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Memory, Pain, and Harm: Ethical Perils in Procedural Amnesia

Introduction

It is the aim of general anesthesia to afford patients physically and psychologically safe passage through an operative experience which is medically indicated but otherwise intolerable, and traditionally this is achieved with several components of an anesthetic working in concert: hypnosis, analgesia, and amnesia, as well as akinesia and hemodynamic support for specific circumstances (1). In this context, hypnosis functions centrally to render a patient unconscious (unaware and unrousable) (2), analgesia centrally and/or peripherally to mitigate the perception of pain (3), and akinesia at the neuromuscular junctions to provide muscle relaxation and thereby prevent involuntary movement (4). Amnesia is unique among the elements of anesthesia: rather than facilitate an operation per se, its focus is on interfering with a patient's consolidation of experience into memory (disrupting new memory formation in a process called "anterograde amnesia") (5,6). Although amnestic agents regulate future recollection rather than immediate experience and perception, they are a critical component of anesthesia because of the many demonstrable

risks of intraoperative memory formation: even brief moments of unintentional awareness during surgery can facilitate consolidation (7), and the ability to recall surgical experience is associated with long-term psychiatric sequelae such as post-traumatic stress disorder (8).

On its face, the simultaneous use of analgesics and amnestics may seem redundant. If a patient is completely insensate to pain, what is gained by using an amnestic? Two arguments are that (1) pain may not be the only experience of an (unfamiliar and sterile) operating room that a patient may reasonably elect to forget, and that (2) amnestics serve as a safety net in case of inadvertently inadequate hypnosis or analgesia. The inverse scenario fundamentally belongs to the field of metaphysics: why is an analgesic necessary for a patient with adequate amnesia?

Analgesics and Amnestics

Analgesic agents such as opioids bear several risks, ranging from post-operative nausea and constipation to respiratory depression and physical dependence (9). Acknowledging that this is an oversimplification of a broad class of pharmacological agents, amnestic medications such as benzodiazepines tend to offer a relatively large therapeutic index (10). For this reason, it could be seen as attractive to use only the latter to limit the psychological consequences of pain, rather than subjecting a patient to the potential side effects of both. Obfuscating any direct comparison between these two categories of effect,

however, is a lack of clearly demarcated amnestics in modern anesthetics. Many anesthetic medications provide some amnestic effect, but we do not have access to “pure” or “perfect” amnestics: common agents like midazolam also have analgesic, sedative, and anxiolytic effects (11,12), and although they are able to disrupt the genesis of conscious memory, they cannot necessarily do the same for implicit memory (13). In addition, there is strong evidence to support the treatment of surgical pain manifested in its physiological consequences (not mediated by psychological experience or memory): unmanaged, the wide-ranging effects of acute pain perception include an immediate hemodynamic and neuroendocrine response (e.g., heightened blood pressure, cortisol, and blood sugar), and myriad downstream complications like poor wound healing, infection, respiratory splinting, thromboembolism, and the acquisition of chronic pain (14–16).

Notwithstanding these limitations in clinical amnesia, its conception provides a unique milieu for philosophical dialogue relating to the experience of pain and the ethical reasons to treat it (as opposed to not treating it, or using only enough analgesia to limit its physiologic consequences) when it will not be remembered. Walter Glannon, in 2014, expanded this discourse through a practical example of a patient awakening during anesthesia, and an exploration of the ethics of providing an amnestic which could “erase” consolidated memory in retrograde (if such a drug existed) (17). Responding to this, Andrew Davidson raised two intriguing points about Glannon’s line of reasoning: that it is not entirely hypothetical, because

there are real situations which mirror a "perfect" amnestic (e.g., infants or patients with dementia, who are unable to form long-term memories); and that the practice of conscious sedation constitutes a real example of the broader medical community acting on a suggestion that the experience of some amount of pain is permissible when an amnestic is used to prevent its consolidation into memory (13).

Davidson's examples of "perfect" amnesia can be extended even further to patients who lack the neurobiological capacity to form memories at all—for instance, the well-known patient H.M. who underwent a bilateral medial temporal lobectomy for severe epilepsy (18)—and his example of conscious sedation falls on a spectrum of medical therapies representing different points of permissibility or reprehensibility in the context of Glannon's questions surrounding the experience and memory of pain (13,17,19). On one end of this spectrum is traditional general anesthesia, wherein a patient is pharmacologically induced into a reversible coma in order to avoid any adverse experiences (pain or otherwise) during a procedure. The other end of the spectrum would represent amnesia without any analgesia, which risks the aforementioned physiological consequences of acute pain and is not known to be practiced in any setting (and rightly so). Somewhere in the middle of this spectrum are procedures performed with an amnestic but limited analgesia, such as conscious sedation provided for the reduction of a fractured bone (13) or awake-awake-awake craniotomies during which patients undergo surgery on the brain while awake in order to limit the risk of iatrogenic damage to critical structures (20), both of which

feature in North American practice. In these cases, patients are typically drowsy although able to wince or vocalize in response to sensations of pain or pressure—but unable to recall the experience shortly after it ends.

This paper explores the concepts of pain and harm as they relate to phenomenal experience and memory, and therefore also to the use of analgesic and amnestic agents. In doing so, it seeks to understand the ethical motivations and parameters underpinning the use of amnestics, analgesics, or both in concert, and how this informs our willingness to allow the experience of pain without memory for some procedures (e.g., an endoscopy) but not others (e.g., removing an appendix). While the benefits and risks associated with the use of amnestics and analgesics are recognizable, a concrete and objective standard for their use cannot be neatly articulated due to the subjective nature of pain—ultimately, though, the degree to which certain combinations of amnestics and analgesics should be used ought to be commensurate to the possibility of avoidable harms.

Pain, Permissibility, and Harm

A philosophical view of pain implicates conceptions of permissibility and when (if ever), in a medical context, we are permitted to either induce pain or fail to relieve it when we have access to the means of doing so (21). Many patients associate receiving an injection with pain, but rarely is it recommended to

administer anesthesia to mitigate the experience. A priori, it can be assumed that either the risks of using an analgesic or amnestic agent outweigh the potential benefits (i.e., patient comfort), or that the perceived pain is better dealt with in other ways. This logic does not extend to the pain associated with an extensive Whipple surgery, which can be recognized as likely to be detrimental to a patient. These two examples reflect an intuitive scale of permissibility for the allowance of pain in some clinical circumstances but not others.

Philosophers outside of the clinical environment have looked for answers to the question of permissibility by developing abstract and metaphysical definitions of pain (22), often delineating it variably as a form of sensory experience such as a physical feature or condition of the body, a form of psychological experience or perception, or a miscellany of both (23). While these definitions of pain have provided intrinsically compelling and provocative arguments to metaphysical discourse, their application in the question of harm—what kind of sensory or psychological experience of pain, or both, it is derived from—can be operationalized to inform the roles of analgesia and amnesia in medical practice. To do this, the present paper borrows the a priori premises from traditional metaphysics and modern clinical practice, respectively, that: (1) pain is either an experience of physical perception, an experience of non-physical (or psychological) perception, or both, and (2) inducing and/or allowing pain is permissible in some contexts but not others. Given these assumptions, the arguments in support of amnesia with limited analgesia (e.g.,

in conscious sedation) arise from a moral chasm within the notion of harm as it is applied to physical pain and psychological pain. In exploring these categories of pain and the relationship each maintains with harm, this paper seeks to offer a richer conception of our profession's prima facie intuition to aggregate the ethical permissions surrounding analgesia and amnesia across various types of medical procedures.

Phenomenological and Abstract Conceptions of Pain

The delineation of two principal classes of pain experience serves as a starting point for the ethics of analgesia and amnesia. The first class refers to a sensory experience defined by concrete spatiotemporal characteristics (23). Philosophers Ned Block and Walter Glannon, among others, have deployed the terminology of phenomenal pain to describe this immediate physical experience of pain perceived through nociceptors (17): for example, the acute perception of an uncomfortable sensation in one's toe when a hard external stimulus has impinged on its soft tissue. While the use of the word phenomenal in the philosophical tradition often refers to the what-it-is-likeness of experience, here it refers strictly to the (objectively or subjectively) localizable, tangible experience of pain. Phenomenal pain is classically situated in and bounded by specific tissue damage, although this is not definitionally imperative with respect to chronic pain (24). In all cases, it is an immediate sensory or phenomenological experience of pain in physical sensations and properties.

While references to pain classically describe this phenomenology, pain can also be described in terms separate from immediate, physical experience. This latter interpretation of pain, termed here as "abstract pain", resists conflating the perception of a physical feature or condition with the physical feature itself (23). Rather, abstract pain represents an often unlocalizable inner perception of an undesirable experience; put another way, it is all the components of painful experience except for its immediate perception. With this definition, abstract pain follows from the encoding of phenomenal pain experience into memory, from which it can be recalled or re-experienced, and manifests more subtly—for example, in care-avoiding behaviors or alterations of thought and emotion reflecting an unpleasant prior experience. Phenomenal pain (e.g., with the experience of receiving an inoculation and experienced until local nociceptors cease to signal tissue injury) and abstract pain (the auxiliary or lasting negative effects of having undergone the phenomenal pain experience) are both necessarily mediated by the nervous system, and together provide a composite definition of pain which can be operationalized to explore the ethics of its management with more granularity.

In practice, phenomenal and abstract pain may be thought to represent unique therapeutic targets. In the context of anesthesia, for example, local or general analgesic formulations are used to numb physical sensations and ameliorate the experience of phenomenal pain. Amnestic agents are similarly provided with the aim of preventing the consolidation of phenomenal pain experiences into memory (therefore sharing in

prevention of the undesirable functions of pain). While both analgesics and amnestics are therefore tools for the mitigation of pain experience, the use of each is grounded in a unique and independent conception of pain.

Broadly Defining Metaphysical Harm

Motivations to pacify these different notions of pain are grounded in their relationships with each other and with the related concept of harm. What constitutes individual harm requires several further considerations, as the subjective and individual factors which contribute to harm exclude the possibility of one unambiguous, universal conception. Colloquially, for example, we recognize the concept of a pain threshold, noting that a person's psychological or genetic disposition may leave predispose them to different kinds or degrees of experience. An experience like receiving a tattoo may be experienced as intolerable for some, but unremarkable or even pleasurable to others. The author C.S. Lewis, in *The Problem of Pain* (1940), provides an initial framework with which to examine the experience of pain and its relationship with harm:

> "[…] the truth is that the word Pain has two senses which must now be distinguished. **A.** A particular kind of sensation, probably conveyed by specialised nerve fibers, and recognisable by the

> patient as that kind of sensation whether he dislikes it or not (*e.g.*, the faint ache in my limbs would be recognized as an ache even if I didn't object to it). **B.** Any experience, whether physical or mental, which the patient dislikes. It will be noticed that all Pains in sense A become Pains in sense B if they are raised above a certain very low level of intensity, but that Pains in the B sense need not be Pains in the A sense. Pain in the B sense, in fact, is synonymous with 'suffering', 'anguish', 'tribulation', 'adversity', or 'trouble' […]." (25)

While some objective factors of experience can be generally recognized as harmful or causally connected to harm, the approach to defining harm ought to be inclusive and sensitive to the various subjective factors which contribute to an individual's harm threshold, allowing for the breadth of both physical and psychological experiences that can be harmful. This understanding prioritizes neither outcomes nor means, and is therefore consistent with both consequentialist and deontological traditions, accepting that both an individual's actions and their consequences can constitute harm in and of themselves.

Simultaneously, a rational conception of harm must be appropriately specific, because while there is a degree to which an understanding of harm may be influenced by personal opinion, subjectivity, and lived experience, the potential for any experience of pain to be conflated with harm is not tenable in the context of professional obligations to do no harm. Primarily, such a conflation could stand to prohibit any

medical intervention associated with even mild discomfort. The duty of clinicians to avoid doing harm is an imperfect, prima facie duty (26), balanced against other competing duties (e.g., to provide beneficent care to patients); nevertheless, it must be possible for some experiences of pain not to constitute harm, or this duty is an indictment of most medical interventions. In practice, the ethical obligation of clinicians appears to be offering interventions which balance the assumed risks and benefits, and to avoid subjecting patients to unreasonable degrees of harm without consent. This may also mean balancing the risks of analgesic and amnestic therapies, along with practical considerations in their use such as cost resource stewardship, against risks associated with experiences not mediated by these therapies.

Harm can therefore be more conservatively defined as the lasting phenomenon of an individual's wellbeing falling below that threshold which a rational individual experiencing it could consider reasonably acceptable. This definition loosely borrows conceptions of wellbeing and harm from Powers and Faden (2006) which suggest that, though the exact threshold is never articulated, harm arises when an individual is deprived of or significantly deficient in a core dimension of wellbeing such as health (27). This would suggest that reasonable action be taken to afford individuals a sufficient state of wellbeing and a minimization of avoidable harm, while also recognizing the intersectional and subjective nature of the phenomena. The definition also allows for the possibility that a single experience of pain may impact two individuals differently, both with respect to its subjective experience and its capacity to cause harm, while

still remaining consistent with the motivations of clinicians to do no harm despite their engaging in practices which sometimes do induce pain (for example, giving a vaccination without prior topicalization with a local anesthetic). However, the forwarded notion of two distinct types of pain experience challenges providers to identify the appropriate permissions surrounding each, and therefore to engage meaningfully with the relationship each type bears with harm.

Treating Phenomenal and Abstract Pain

Earlier, it was suggested that pain can be philosophically disaggregated into a dichotomous experience. The concept of phenomenal pain informs the use of analgesics as a practice seeking to ameliorate the acute physical experience of pain by forestalling its signals' transduction or transmission through the nervous system. In the absence or failure of an analgesic, a subject undergoing an acute physical experience of severe pain can sustain harm, for example in a physiological stress response which precipitates a stroke. Abstract pain, in contrast, informs the use of amnestics as a practice seeking to mitigate the consolidation of negative experience into memory. In the absence or failure of an amnestic, the harm done to an individual by way of undesirable mental/emotional states and behavioral modification can manifest immediately, but is also capable of extending beyond the immediate present to encompass a broad class of enduring psychological harms.

Two moral questions arise from this framework, which we endeavor to outline and offer responses to. First, if it is the case that allowing (or even causing) either phenomenal pain or abstract pain can be harmful, then how can we be justified in allowing one or the other—or some uneven combination of both—in clinical practice? For example, why is it that we utilize predominately amnestics with limited analgesic effect for some brief procedures such as endoscopy, whereas traditional general anesthesia a requirement for more complex and invasive procedures like cardiac surgery? What are the morally relevant aspects of the dichotomous pain experience that inform this practice? Secondly, at what point within each category does the experience of pain become constitutive of a harm? Though we can attribute both phenomenal and abstract pain to a specific experience, does their existence (or representation in consciousness) necessitate the occurrence of harm?

Relationships Between Pain and Harm

Both phenomenal pain and abstract pain have the potential to be harmful, but the means by which they act as causative agents of harm (and the means by which we can prevent this process) are unique. With respect to phenomenal pain, the practice of avoiding or ameliorating harm arising from sensory experience seems prima facie intuitive: by preventing sensory pain with analgesics or similar modes of therapy, an inherently undesirable experience can be avoided, and therefore precluded from causing harm to an

individual. Complicating this framework, the translation of phenomenal pain into harm relies on several mediating physiological factors: for example, the perception of pain causing changes in sympathetic drive, which in turn lead to hemodynamic stress and the potential for end-organ damage. Rather than eliminating the pain experience with analgesics, it is conceivable that providers could instead think to treat the mediating response—blood pressure with beta-blockers, blood sugar with insulin, and so on to the extreme of yet-unknown molecular stress responses to pain and yet-unknown means of terminating them. The possibility therefore arises for a perception of phenomenal pain which may not be directly causative of harm, though still potentially harmful via its encoding into memory and re-experiencing in the form of abstract pain.

The relationship between abstract pain and harm is more complex, given that this pain cannot be ascribed to a spatial location in the same way that a physical injury might be. This notion of abstract pain refers to many components of a pain experience beyond the immediate sensation. For example, in the way that we respond to an unpleasant stimulus by encoding knowledge and memory of its experience into our nervous systems, we may form an aversion to that stimulus (just as we might form a predilection for a pleasant one). The harm associated with abstract pain may not necessarily be immediately impairing, but it informs our beliefs, behaviors, attitudes, practices, and judgements. For example, consolidating the memory of a traumatizing surgical experience may lead to symptoms of post-traumatic stress disorder (e.g.,

hypervigilance and recurrent memories about that experience), and a patient who has experienced trauma resulting from awareness under anesthesia may later elect not to undergo another surgical procedure even in dire circumstances. The consequences associated with abstract pain therefore have the capacity to extend beyond the bounds of an original stimulus, encompassing a broad class of enduring and undesirable harms, and warranting the use of amnestic therapy when feasible. Similar to the caveat provided with respect to the prevention of harm via phenomenal pain, it is worthwhile to note that the harms of abstract pain are also mediated by our ability to (consciously or subconsciously) call them forth from memory, presenting another therapeutic target for pharmacologic agents which do not yet exist (retrograde amnestics or memory recall inhibitors) but which would intuitively warrant similar ethical considerations.

In the case of both phenomenal and abstract pain, not all instances of pain are constitutive of harm. For example, the experience of being pinched by a needle and that of sustaining injuries in a car accident both involve experiential pain, but describing the former as harmful in any meaningful sense depreciates the term. In the latter, the pain experience has the unique possibility of rendering long-lasting decreases in physical wellbeing (e.g., the loss of a limb) and mental wellbeing (e.g., phantom pain or an adjustment disorder). Although the threshold beyond which an experience becomes harmful evades precise definition (in part due to its inherent subjectivity), two conclusions seem plausible: (1) there are general, objective instances which we recognize as *potentially* harmful that can inform motivations to administer analgesics

and amnestics, and (2) these objective considerations can supplement the subjective experience and understanding of harm, and inform the balance of expected benefits and risks associated with the mitigation of pain experience. The practical application of this theoretical threshold can be informed pragmatically by the unique clinical efforts to treat phenomenal and abstract pain in modern medical practice.

Implications for the Use of Amnestics and Analgesics

The nature of the relationships between phenomenal, abstract pain, and harm reflect the existence of an ethical threshold unique to each type of pain, which divides experiences as harmful (to varying degrees) or harmless. While the present paper cannot claim to offer a clear and practical injunction for the permissions surrounding pain and harm, it submits the observation that clinical permissions are dictated by whether a particular course of action surpasses a given limit with respect to the possibility of harm proportional to the action in question. Factors which link pain experiences to harmful outcomes appear likely to include both objective features (e.g., stimulus intensity or timescale) and subjective patient features (e.g., individual tolerance) of the experience, which may serve as a starting point for attempts to delineate the separation between permissible and unacceptable pain experiences.

Because harm thresholds are modified by patient-specific variables, we may never be able to anticipate every individual's tolerance for pain before it broaches harm. In the absence of objective

frameworks for the measurement of pain, the medical system relies on incomplete evidence to anticipate which procedures require complete analgesia or complete amnesia, and which can afford to forego the potential negative effects of either of these interventions. Our permissions to allow pain therefore appear to be guided by a judgement relating to what an average individual can reasonably be expected to tolerate (e.g., a reasonable person can be expected to tolerate the discomfort of endoscopy mitigated by the use of an amnestic with only slight analgesic properties, whereas these permissions cannot be extended to an open thoracic surgery). The gravity of reasonably anticipated effects is also worth considering: our permissions may take into account what negative effects are likely or logically expected to occur in the absence of interference from an amnestic and/or analgesic and, when it can be anticipated that a patient would experience severe pain, we are ethically obligated to mitigate it with the means available to us. When phenomenal pain can be controlled to the extent that physiologic harms are avoided, the further reduction of pain (e.g., providing local anesthetic through a small-bore needle before establishing intravenous access with a larger-bore one) is a purely ethical imperative.

Recognizing the possibility of causing harm through the administration of analgesic or amnestic medications themselves, it may be reasonable to suppose that the overall risk of harm posed to a patient undergoing a brief but stimulating procedure can be furthest reduced by titrating analgesic agents to the point where phenomenal pain experience is maintained below the threshold of physiological harm, and

supplementing this regimen with an amnestic to preclude the possibility that any unchecked phenomenal pain may gain access to memory and result in abstract pain or later harms. The present article posits that this theory is the unspoken ethical justification for conscious sedation, and that a more nuanced understanding of the precise relationships between pain and harm will inform more accurate thresholds to guide the optimization and application of such combined analgesic/amnestic therapy. To this end, the work of elucidating where these thresholds between pain and harm exist, precisely, remains an ongoing project of medical ethics.

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