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The Quest for Anesthetic Depth: Albert Faulconer, Electroencephalography and the Servo-Controlled Anesthesia Machine

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Introduction

In October 1996 the Food and Drug Administration approved the use of a new monitoring device of anesthetic effect that integrates various electroencephalogram (EEG) descriptors into a single dimensionless, empirically calibrated number, the Bispectral Index (BIS, Aspect Medical Systems, Natick, MA).[1] The BIS monitor is the latest innovation in the quest for a reliable monitoring device of anesthetic depth, the "holy grail" of monitoring for anesthesiologists.[2] This new monitor is gaining acceptance in the anesthesia community, but the basic concept of this idea goes back to the early 1950's. At that time Albert Faulconer and Reginald Bickford from the Mayo Clinic first systematically investigated EEG changes induced by various anesthetic agents.[3-5] In a pioneering project, they went a step further and attempted to create the first closed-loop anesthesia delivering device, the servo-controlled anesthesia machine, aimed at automatic control of anesthetic depth via EEG guided delivery of anesthetic agents.[6] The following is an illustration of some of the problems associated with this groundbreaking idea.

Electroencephalography and anesthesia: the early years

Richard Caton, a physician in Liverpool, first noted the occurrence of electric potentials in the brains of animals in 1875.[7] In 1890, von Marxow described the effects of chloroform anesthesia on brain waves.[8] In 1929, Hans Berger, a psychiatrist in Jena, Germany and the "father of electroencephalography," demonstrated that the electric potentials of the human brain could be recorded from electrodes placed on the surface of the head.[9] Four years later he described the loss of alpha-waves in the EEG caused by chloroform anesthesia.[10] In 1937, Gibbs and associates noted that the EEG was sensitive to anesthetic agents and postulated:

> A practical application of these observations might be the use of the electroencephalogram as a measure of the depth of anesthesia during surgical operations. The anesthetist and surgeon could have before them on tape or screen a continuous record of the electrical activity of both heart and brain.[11]

Shortly thereafter, EEG changes were reported with the use of cyclopropane[12] and barbiturates.[13] In the early 1950's, Faulconer and his colleagues studied the EEG changes produced by ether,[3] sodium thiopental,[4] and cyclopropane[5] under actual surgical conditions. They classified the results of administration of an anesthetic agent into distinct patterns identifiable on the EEG, based upon the observation that "the electric output of the brain would decrease progressively from the stage of light anesthesia to that of deep anesthesia."[14] After identifying 7 distinct EEG levels (Fig. 1) with ether administration,[3] 6 with cyclopropane anesthesia,[5]

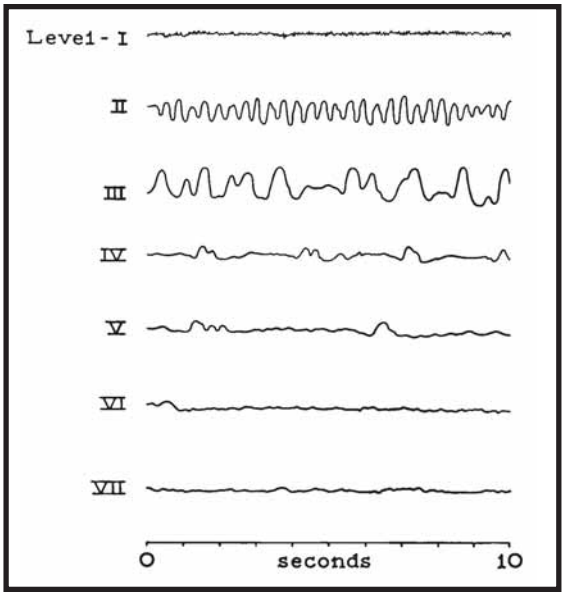

Fig.1: Characteristic patterns of successive electroencephalographic levels of ether anesthesia as described by Courtin, Bickford and Faulconer in 1950.[3] Levels IV to VI represent progressively increasing suppression to burst intervals. Level VII is isoelectric. (From Faulconer A, Bickford RG: Electroencephalography in Anesthesiology. Springfield, Charles C Thomas, 1960. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois).

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and 5 with pentothal anesthesia,[4] Faulconer was convinced that the EEG could be used "as a reliable index of the depth of anesthesia."[15] His finding that increased arterial ether concentrations correlated nicely with greater EEG depression linked the electrophysiologic effect of ether to a measure of anesthetic uptake and lent further credence to the use of EEG as a measurement of anesthetic depth.[16]

The development of the servo-controlled anesthesia machine

Faulconer was searching for a more scientific basis to assess anesthetic depth, as he recognized that since John Snow's early clinical observations in 1858[17] "the diagnosis of depth of anesthesia in this manner has never been an exact science but is truly an art."[6] Convinced that "EEG changes occurring during surgical anesthesia might provide a basis for a more objective and exact estimate of the depth of anesthesia,"[6] he and Bickford developed the first automatic EEG controlled anesthesia delivering system. Bickford was the driving engineering force behind the project.[18]

Their servo-controlled anesthesia machine was based upon the principle that "the output of cortical electrical energy falls off consistently in relation to increasing depth of surgical anesthesia"[19] and consisted of an EEG monitor recording cortical electrical activity obtained from a single fronto-occipital electrode pair placed on the scalp of the patient. The EEG voltages were summated with an integrating circuit and converted to pulses proportional in number to the time-integrated EEG potential. These integrator output pulses triggered a stepping relay leading to a syringe pump-driven administration of a unit dose of the anesthetic agent into the circulation or anesthesia circuit (Fig. 2). The frequency of dosing and thus anesthetic depth was independently adjustable by changing the gain of the EEG voltage output. Thus the servo-controlled anesthesia machine delivered a predetermined unit dose of anesthetic agent at a rapid rate when the summated EEG potential was high (fast or high amplitude EEG activity), and at a slower rate when the pattern revealed less activity. Bickford compared the principles of this design to "application of engineering principles to the human that have been known since James Watt invented the governor for his steam engine."[6]

Testing this closed-loop system in animals showed "that a desired level of surgical anesthesia could be maintained automatically for long periods of time (two to three days) without human interference."[6] In 1950, the first human trial with 50 patients undergoing major abdominal surgery was presented before the section of surgery, general and abdominal, at the 99th annual session of the American Medical Association in San Francisco. The authors concluded that "as an outcome of this work it was seen that there were changes in the electroencephalographic pattern of sufficient clarity, magnitude and consistency to allow these changes to be related to depths of anesthesia progressing from loss of consciousness to complete respiratory paralysis."[6] The researchers also noted that "the EEG foretells a change in depth of anesthesia many seconds before the change is apparent to an anesthetist. Thus the system is more capable than an anesthetist of maintaining a constant level."[6] In a letter of discussion accompanying the publication, William Estes, a surgeon from Bethlehem, PA remarked:

> My only qualification to discuss this report is that I have seen this remarkable machine in action. It is most uncanny and dramatic to observe the automatic record of the patient's condition unfold, including both the electrocardiographic changes and the electroencephalographic record, while the little click every few seconds indicates the automatic administration of small increments of the anesthetic agents. The mechanism by which all this is accomplished is most baffling to a

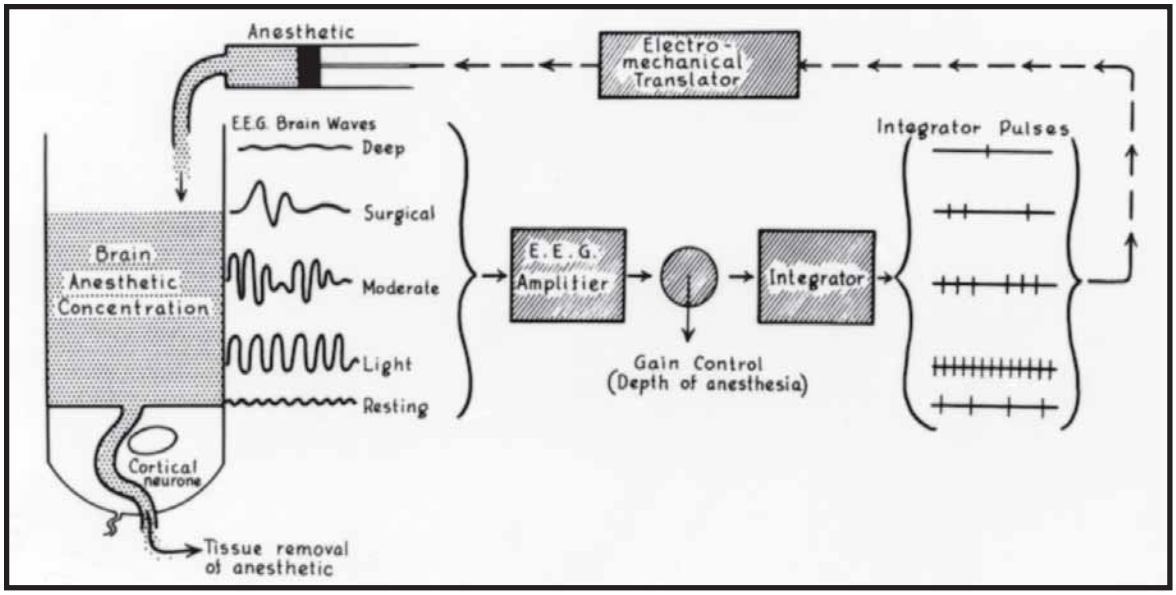

Fig. 2: The principle of the servo control mechanism after Faulconer and Bickford [15]. The patient EEG (left) is the physiologic variable measured and ultimately drives the electromechanical translator (top center) of the drug delivery system (top left). The raw EEG is integrated over specified time intervals and amplified to increase output (see integrator pulses on right) to the drug delivery system as a function of total EEG amplitude. (From Faulconer A, Bickford RG: Electroencephalography in Anesthesiology. Springfield, Charles C Thomas, 1960. Courtesy of Charles C Thomas, Publisher, Springfield, Illinois).

> mere surgeon. Although the full significance of a machine of this character in the field of anesthesia is at this time difficult to predict, the immediate potentialities are most impressive and seem epoch making.[6]

With limited data-processing resources at that time, Faulconer and Bickford refined the servo-controlled anesthesia machine by trying to minimize outside electrical interference from sources other than the EEG signal.[20]

Faulconer also noted significant individual variability in observations early in his research.[16] But in contrast to "the transient and somewhat inconstant nature of the clinical signs, and the variations in their interpretation by different individuals,"[16] he found the EEG patterns of anesthesia to be more objective[6] and believed in the clinical and research applications of his "servo-anesthesia";[19] a notion that was not shared by all of his colleagues.[21] However, both Faulconer and Bickford were well aware, that "automatic control cannot be more reliable than the electroencephalographic information on which it operates."[22]

This statement reflects one of the fundamental problems associated with automatic anesthesia control: the need for a reliable neurophysiologic endpoint to provide an assessment of anesthetic depth to guide the unit dosing of a closed-loop anesthetic administration system. While the spectrum of effects constituting general anesthesia and anesthetic depth is still hotly debated,[23,24] blocking the somatic motor response to painful stimuli is widely used as an indicator of anesthetic adequacy. The end-tidal concentration of anesthetic agent required to achieve this unresponsiveness (MAC) remains the benchmark of anesthetic potency.[25,26]

More than a decade before the concept of MAC was introduced, and in an era where muscle relaxants were not yet routinely used, the servo-controlled anesthesia machine was designed to achieve immobility during surgical stimuli by increasing the concentration of the anesthetic agent until burst suppression in the EEG occurred.[19] Although this level of anesthesia would be considered unnecessarily deep by modern standards, it was an appropriate way to provide satisfactory surgical conditions at a time when sophisticated pharmacological tools and monitoring equipment were limited.

Why the servo-controlled anesthesia machine did not gain widespread popularity following its introduction into clinical practice remains unclear, but the need for constant supervision and adjustment and the development of new pharmacologic agents, particularly muscle relaxants, may have played significant roles (Professor P. Southorn, Mayo Clinic, Rochester, MN; personal communication). Faulconer and Bickford, however, deserve recognition for opening a new chapter in the quest for monitoring anesthetic depth by first recognizing the potential usefulness of EEG monitoring to guide the delivery of anesthetic agents almost half a century before the BIS monitor.

New research over the last decade has painted an even more complicated picture about monitoring anesthetic depth than originally anticipated. Recent research attempts to relate sophisticated computer-processed EEG to clinical anesthetic depth have resulted in inconclusive findings.[27,28] Other autonomic or electrophysiologic measurement techniques, such as auditory evoked potentials[29] or contractility of the lower esophagus[30] do not consistently correlate with anesthetic depth either.[31] The BIS monitor, designed to measure the hypnotic component of an anesthetic regimen, has been shown to predict loss of consciousness and loss of recall with good probability under certain clinical conditions.[32,33] Recent case reports showing intra-operative awareness despite adequate BIS values illustrate the complexity of the problem of measuring adequate anesthetic depth using cortical neurophysiologic monitoring.[34,35] Furthermore, animal studies over the last decade suggest that anesthesia-induced immobility to surgical stimulus may be a subcortical or spinal cord phenomenon.[36,37] With accumulating evidence that anesthetic actions at the spinal cord level determine MAC,[36,38,39] we can now appreciate why measuring cortical electrical activity from the surface of the human brain does not correlate reliably with anesthetic depth as we currently define it.

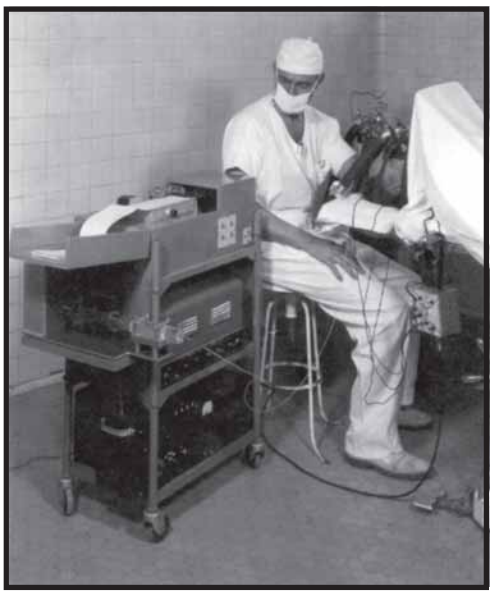

Fig. 3: Donald Sotero, a colleague of Albert Faulconer, with the servo-controlled anesthesia machine. This model automatically delivered pentothal anesthesia. The syringe pump is on the left side of the servo-anesthesia machine. This system was also adopted for administration of ether anesthesia, wherein ether was injected from the syringe pump into the inspiratory limb of the anesthesia circuit. (From Rehder K, Southorn P, Sessler A: Art to Science. *Mayo Foundation for Medical Education and Research, Rochester, Minnesota, 2000. By permission of Mayo Foundation for Medical Education and Research).*

Conclusions

Assessment of anesthetic depth even in the 21st century is still an art rather than a science. Albert Faulconer and Reginald Bickford from the Mayo Clinic established the first electrophysiologic attempt of measuring anesthetic depth based upon EEG monitoring. They also designed the first automatic anesthesia-delivering device, the servo-controlled anesthesia machine (Fig. 3). More than 40 years later the same idea, EEG monitoring to assess anesthetic adequacy, has been reintroduced to the anesthesia community in the form of the BIS monitor. An increasing number of recent publications in the anesthesia literature indicate the great interest as well as the ongoing controversy, but the quest for adequate monitoring of anesthetic depth continues.

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