IT is a natural human tendency to internally construct the world around us largely as we learned to see it while growing up, just as it is our tendency to prefer simplified, intuitive constructs over ambiguous complexity. As anesthesiologists, we largely learned the binary concept that patients were either awake or asleep. Asleep was good, and awake was not so good. This elegant simplicity was both convenient and reassuring and enabled us to summarize the mysteries of anesthesia to patients without delving into the language and nuances of cognitive neuroscience. What our patients heard, and what we mostly intended them to hear, was that they would be asleep. Completely. Every time.

These binary divisions are no longer applicable. It is now clear that there are states of consciousness that do not fit conveniently into our understanding of being perfectly awake or perfectly asleep. They are hiding in plain sight, well disguised, in part, because we instinctively assess behaviors as surrogates to decide whether a person is conscious or unconscious. We intuitively assume that a person behaving as though they are conscious actually is conscious and vice versa. This interpretation of behavior as signaling cognitive state is mostly reliable, but it is nonetheless flawed, and perhaps no more so than when drugs alter neural function to create states that do not occur naturally.

In this regard, the anesthesiologist’s impression of whether patients were awake or asleep is confused because it has characteristically relied on probing their memory—a behavior for which consciousness is necessary but not sufficient. A patient who is under the influence of an amnesic drug such as a benzodiazepine interacts with the world with behaviors that suggest they are awake. However, on the following day, with no recollection of events, their behavior is grossly indistinguishable from what it would be had they been completely unconscious. What exactly is the nature of this state, and where does it fit along the good—not so good spectrum? If a patient is aware of an event but develops no memory of it, is this neutral or rather worse that being unconscious during those same events?

The current issue of Anesthesiology presents a study by Sanders, Gaskell et al. that forces us to pointedly confront this question. The authors conducted an international, six-center study of 260 patients to assess responsiveness to command after intubation, using the isolated forearm technique (IFT). It is by no means the first study using the IFT, but it can lay claim to being the most methodologically robust. The incidence they report, using conservative criteria, is 4.6%. This is an order of magnitude less than the estimate of approximately 40% suggested by previous studies and provides reassurance to assuage the uncomfortable prospect that nearly half of our patients possess some level of consciousness at a time when we assume they are distinctly otherwise. But 4.6% still represents a 20- to 50-fold increase over the incidence of awareness reported in randomized controlled trials using the Brice protocol and is approximately 1,000 times the incidence of spontaneously reported awareness.

If we routinely informed our patients that there was a 1 in 20 chance that they would have some form of connected consciousness during their anesthesia, would their initial unease be relieved by next telling them that they would form no memory of it? Could we tell them, with intellectual confidence, that awareness not remembered is effectively the same as no awareness at all? Could we tell them that while...
they might not be completely unconscious, the state they will be in is not consciousness as they normally experience it.

Controversy arises with this question, in no small part fueled by our incomplete knowledge and misconceptions, which Sanders, Tononi et al. captured elegantly in the title of a previous 2012 review: Unresponsiveness ≠ Unconsciousness. As our understanding of the mechanisms of anesthetic-induced unconsciousness unfold, it is not surprising that additional states of being emerge near the borders. However, knowing of their existence mostly serves only to heighten the mystery and elusiveness of their nature. It is suggested, for example, that anesthetics can induce a state of being termed dissociated awareness or dysanesthesia. Here, one is for all purposes awake during a period when being otherwise is expected yet unperturbed by this strange state of perception–sensation uncoupling. Dysanesthesia is a nascent construct open to question: an exemplar of how it is expected and appropriate that, as our exploration of multi-modal states evolves, controversy will first surround whether a new entity exists. But as clinical relevance is considered, the question should then evolve into whether such an entity is desirable, or more relevantly does no harm. As new evidence mounts, new entities are finally incorporated in some fashion into an updated model of the world, much as physics continuously reveals to us strange things such as spooky actions at a distance. Neurologists are couring a similar path, investigating states of consciousness between awake and asleep on the basis of structural and functional changes in the brain.

The study that Sanders, Gaskell et al. present is an important replication, a milestone in objectively identifying evidence supporting a novel, intermediate state of consciousness, confirming multiple single-site studies from a small number of investigators reporting what some had argued were observations under contrived conditions. The current replication revealed an effect size smaller than that in previous reports, a phenomenon consistently observed across many spheres of research. Perhaps the most prominent discussion of diminishing effect size and nonreproducibility has been focused on the psychology literature, which is of special relevance to the current study because the experimental method is in essence probing the neuropsychology of modulated consciousness. As a staggering 60% of well-regarded psychology studies cannot be replicated, the fact that Sanders, Gaskell et al. have done so with IFT observations in a multicenter pragmatic trial puts this anesthetic-induced state of being on substantially more solid ground. Nonetheless, it must be noted that even a pragmatic IFT experiment introduces potential effects that may challenge the generalizability of the finding. The very act of informed consent may create an unusual Hawthorne effect, priming the patient for input from the external world during anesthesia. The use of muscle stimulation to test for nonparalysis may represent a priming stimulus infrequently present outside of the experimental setting, and the brain response to salient or primed stimuli can be greater than that to random stimuli. The authors have demonstrated that a form of connected consciousness is able to occur during the early minutes of a general anesthetic but not that it routinely does. In this sense, the authors’ statement that this is a conservative estimate of connected consciousness may not be as conservative as they contend.

If we can now accept that the IFT is a real, replicable phenomenon, it is time to move on to investigating the exact nature and implications of this mysterious state. One can now hope to apply the big hammers of systems neuroscience to understand what is going on in the brain, with the added advantage that, unlike equivalent investigations of the vegetative state, provides a definitive behavioral response. But our curiosity to understand the neuroscience should not dwarf the need to evaluate the neuropsychology. We must look forward to the next phase of investigations with more objective data to decide whether this state is benign and to be expected in the natural course of anesthesia or whether it retains a potential for harm, at least until proven otherwise, as has been suggested by several investigators. It may also be time to weigh and debate how a loss of the illusion of simplicity should modify the way we describe the anesthetic state to our patients and the expectations that we set.

Competing Interests

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REFERENCES