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To cite this article: Christopher Scott Stauffer (2025) Psychedelics and Psychotherapy: What Can be Learned from a Historical Analysis of General Anesthesia and Surgery?, The American Journal of Bioethics, 25:1, 56-58, DOI: [10.1080/15265161.2024.2433453](https://doi.org/10.1080/15265161.2024.2433453)

To link to this article: <https://doi.org/10.1080/15265161.2024.2433453>



Published online: 13 Jan 2025.



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Psychedelics and Psychotherapy: What Can be Learned from a Historical Analysis of General Anesthesia and Surgery?

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This Special Issue on Psychedelic Ethics highlights that while psychedelic medicine may not be “exceptional” in its therapeutic value and risk (Cohen and Marks 2025), it is “distinctive” in that it represents “a unique combination of characteristics that are all separately present in other medical and psychological interventions,” including aspects of major surgery under general anesthesia (Cheung et al. 2025). Using historical case analysis and analogical reasoning, I’d like to further explore this example.

The unfolding ethical landscape of psychedelics paired with psychotherapy within a medical framework shares noteworthy parallels with the introduction of general anesthesia in 19th-century surgery. Just like early anesthesia, psychedelic-assisted psychotherapy holds transformative potential that stands to redefine practice, involves risks associated with consciousness-altering substances used to facilitate probing clinical interventions, and withstands heightened scrutiny due to ethical concerns around safety, public perception, and professional acceptance. Keeping in mind there are limitations to any comparative framework, these parallels offer valuable insights when weighing the benefits and risks of psychedelic medicine.

The first known use of general anesthesia in surgery occurred on March 30, 1842, when Dr. Crawford Williamson Long used sulfuric ether to sedate a patient and painlessly remove a tumor from his neck (Anaya-Prado and Schadegg-Peña 2015). An acquaintance of Dr. Long reflected on an angry mob gathering outside his office on that day:

“They vowed that should the boy fail to arouse from the effects of the ether, they would lynch Long. I did not see the operation, but I did station myself at the steps of the office in which the operation was being done, to beg the crowd to stand back and quietly await the result.” (Marston 1942)

The procedure was a success, though Dr. Long was uncertain if this was due to the ether or to

mesmerism—a hypnotic technique used to reduce awareness of pain during surgery (Anaya-Prado and Schadegg-Peña 2015). Nonetheless, the public’s reactionary response perhaps reflected concern over combining what was, at the time, a party drug (Habchi et al. 2020) into an already risky medical procedure. Dr. Long’s inspiration for this experiment came from “ether frolics,” trendy social gatherings where partygoers inhaled ether recreationally. Dr. Long noted that he and his friends would often flail about and experience minor injuries without pain or memory of the event.

Professional disputes and various major objections to the adoption of anesthesia into medicine (i.e., “ether controversy”) continued for decades, including arguments that patients undergoing surgery have a “moral obligation” to endure pain (Meyer and Desai 2015). James Young Simpson, the first to apply ether to midwifery on January 9, 1847, countered:

“the same arguments that forty or fifty years ago were urged against the propriety and safety of vaccination, or a hundred years ago against small-pox inoculation, have, within the last few months, been again involved and used against the employment of etherisation” (Farr 1980).

For most of human history, surgery without anesthesia was a grueling reality, which is almost unthinkable nowadays given the ubiquity of sedation in the operating room. For individuals with severe posttraumatic stress disorder, trauma-focused therapy can be akin to “surgery without anesthesia”. Gold standard treatments like prolonged exposure and cognitive processing therapy are effective for many of those willing and able to engage with them but have high drop-out rates in real-world clinical settings. Qualitative studies reveal that many military veterans discontinue these interventions due to inadequate trust built with providers or finding the intervention too distressing. MDMA-assisted psychotherapy for posttraumatic stress disorder may offer an advantage by enhancing the

therapeutic alliance and widening the “window of tolerance” for processing trauma, reducing the likelihood of premature treatment termination. Just as anesthesia enabled surgeons to develop more nuanced understanding of disease processes and more sophisticated surgical interventions, MDMA may empower therapists to do the same for PTSD and trauma processing.

The first public demonstration of ether anesthesia occurred on October 16, 1846 (i.e., “Ether Day”) in what later became known as the “Ether Dome” in Boston, Massachusetts. Less than a year later, the first reported case of sexual abuse of an anesthetized patient occurred in Paris, France.

“The case of the dentist recently on trial in this city for an alleged outrage on the person of a patient while under the influence of inhaled ether has painfully attracted the attention of our whole community, notwithstanding the revolting nature of its details....It has inflicted a lasting shock upon the public sentiment in relation to the use of anæsthesia in the absence of third parties and for trivial operations....” (Hartshorne 1854)

While it is difficult to estimate the prevalence of sexual boundary violations committed by surgeons, dentists, and anesthesiologists toward sedated patients due to the issue being underreported, underdisciplined, and understudied, it continues to be a serious ethical and professional concern. The cases outlined in this issue by Harrison et al. (2024) of sexual violations in the psychedelic medicine field perhaps serve as a call for greater accountability, not just in psychedelics but more broadly in medicine and mental health.

Another pertinent parallel is the risk of substance misuse. Inhaled anesthetic agents are highly regulated nowadays, and their recreational use is exceedingly rare—even among anesthesiologists with substance use disorders (Habchi et al. 2020); though, Horace Wells, a dentist who tried and failed to claim the discovery of anesthesia, developed an addiction to ether and chloroform and died tragically in prison from suicide in 1848 (Finder 1995). In the 19th century, drinking ether as an inexpensive substitute for alcohol was not uncommon—particularly in places like Ireland during periods of alcohol prohibition, where psychological dependence, or etheromania, was an issue (Kerr 1891). While recreational misuse of MDMA raises concerns, this risk may be exaggerated due to misguided comparison to the opioid epidemic. Today, patients undergoing surgery are at increased risk for developing chronic opioid use disorders due to the widespread expansion of pain management practices from intraoperative to the post-operative period starting in the mid-20th century and the

subsequent development and aggressive marketing of more potent opioids. However, proposed clinical protocols of MDMA-assisted therapy call for only two or three dosing sessions administered on-site to patients who are monitored throughout the duration of acute effects, reducing the risk of diversion in a manner more similar to general anesthesia than take-home narcotics.

Ketamine was approved by the FDA as an anesthetic agent in 1970. Beyond its role in supporting surgical interventions through its unique blend of amnesic, analgesic, and hypnotic effects, ketamine has rapid antidepressant effects and can effectively address acute suicidal ideation (Kohtala 2021). However, the duration of these therapeutic effects seems to be limited. Through its off-label use, some clinicians report benefits from combining “psychedelic” doses of ketamine with psychotherapy (i.e., ketamine-assisted psychotherapy) to extend the duration of antidepressant effects or to address complex issues like posttraumatic stress disorder or substance use disorders (Drozd et al. 2022). Ketamine-assisted psychotherapy protocols vary significantly as far as dosage, formulation, and amount and type of psychotherapy support provided. More research is needed to determine the risks and to compare this modality to ketamine without psychotherapy.

Ketamine, representing both an anesthetic agent and a psychedelic, provides a stark example of the limitations of our analogy between anesthesia-assisted surgery and psychedelic-assisted psychotherapy. Namely, despite the broad use of ketamine to assist a countless array of emergency and surgical procedures over five decades, the term “ketamine-assisted surgery” never entered common lexicon. Neither did “ether-assisted surgery”. Yet the standard phrasing of “ketamine-assisted psychotherapy”, “MDMA-assisted psychotherapy”, and others reflects differences in perception, function, and stigma across medical fields, highlighting how mental health treatments must navigate additional barriers to legitimacy. Despite the obvious risks of surgery, it tends to address disease processes we can physically observe and readily understand mechanistically; while the psyche remains a black box for most laypeople and our medical institutions. Even within mainstream psychiatry, psychedelic medicine is still often referred to as a nascent field, despite psychedelic research pre-dating most of our modern psychiatric interventions. Despite the impact of stigma from both mental health and mind-altering substances on the wider acceptance of psychedelic medicine, “many of the bioethical issues engendered by psychedelics in clinical contexts may not be so fundamentally different from issues raised in other areas of medicine” (Neitzke-Spruill et al. 2024).

In most industrialized countries over the past five or six decades, ether has been replaced as the inhalation anesthetic of choice by safer and more efficient halogenated ethers (e.g. sevoflurane). These agents were FDA approved after being evaluated for their ability to induce and maintain the desired state of anesthesia safely during surgery, with predictable onset and recovery times. The FDA does not play a role in determining the type of surgical procedures conducted with specific anesthetic agents. Clinical best practices are determined by professional medical organizations and institutional policies. Today, it is widely accepted in the medical community that the benefits of general anesthesia outweigh the risks. Similarly, MDMA-assisted therapy and others, when administered by trained professionals with proper consent for appropriate indications, may advance into mainstream practice as a transformative yet carefully regulated intervention.

DISCLOSURE STATEMENT

The author was as a contractor for psychotherapy trainings for Lykos (formerly MAPS PBC) between 2021 and 2023.

FUNDING

The author(s) reported there is no funding associated with the work featured in this article.

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