

# Integrating the Science of Consciousness and Anesthesia

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The nature and mechanism of human consciousness is emerging as one of the most important scientific and philosophical questions of the 21<sup>st</sup> century. Disregarded as a subject of serious inquiry throughout most of the 20<sup>th</sup> century, it has now regained legitimacy as a scientific endeavor. The investigation of consciousness and the mechanisms of general anesthesia have begun to converge. In the present article I provide an introduction to the study of consciousness, describe the neural correlates of consciousness that may be targets of general anesthetics, and suggest an integrated approach to the science of consciousness and anesthesia.

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**R**ecent advances in neuroscience and psychology are now providing the tools and intellectual framework to address the mechanism and function of human consciousness. The investigation of consciousness is emerging as a new science, drawing upon philosophy, cognitive neuroscience, mathematics, physics, and various other disciplines. Although the rigorous investigation of consciousness is still in its nascent stages, the pursuit has gained scientific legitimacy and the field of anesthesiology is poised to play an important role. The present article reviews the basic history and principles of the scientific investigation of consciousness, discusses proposed mechanisms of anesthesia that explicitly consider neural correlates of consciousness, and argues for an integrated approach to the study of consciousness and anesthesia.

## The Emerging Science of Consciousness

The 19<sup>th</sup> century concluded with the belief that consciousness was a legitimate scientific pursuit (1). In the early 20<sup>th</sup> century, however, consciousness lost legitimacy as a topic of serious inquiry in the two dominant paradigms of psychology. Freud's psychoanalytic theory emphasized the investigation of unconscious processes, while behaviorism placed consciousness and science on opposite ends of a spectrum. The behaviorists did not find scientific value in the notion of subjective experience but instead regarded the relationship between stimulus

and observed response as the basis for a rigorous psychology. This antipathy toward consciousness as a scientific pursuit was to persist through the latter part of the 20<sup>th</sup> century, until a recent renaissance of interest (1).

In the 1990s, a number of events reinvigorated the study of consciousness and the beginnings of a "science of consciousness" emerged. In 1994, a landmark interdisciplinary conference of philosophers, neuroscientists, cognitive scientists, physicists, and physicians converged to discuss the possibility of a rigorous interdisciplinary study of consciousness (2). During this time, a number of prominent scientists, including physicist Roger Penrose, as well as Nobel Laureates Gerald Edelman and the late Francis Crick, publicly turned their attention to the study of consciousness. Books began to proliferate on the subject and articles in journals such as *Nature* discussed the neuroscience of consciousness directly (3). As a result of the confluence of these events, the legitimate scientific pursuit of consciousness was re-established.

Currently, there are three basic approaches to the question of consciousness: the philosophical, the physical, and the neuroscientific. The subject of consciousness has a number of unique features distinguishing it from other scientific subjects, and a number of theories have been elaborated (Table 1). These theories, although intellectually fascinating, do not hold promise as foundations for a scientific approach to the subject. Some have argued that the unique features of quantum physics can explain the mysteries of consciousness (4), but using physics to explain consciousness is at present theoretically controversial and experimentally unproven. Although the ultimate explanation may, indeed, require a novel application of physics, it is the neuroscientific approach that has established a successful starting point for the endeavor.

The neuroscientific approach to the study of consciousness is characterized by the search for the "neural correlates of consciousness" (5). For the sake of the present arguments, consciousness is defined as "explicit awareness." The term "awareness" is chosen

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**Table 1.** Selected Positions in the Philosophy of Consciousness

Philosophical position	Basic tenets
Connectionism	Proposes that consciousness arises from the activity of neural networks
Dualism	Proposes mind and brain as distinct, yet interacting, entities
Epiphenomenalism	Proposes that consciousness serves no basic evolutionary purpose itself but rather arises as an epiphenomenon of evolved information processing in the brain
Functionalism	Proposes that a particular functional arrangement is required for consciousness and that this arrangement can be nonbiological (e.g., computer, robot)
Mysterianism	Proposes that the question of consciousness is a mystery that cannot be solved scientifically
Panprotopsychism	Proposes that consciousness is a basic feature of the universe
Panpsychism	Proposes that all matter has some form of consciousness
Phenomenology	Proposes that consciousness can only be understood from the subjective perspective through first-person analysis of its contents
Reductionism	Proposes that all mental events can be reduced to physical or biological events

because of its consistency with the current terminology of anesthesiology; i.e., awareness is typically regarded in contradistinction to anesthesia. Awareness implies both that the brain is aroused and that there are specific perceptual qualities of an experience (e.g., the redness of a rose). The modifier “explicit” distinguishes conscious awareness from other cognitive processes in the brain that remain implicit or unconscious. It is important to note that “explicit awareness” does not necessarily imply “explicit recall,” as it often does in the discussion of awareness under anesthesia.

The phrase “neural correlate” denotes the specific and minimally adequate brain state that corresponds to a specific state of consciousness. There are numerous philosophical subtleties and difficulties regarding the very definition of consciousness and its neural correlates that will not be reviewed here but have been discussed elsewhere (6,7). Neural correlates of consciousness may be identified through a number of

methods, including clinicopathologic correlation (e.g., in stroke or epilepsy), functional neuroimaging, and neurophysiologic recording in association with a cognitive task. Chalmers (7) has summarized some of the initial candidates for the neural correlates of consciousness that developed in the 1980s and 1990s:

- Re-entrant loops in thalamocortical systems (8)
- Neurons in the superior temporal sulcus (9)
- Recurrent processing from higher to lower cortical areas (10)
- Extended reticular-thalamic activation system (11)
- Anterior cingulate system (12)
- Temporally-extended neural activity (13)
- 40-Hz rhythmic activity in thalamocortical systems (14)
- Neural assemblies bound by *N*-methyl-D-aspartate (NMDA) glutamate receptors (15)
- Intralaminar nucleus in the thalamus (16)
- Neurons in extrastriate visual cortex projecting to prefrontal areas (3)
- Neural activity in visual area V5/MT (17)

This list illustrates the diversity of possible neural correlates, ranging from neurons, to brain nuclei, to brain regions, to integrated processes of brain function. Rees et al. (18) have discussed the evidence for many of these neural correlates of human consciousness.

It should be clear that the neural correlates of particular conscious modalities (e.g., the visual) must ultimately be combined with other modalities (e.g., the auditory) to generate perception. This is also true of the various submodalities of sensory perception (such as color, form, and motion in visual processing). Although the brain processes these modalities and sub-modalities in a number of discrete neuronal populations, our experience of the world is nonetheless singular and seamless. This “seamless” quality of our perception is often referred to as the “unity of consciousness.” The mechanisms by which modular perceptual processing in the brain is synthesized into a single experience appear to be interrupted by the actions of general anesthetics. The neuroscientific basis of cognitive information integration will now be discussed, as well as its relevance to the mechanism of general anesthesia.

### The Unity of Consciousness

The unity of consciousness is an important concept in the study of consciousness, and its philosophical origins date to the 18th century, when Immanuel Kant (19) discussed the basic unity that he regarded as an essential prerequisite of consciousness. Kant described the mind as comprised of many distinct faculties particularly suited to perceive different aspects of the world. Despite this “division of labor” in the mind, Kant recognized that we do not perceive the qualities of objects as divided or separated. For example, we do not experience the color and the shape of a rose at different times but, rather, simultaneously. According

to Kant, for a perception to have meaning its distinct qualities must be brought together into a single experience. Kant also recognized that there must be some mechanism by which the diverse and complex processes of the mind are synthesized to generate a single perception. Thus, he was remarkably prescient with respect to the development of cognitive neuroscience.

In the late 19<sup>th</sup> century, clinicopathologic correlations by neurologists such as Broca and Wernike led to the realization that specific brain regions serve specific cognitive functions. Neuroscientific progress over the 20<sup>th</sup> century refined these initial observations, demonstrating cortical localization for distinct sensory modalities (such as vision), as well as specialized neuronal subgroups that process submodal properties (such as motion or color). The visual system has been a model for the study of consciousness, attempting to elucidate neural correlates in the sites or pathways from the occipital cortex (primary processing), to the temporal and parietal cortices (the “ventral” and “dorsal” streams, respectively), to the prefrontal cortex. In the 1980s, the quandary recognized by Kant was formulated in neuroscientific terms: how does the brain synthesize the elements of visual processing in these discrete cortical loci to generate a unified visual perception? This question has come to be known as the “cognitive binding problem” (20,21).

Cognitive binding is thought to occur within and across sensory modalities and is thought to be necessary, although not sufficient, for consciousness itself. There are several proposed mechanisms for cognitive binding in the brain, including binding by convergence, binding by assembly, and binding by synchrony. Binding by convergence is the transmission of information from more primary processing areas to another region of the brain for integration. Binding by assembly refers to information being synthesized or bound in a Hebbian cell assembly, i.e., a group of inter-related neurons whose connections grow stronger with repeated firing together. Binding by synchrony is the coordination of neural firing in time and is thought to be associated with neural events at the frequency of 40 Hz. A discussion of the strengths and weaknesses of each of these proposed mechanisms can be found elsewhere (22,23). The present discussion will focus on convergence and synchrony, as they represent binding processes on the cellular and global brain level that are directly relevant to general anesthesia.

Cognitive binding by convergence denotes the process of lower-order neural processing becoming synthesized in higher-order brain regions. Such neuronal subpopulations have been found to be selectively responsive to specific sensory stimuli. For example, the recognition of faces is linked to the fusiform gyrus of the temporal lobe (24), suggesting that the various features of a face processed in primary visual areas (such as V1 in the occipital lobe) converge and are bound in this region. Cortical area MT is another temporal lobe locus of visual processing for object recognition processing visual motion (25). Again, it is

suggested that primary and secondary order features converge and are bound in this cellular subpopulation (26). The extreme example of binding by convergence is the concept of a “grandmother cell,” which binds all of the features of a particular object (such as your grandmother).

Although binding by convergence suggests neural information integration in space (i.e., another brain region), binding by synchrony suggests neural information integration in time. There is abundant evidence for synchronization at all levels of neural processing that has been associated with perceptual tasks and cognitive binding (27). There has been considerable focus on cortical activity in the  $\gamma$ -band frequency of 40 Hz as a mechanism of binding (28). It has been suggested that cortical 40-Hz activity coordinated by the thalamus serves to bind information that is processed within the 12–15 ms timeframe in which these oscillations propagate across the brain (14). The 40-Hz oscillations of thalamocortical circuits have been proposed as neural correlates of consciousness and will become particularly relevant in the consideration of general anesthetic mechanism.

Consistent with the philosophy of Kant and the neuroscience of cognitive binding, Giulio Tononi (29,30) has proposed an “information integration” theory of consciousness, as well as a theoretical model that expresses the capacity of neural systems to integrate information (a value denoted as  $\Phi$ ). Tononi suggests that certain neural systems have a higher capacity to integrate information, which is why, for example, thalamocortical circuits are more relevant to conscious processes than cerebellar circuits. This higher integrative power is correlated with a higher value of  $\Phi$ . Because  $\Phi$  is a mathematical expression reflecting the capacity for consciousness, it is increased in systems maintaining consciousness (e.g., thalamocortical processes) and decreased in those that do not (e.g., cerebellar processes, sleep).

In philosophy and neuroscience, as well as in current theories of consciousness, the synthesis of cognitive information appears to be an essential requirement for conscious processes. Furthermore, such integrative functions appear to be operational from the cellular to the global brain level. It is of interest that current theories of general anesthesia grounded in the neurophysiology of consciousness either implicitly or explicitly suggest that this synthetic process is the functional substrate of general anesthetic mechanism.

### A Brief History of General Anesthesia

Anesthesia was first demonstrated successfully in 1846 at the Massachusetts General Hospital and over the next decade chloroform, ether and nitrous oxide were administered as general anesthetics. The clinical use of these diverse agents also led to a fundamental scientific question: what is the mechanism of general anesthesia? As early as 1847, von Bibra and Harless (31) suggested that anesthetics dissolve and remove

lipids in the brain. In 1875, Claude Bernard (32) formulated the original “unitary hypothesis” of general anesthesia, suggesting that all of these structurally and pharmacologically diverse agents have a final common mechanism. Around the turn of the 20<sup>th</sup> century, Meyer and Overton (33,34) independently observed that the potency of volatile anesthetics was correlated with their solubility in olive oil. The synthesis of these ideas led to the “lipid hypothesis” of general anesthesia, the proposition that anesthetics act by nonspecific perturbation of lipid cell membranes in neural tissues.

Variations on the lipid membrane hypothesis of general anesthesia persisted late into the 20<sup>th</sup> century, until Franks and Lieb (35) demonstrated in 1984 that anesthetics inhibit lipid-free preparations of the enzyme firefly luciferase in parallel with their hydrophobicity. Since the time of this discovery, the specific actions of anesthetics on protein substrates have been investigated. Despite the potentially “promiscuous binding” of anesthetics (36), the primary focus of molecular targets has been ion channels. Ion channels serve a number of functions within the neuron and are the molecular mediators of the neurophysiology that forms the basis of consciousness.

As the focus of anesthetic activity shifted from lipids to proteins, the understanding of anesthetic mechanism shifted from unity to diversity. General anesthetics affect a number of different neurotransmitter receptors, including  $\gamma$ -aminobutyric acid (GABA) type A, nicotinic acetylcholine, and glutamate receptors in the brain, as well as glycine receptors in the spinal cord (reviewed in 37,38). The characterization of anesthetic activity on different channel subunits was further refined through the use of genetic techniques such as in transgenic and knockout mice (reviewed in 39). Furthermore, distinct neuroanatomic sites were correlated with distinct anesthetic properties: hypnosis appears to be associated with cerebral cortical effects (discussed below), amnesia with limbic system effects (40–42), and immobility and analgesia with spinal cord effects (43–47). Neuroanatomical structures affected by general anesthetics include thalamus, cuneus, and precuneus, posterior cingulate cortex, orbitofrontal cortex, and right angular gyri (48). The molecular, neuronal, and neurophysiologic effects of general anesthetics have been extensively reviewed elsewhere (37–39,49).

### Current Theories of General Anesthesia and Consciousness

Given the multitude of anesthetic substrates and effects, it appears as if Bernard’s unitary hypothesis of anesthetic mechanism is no longer tenable. The substrates of anesthetics that are typically considered have been structural entities such as lipids, proteins, or neuroanatomical sites. Because these substrates are diverse, it would appear that no unitary construct is possible. This argument, however, confuses the *actions*

of general anesthetics with the *mechanism of general anesthesia*. Describing the mechanism of anesthesia as, for example, the potentiation of GABA transmission epistemologically begs the question, as it says little about how the state of general anesthesia is actually generated. Thus, the potentiation of GABA may be more accurately regarded as an *action* rather than a *mechanism*.

A proposed mechanism of general anesthesia must in some way describe how anesthetic actions affect functional end-points, such as the loss of consciousness. Current theories that attempt to explain general anesthetic mechanism have, indeed, focused on functional processes related to the neural correlates of consciousness. The information processing theory of Flohr (50), the unified narcosis theory of Alkire et al. (51), the cognitive unbinding theory of Mashour (52), and the proposed anesthetic cascade by John and Prichep (49), have all in some way considered synthetic processes in the brain as the functional targets of general anesthetics.

In 1995, Flohr (50) proposed an “information processing” theory of anesthetic mechanism. The premise was based on the role of glutamatergic NMDA receptors in the function of Hebbian cell assemblies responsible for cortical representation of conscious perceptions (53). A Hebbian assembly denotes a set of interconnected neurons that are functionally and anatomically linked, primarily through repetitive synaptic activity among the interconnected cells (54). As mentioned above, “binding by assembly” is indeed another mechanism posited to mediate information synthesis in the brain. Flohr postulates that general anesthesia results because of the interruption of NMDA receptor-mediated higher-order representation, as supported by the anesthetic actions of known NMDA-receptor antagonists such as ketamine, nitrous oxide, and xenon (55). GABA-mediated actions of anesthetics are posited to have an indirect and common final effect through NMDA pathways. This theory represented an important step in linking a molecular action of anesthetics to a functional neural correlate of consciousness.

In 2000, Alkire et al. (51) described a “unified theory of narcosis” based on the finding that thalamocortical circuits were disrupted under general anesthesia. The resonance of thalamocortical circuits has been proposed as the “dynamic core” of consciousness by Edelman (8) and is consistent with cognitive binding by 40-Hz oscillations (14). Functional neuroimaging by positron-emission tomography during either isoflurane or halothane anesthesia demonstrated reduced cerebral glucose metabolism in the thalamus, midbrain reticular formation, basal forebrain, cerebellum, and occipital cortex. Thus, like Flohr, the work of Alkire et al. suggests that neural correlates of consciousness related to binding are suppressed under anesthesia.

In 2004, Mashour (52) proposed the “cognitive unbinding” paradigm of general anesthesia, stating

explicitly that anesthetics may function by interrupting various cognitive binding processes from the cellular to the global brain level. This was, in part, based on findings by John et al. (56) that demonstrated a functional uncoupling of 40-Hz activity between the hemispheres and rostrocaudal axis of the brain (interruption of synchronous binding). The cognitive unbinding paradigm was also based on the interruption of synthetic processes in cortical area MT under isoflurane (interruption of convergent binding) (57). A causal relationship between anesthetic activity on the cellular and global brain level was not posited and the theory was not restricted to particular molecular mediators; rather, it was suggested that cognitive unbinding was a common functional outcome among different pharmacological agents, as well as at different levels of neural processing. Peltier et al. (58) demonstrated loss of functional connectivity in the cerebral cortex during sevoflurane anesthesia. This supports cognitive unbinding as a potential anesthetic mechanism by providing further evidence that anesthetics uncouple the activity of brain regions that would otherwise influence one another in the waking state.

In 2005, John and Prichep described the "anesthetic cascade" (49). This proposed mechanism of general anesthesia endorsed the concept of cognitive unbinding, while at the same time postulating a specific stepwise process by which anesthetics suppress consciousness. The proposed "cascade" is as follows:

1. Depression of the brainstem reduces the influences of the ascending reticular activating system on the thalamus and cortex.
2. Depression of the mesolimbic-dorsolateral prefrontal cortex interactions leads to blockade of memory storage.
3. Further depression of the ascending reticular activating system leads to hyperpolarization of GABAergic neurons in the nucleus reticularis of the thalamus, resulting in
4. Blockade of thalamocortical reverberations and the associated  $\gamma$ -oscillations underlying perception, as well as
5. Functional uncoupling of parietal-frontal cortical activity, interrupting cognition, and finally
6. Reduced awareness and increase of frontal  $\delta$  and  $\theta$  band activity.

Interestingly, the cascade is organized by first describing molecular actions of anesthetics then linking these actions to neural correlates of consciousness such as thalamocortical resonance and  $\gamma$  oscillations. It is unclear how drugs such as ketamine or nitrous oxide, which can lead to electroencephalogram activation rather than depression (59,60), fit within the proposed anesthetic cascade. The previously discussed frameworks of consciousness and anesthesia are not dependent on depressive actions of anesthetics but instead focus on the disorganization of processes

that bind information together. Thus, while the anesthetic cascade of John and Prichep incorporates many aspects of proposed mechanisms of general anesthesia that are based on neural correlates of consciousness, perhaps the early steps could be revised to accommodate both excitatory and depressive phenomena.

Although not discussed above, it is of interest to note that Hameroff's quantum theory of consciousness is also grounded in information coherence, albeit by non-classical physical processes (4). Accordingly, he suggests that anesthetic actions in the hydrophobic cavities of microtubules, which are purported to mediate coordinated quantum computation in the brain, disrupt this coherence, leading to the loss of consciousness (61). Thus, even markedly distinct perspectives on consciousness and anesthesia can be based on the integration and disintegration of cognitive processing.

### Converging Neuroscientific Perspectives Of Unconscious States

The frameworks of anesthetic-induced unconsciousness discussed above either directly state or indirectly imply that it is not necessarily the *absence* but the *disintegration* of cognitive processing that characterizes the loss of consciousness. If this were the case, we would expect other physiologic and pathologic states of unconsciousness to be associated with a similar neurophysiology. Recent data on both unconscious vegetative states and sleep indicate that this may be the case, lending support to current theories of general anesthesia and consciousness.

"Effective connectivity" refers to the relationship of activity between distant structures in the brain and can be assessed using functional neuroimaging (62). Effective connectivity is a functional state beyond the anatomic connections of two structures and implies that one brain region causally influences another. Studies of brain-injured patients in vegetative states have revealed fragmented cerebral activity (63) and a loss of such effective cortical connectivity (64). It has therefore been suggested that vegetative states are "disconnection" syndromes (65). There is no one brain area that appears to be exclusively associated with vegetative states but rather a network of areas including frontal cortex, cingulate cortex, association cortices, and thalamus (65). As mentioned above, general anesthetics are thought to target many of these structures. Of interest, recovery from vegetative states is associated with a restoration of the connectivity of thalamocortical networks (66). Similarly, emergence from anesthesia is associated with a return to the coordinated activity of  $\gamma$  oscillations throughout the cortex that were uncoupled during induction and maintenance (56).

As stated above, neuroimaging studies during general anesthesia have also shown decreases in effective connectivity in the cerebral cortex and thalamocortical systems (58,67). Sleep is a state with a number of similar traits to general anesthesia (68), and is often

used as a metaphor for anesthesia in the clinical setting. Using a transcranial magnetic stimulation and electroencephalogram recordings of subjects either asleep or awake, Massimini et al. (69) demonstrated that non-rapid-eye-movement sleep is also characterized by a loss of effective cortical connectivity. The loss of cortical connectivity associated with sleep suggests a common feature with anesthetic-induced loss of consciousness (70).

Loss of effective connectivity, functional uncoupling, and cognitive unbinding are all terms that denote the interruption of functional neural interconnections essential for conscious processing. Recent data on sleep and vegetative states suggest a common neurophysiology underlying the loss of consciousness and support the continued focus on information dissociation as an important mechanism for anesthetic-induced unconsciousness.

## DISCUSSION

As we pursue the specific neural correlates of general anesthesia, we are in a position to understand further the neural correlates of consciousness. Neural networks or anatomic sites that are reversibly and consistently inhibited during general anesthesia present themselves as potential mediators of consciousness. Of equal importance, as we understand the neural activity that *persists* under general anesthesia, we are also in a position to *eliminate* functional or anatomical candidates for the neural correlates of consciousness. The hypnotic property of general anesthetics suppresses consciousness: thus, if particular neural activities are present in the absence of awareness, they are likely to be poor contenders for sufficient neural correlates. As one example, Crick and Koch (3) demonstrated that activation of primary visual cortex V1 is not sufficient for consciousness in the awake nonhuman primate. This conclusion is supported by the finding that primary visual processing can persist under general anesthesia, while higher order processing is interrupted (71,72). A recent study of auditory processing under general anesthesia has reached a similar conclusion (73). Such studies demonstrate the potential for anesthesiology to contribute to the understanding of the neuroscientific basis of consciousness.

The current frameworks of general anesthesia reflect an emerging relationship with the science of consciousness, as they are based on proposed neural correlates of consciousness. In particular, neuroscientific theories of consciousness, as well as those based in physics, suggest that the binding or integration of cognitive processing is an essential neural correlate. Importantly, the validity of this is, in turn, supported by the empirical observations under anesthesia that such binding and integrative functions are interrupted. This further suggests the potential for an integrated science of consciousness and anesthesia: 1)

proposed neural correlates of consciousness may be tested as functional substrates of general anesthetics, and 2) the molecular or neurophysiologic targets of general anesthetics may be tested as neural correlates of consciousness. This relationship could perhaps be formalized as a principle of "mutual verifiability," namely, that 1) any proposed neural correlate of consciousness must be eliminated or altered under general anesthesia, and 2) any proposed mechanism of general anesthesia must link molecular anesthetic action to the elimination or alteration of a neural correlate of consciousness. This could establish a formal and practical scientific dialogue between two pursuits that appear to be linked in principle.

This is by no means the first time that a relationship between the science of consciousness and anesthesia has been proposed. This may, however, be the first time that the field of anesthesiology is ready for such a proposal. There was recognition in the late 1980s and early 1990s that the study of consciousness and anesthesiology shared a common interest (74). It is important to consider that this was a time in which a paradigm shift was occurring: investigation of anesthetics was shifting from lipids to proteins, and the diversity of molecular actions was becoming appreciated. Thus, integrative or unitary hypotheses were not the focus at that stage of investigation. In fact, it is only in recent years that discussions of anesthesia and neural correlates of consciousness have appeared in the literature of anesthesiology (49,52), rather than the literature of psychology (50) or consciousness (51).

It has been suggested that anesthetics may not be a useful tool to study consciousness because of their diverse molecular actions (75). It is arguable, however, that differing molecular actions can nonetheless result in a single common mechanism. An example from oncology is illustrative: although tumors may have high genotypic variability, these diverse molecular mutations may nonetheless result in a neoplasm with a common histological phenotype. Furthermore, there may be a functional outcome of tumorigenesis that is common and essential to all such neoplasms, such as angiogenesis. Similarly, general anesthetics act on diverse substrates on the molecular level, yet may nonetheless result in a similar "phenotype" with a common functional outcome. The common feature that is currently proposed in multiple frameworks of anesthetic mechanism is the disruption of integrated neural processes that are normally required for consciousness. This is supported by data from studies indicating similar processes in sleep or vegetative states.

## CONCLUSION

In 1947, Harvard anesthesiologist Henry Knowles Beecher published a prescient article in *Science* entitled "Anesthesia's Second Power: Probing the Mind" (76). In it, he states that:

“...we seem to have a tool for producing and holding at will, and at little risk, different levels of consciousness—a tool that promises to be of great help in studies of mental phenomena.”

Nearly 60 years later, perhaps the time has come to actualize this “second power.” The scientific pursuit of consciousness and general anesthesia appear to have converged, suggesting the potential for an integrated science. Appropriating the question of consciousness provides anesthesiology with a focus that extends its role beyond the operating suite and into the heart of a fundamental intellectual pursuit. The first power of clinical anesthesia led to a revolution in the 19<sup>th</sup> century and continues to provide benefits to patients worldwide. Perhaps this second power of anesthesia can contribute to yet another revolution, providing critical insights to the science of consciousness in the 21<sup>st</sup> century.

## APPENDIX: RESOURCES FOR THE STUDY OF CONSCIOUSNESS

### Organizations:

Association for the Scientific Study of Consciousness (ASSC): <http://assc.caltech.edu/index.htm>

Center for Consciousness Studies: <http://consciousness.arizona.edu/>

### Journals:

*Consciousness and Cognition* (Official journal of ASSC)

*Journal of Consciousness Studies*: <http://www.imprint.co.uk/jcs.html>

### Conferences:

Annual meeting of ASSC

Biennial “Toward a Science of Consciousness” conference in Tucson; alternates with a smaller conference abroad: <http://consciousness.arizona.edu/>

### Internet Resources:

Science and Consciousness Review: <http://www.scicon.org/>

The homepage of David Chalmers provides access to >2000 online articles on the subject of consciousness: <http://consc.net/online.html>

### Selected Compendia:

Steven Laureys, ed. *The boundaries of consciousness: neurobiology and neuropathology*. Progress in Brain Research Series (150). Amsterdam: Elsevier, 2005.

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### Other Media:

“Consciousness”—multiple lectures on DVD: <http://www.amazon.com/exec/obidos/tg/detail/-/B0007M1294/103-4036929-6747054?v=glance>.

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