Sleep and anesthesia: can we use a physiologic model to decrease risks of a medical intervention

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Abstract

Anesthesiology is one of the most important creations of the modern science, basically based on the anesthetic drugs; however, there are a few concerns regarding the effects of the anesthetic drugs. Would there be any progress in the current trend of anesthesiology, both clinically and basically. There would be a possibility to use the physiologic mechanisms of sleep to be incorporated into clinical practice instead of pharmacologic agents in order to decrease their unwanted effects.

Keywords: Sleep, Anesthesia, Analgesia, Mechanism, Pain

Introduction

Anesthesiology is a relatively new convention of medicine. Many surgeries are nowadays performed just because we can anesthetize patients; otherwise, there was no progress in the many fields of surgery. In the United States, nearly 60,000 patients are anesthetized each day, mainly for surgical operation.

The first time that anesthesia was "created", one of the greatest fears of mankind was overcome (1): since the first patient was anesthetized in October 16, 1846 by Dr William T. G. Morton at Massachusetts General Hospital, Boston, the science and practice of anesthesiology has made many great developments, increasing its efficacy and safety and at the same time, decreasing the anesthesia-related morbidity and mortality (2, 3).

In the current era of modern anesthesiology, the practice and science of anesthesia is composed of 4 basic elements; each being one of its permanent counterparts; without each of them, anesthesia is not complete. These 4 basic elements are (4, 5):

1) hypnosis (an iatrogenic pharmacologic-based coma)
2) amnesia (forgetting the unpleasant events during operation)
3) analgesia (painlessness)
4) akinesia (lack of movements in response to noxious stimuli, including the surgical incisions and manipulations).

Very interesting issue is that all of these basic elements of anesthesia are created after interaction of anesthetic drugs with different parts of the nervous system (including central, peripheral, and autonomic nervous systems). However, CNS remains the primary site of action for "anesthesia". In other words, anesthesia is an iatrogenic, reversible, pharmacologic-based coma; affecting CNS neuronal circuits at many levels including the molecular level; for example, the mechanism of anesthesia in some volatile agents (i.e. Isoflurane and Sevoflurane) is through inhibition of...
orexinergetics neurons; also, ketamine acts through “pyramidal cells and also, seven different types of CA1 interneurons” (6-13) or amnesia is induced primarily through effects of anesthetics on hippocampus neurons (14-16). Also, the majority of CNS anesthetics act through N-methyl-D-aspartate (NMDA) receptor or gamma-amino butyric acid (GABA) receptor subunits (17-30).

Globally, some believe that anesthesia induction is due to “drug-induced global modulation of neuronal function”; meanwhile, termination of anesthesia is spontaneous and passive, occurring after termination of pharmacologic effects of anesthetics from “their sites in the central nervous system”; though this mechanism might be somewhat oversimplification and the neural inertia could have a role (31-36).

But are we doing anesthesia in a right way? Are the modern anesthetic drugs as safe and physiology-compatible as we want? To answer this questions, one could consider the many animal and human studies proving the very safe anesthetic agents and the very diminutive incidence of unwanted effects of anesthetic drugs. Despite the many available proofs for modern anesthesia safety, there are some considerations regarding the effects of anesthetics on organ functions described in the following paragraphs.

If we want to discuss more specifically, anesthesia is not so much physiologic. It is demonstrated in cerebral cortex and hippocampus neurons of rats that neuronal spikes from these sites are “very stable across physiologic states i.e. waking, slow-wave sleep and rapid-eye-movement sleep”; however, these neuronal spikes and avalanches “would collapse during anesthesia”. Also, waiting time distributions obey a single scaling function during all natural behavioral states, but not during anesthesia (34, 36-38).

From another viewpoint, anesthesia is an iatrogenic pharmacologic based coma; of course with a reversible nature. In fact, electroencephalographic studies performed in patients undergoing general anesthesia has demonstrated an EEG pattern similar to patients with coma; in other words, the EEG waves in "comatose patients" and "patients undergoing general anesthesia" both demonstrate high amplitude, low-frequency waves (4, 39, 40).

Now let's discuss the issue from a different viewpoint; i.e. the neurophysiologic point of view. During normal sleep, the arousal status is depressed and we would go unconscious. During the rapid eye movement (REM) phase of sleep, EEG waves have an active high-frequency, low-amplitude pattern; while in the non- rapid eye movement (Non-REM) phase of sleep the EEG waves are high amplitude, low frequency (33, 39-44). In contrast to this dual stage pattern of EEG in sleep, the EEG pattern in "general anesthesia" or "coma" has high amplitude, low-frequency waves. Although coma and general anesthesia have some similarities with the Non-REM phase of sleep, "coma and general anesthesia" are not the same as Non-REM (4, 32, 41, 45, 46). As we see, EEG assessments also suggest us that possibly; the current anesthetic pharmacologic agents are not as physiologic as we need.

Concerning the clinical point of view may be all above comments are not as worrying as the following lines of this paragraph; which addresses a sample of the many studies published mainly in the last decade. There are an increasing number of evidence demonstrating the unwanted effects of anesthetic agents on the synaptogenesis processes in the animal neonates receiving modern anesthetic agents; these animal and lab studies have demonstrated the clues to apoptotic effects of anesthetics; some even well demonstrating these effects on animal CNS; though human CNS studies are not so much available due to technical problems (12, 46-74); also, there are a number of studies raising the questions regarding the effects of some of the current anesthetic agents on the behavioral and learning aspects of the human neonates, though none of them still have not presented definite proof for this effect (75).

There are some new windows which could help us use the sleep mechanism as a “physiologic mechanism” instead of the current “pharmacologic mechanism” for anesthesia. In one direction, there is a concordance between interventions which disturb sleep and/or cause some types of somatic pain; in other words, these interventions have the “same direction effects” for pain and sleep; i.e. there is a concordance between them (76-79); so, possibly we
could use the physiologic mechanisms maintaining normal sleep for suppressing those surgical stimuli which create pain. On the other hand, we could use some newer molecules like urethane which could induce anesthesia with mechanisms different from current anesthetics; it means that urethane induces anesthesia with a mechanism “closely mimicking natural sleep” (8, 80-83).

**Conclusion**

The above paragraphs are brief concerns regarding the importance of a new look at our current approach for a very common medical practice. In other words, in the current era of clinical and basic studies, the effects of anesthetic agents in creating the "pharmacological coma" is a very important concern with high priority, in medicine, in pharmaceutical studies and more importantly, in neuroscience. We anticipate a very important turning point, which would add another improvement to the safety of anesthesia and add another revolution to the previous “jump up’s” of this field of medicine, as a number of relatively safe anesthetic agents have emerged and shown to be neuroprotective (5, 84-90); however, this time, the turning point would be at the cellular and subcellular levels.

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**Conflicts of Interest**

The authors declare that there are no conflicts of interest.

**References**

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