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Surges of Electroencephalogram Activity at the Time of Death: A Case Series

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Abstract

Level of consciousness at the end of life in critically ill patients is poorly characterized. We report a case series of seven patients who were neurologically intact before the decision to withdraw care due to extensive systemic critical illness. As part of our end-of-life care protocol, bispectral index (BIS) monitor (Aspect Medical Systems, Newton, MA) or SEDline™ (Hospira, Lake Forest, IL) monitoring devices are placed on each patient to ensure adequate comfort. Both monitoring systems use an integer-based system (BIS or PSI, respectively) to reflect the level of consciousness/effect of anesthesia. In each case, loss of blood pressure, as monitored by indwelling arterial line, was followed by a decline is BIS/PSI activity followed by a transient spike in BIS/PSI activity that approached levels normally associated with consciousness. This spike in electroencephalogram (EEG) activity had short duration and the activity then declined to a level of activity associated with burst suppression. In one case of a patient who had a SEDLine™ device, we were able to capture and analyze the raw EEG signal, and confirm that the EEG waveform was not artifact, and in fact a high frequency waveform was present during the spike activity. We speculate that this level of BIS/SEDline™ activity is related to the cellullar loss of membrane polarization due to hypoxemia. We further speculate that since this increase in electrical activity occurred when there was no discernable blood pressure, patients who suffer "near death" experiences may be recalling the aggregate memory of the synaptic activity associated with this terminal but potentially reversible hypoxemia.

Introduction

The first report of research into the electrical activity of the brain was in 1875, when Richard Caton presented to the British Medical Association his description of the electrical activity of exposed rabbit cortex.[1] Subsequently, the first pictorial electroencephalogram (EEG) tracing was recorded by Pravdich-Neminsky in 1912; he also described slowing of the EEG as a response to cerebral ischemia.[1] The first human EEG was reported by Berger in 1929.[1] Clinical research into EEG continued throughout the 1930s, and by the 1950s, EEGs were in widespread clinical use.[1]

The bispectral index (BIS) monitor (Aspect Medical Systems Newton, MA) and SEDline™ monitor (Hospira, Lake Forest, IL) are devices that incorporate frontal cortex EEG activity with electromyograghic (EMG) data to produce a numeric assessment that correlates with level of sedation. A complete review of the development of the BIS and SEDLine™ monitors is beyond the scope of this case series. A brief overview is given here.[2,3]

During anesthesia, the EEG develops decreased average frequency and also shows increased synchronicity as deep brain structures pace cortical signals. However, these changes are too complex to be accurately displayed in an operating room monitoring system. The BIS monitor and the SEDLine™ monitor are systems that were developed to provide clinicians with an objective measure of level of consciousness for patients in the operating room and in the intensive care unit (ICU). The objective measure of level of sedation is a tool that can be used to help prevent "consciousness during an operation" known as "awareness." Both systems utilize independent proprietary technologies to process an EEG signal into an integer score related to clinical end points of sedation and hypnosis.

The BIS and SEDLine™ monitors analyze a frontal cortical EEG signal, convert that into digital data, process it, and then produce a score between 0–100. The processing algorithm was honed through review of thousands of full EEGs on patients receiving various sedative regimens. Multiple analyses were performed on those EEGs to develop variables; multivariate

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Table 1. Demographic Data

Age	*Gender*	*Diagnosis*	*Ethnicity*	*Sedation*
47	Male	Cirrhosis & HIV	White	Midazolam/morphine
74	Female	Multisystem organ failure	White	Midazolam/morphine
34	Male	Septic shock	African American	Midazolam/fentanyl
60	Female	Cardiac arrest	African American	Midazolam/fentanyl
52	Female	Inoperable C-spine tumor	White	Midazolam/morphine
66	Female	Septic shock	African American	Midazolam/fentanyl
53	Female	Metastatic breast cancer	African American	Midazolam/morphine

HIV, human immunodeficiency virus.

and other statistical rankings were then applied to weight those variables most closely associated with clinical observation of sedation. The algorithm has been refined through several iterations, and the BIS score (BIS monitors) or PSI (SEDLine™) have been shown to correlate with clinical sedation, recall, and anesthesia titrated to quicker recovery times. The output BIS score and PSI are dimensionless, and can vary between 0–100. Higher scores correlate to higher levels of alertness. As the score diminishes from 40 toward 0, it indicates increasing amounts of burst suppression on the underlying EEG. A score of 0 approaches burst suppression.

Case Series

We report seven critically ill patients (Table 1) who were previously neurologically intact, who for various reasons had life support withdrawn. Per standard ICU procedure, patients for whom life support is being withdrawn are placed on a comfort care protocol. This protocol includes a morphine infusion, minimal ventilator settings, weaning of vasopressor agents, and as-needed midazolam. A BIS or SEDLine™ monitor is placed as part of the protocol in order to ensure that the patient is comfortable. In each case that we report, the PSI or BIS score decreased but did not reach 0 as the blood pressure decreased. Once the blood pressure became undetectable, as assessed by indwelling arterial line, a surge in BIS or PSI signal was captured by the respective device and the signal then rapidly declined to zero. Typically, the EKG displayed a ventricular escape rhythm or an isoelectric EKG. After the patients EKG became isoelectric the patient was pronounced dead, and the device was removed.

In one of the cases, we used a SEDLine™ device. This device has the capacity to store the raw EEG signal in an archive. We were able to retrieve and analyze the raw EEG signal during the period of the spike and found that during the period of electrical spike, a high frequency signal was in fact present, and that signal dissipated as the observed surge diminished. High frequency signals typically represent EMG or gamma wave activity. Gamma wave activity is consistent with cerebral arousal.

Discussion

Previous reports of EEG surge and potential artifact

Initially, we ascribed these spikes to electrical artifact; pulse wave artifact has been previously suggested in a case of BIS spike in a patient with brain death.[4] Multiple etiologies of BIS artifact causing artificial increases in the BIS index have been reported. The causes of artifact have been ascribed to pulse wave sensation, cardiac pacemaker, and forced warm-air therapy.[4–7] In addition, there has been a single case wherein EMG artifact was thought to be the cause of an increase BIS activity.[8] However, in all of the cases we assessed, the patients were pulseless, motionless, and the EKG showed asystole or a deteriorating ventricular escape rhythm. In addition, none of the patients were being treated with forced air warming therapies. We excluded other types of artifact, such as patient

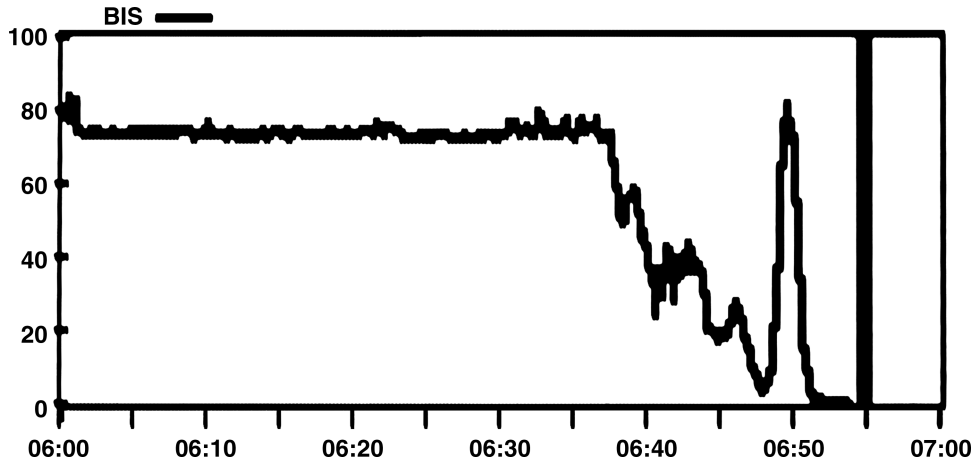

FIG. 1. BIS tracing of patient number 1.

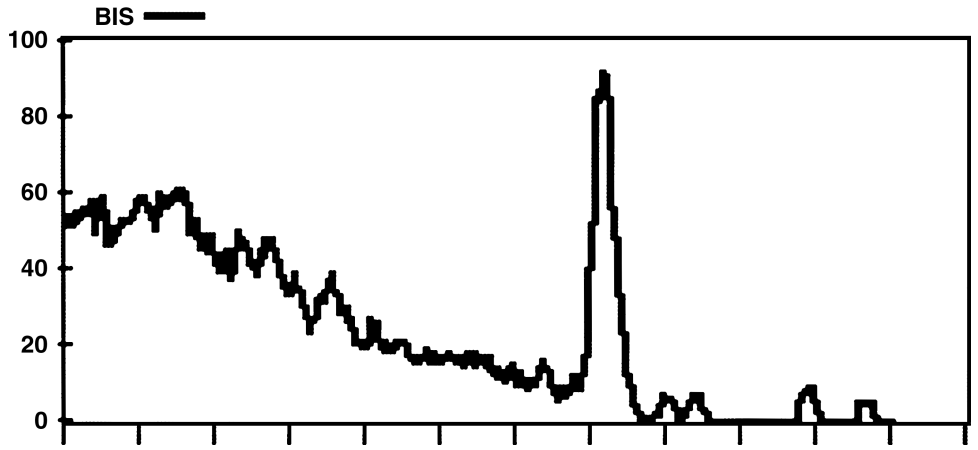

FIG. 2. BIS tracing of patient number 2.

or bed motion, other electrical devices (e.g., cell phones, beepers, sequential compression devices, etc.).

We have observed a multitude of these BIS spikes (>20) in other patients who were immediately ante-mortal, and the timing of these spikes are consistent, although not all patients will demonstrate a surge of activity. We only report the patients in whom we were able to capture the spike activity on the monitor. In our review of the literature, we were able to find one published report of a BIS spike in a similar clinical scenario.[9] The shape and timing of the spike reported is congruent with our seven patients in this report.

EEG and ischemia

The classic EEG findings during cerebral ischemia have been demonstrated in both clinical and research models. In animal models, human experiments and clinical settings, during progressive hypoxemia the EEG shows an initial brief increase in activity, followed by slowing and then decreasing amplitude to the point of an isoelectric EEG.[1,10,11] These EEG findings initiate below a critical cerebral oxygen delivery threshold value of near 15 mL/100 g brain tissue per minute.[11,12] After the EEG becomes isoelectric, stimulated evoked potentials are then lost as oxygen delivery decreases further and ischemia progresses.

The mechanism behind the diminished electrical activity is not entirely clear.[11] As oxygen delivery decreases, the neurons are no longer able to use aerobic metabolism to generate adenosine triphospate (ATP), and energy stores within the brain decrease. As the Na^+-K^+–ATPase pump fails, the normal concentration gradients for cerebral cations diminish. However, the suppression of electrical activity occurs earlier than the drop in ATP. Postsynaptic inhibition may be a mediator of the early loss in electrical activity during ischemia.[11]

Anoxic depolarization

There is a second threshold for ischemic-induced cerebral metabolism. At oxygen delivery levels less than roughly 8–10 mL/100 g per minute, interstitial K^+ levels begin to rise beyond levels due to neuronal activity.[11–13] As mentioned above, this change in ion gradients occurs after the loss of electrical activity. This dual threshold model is clinically applied to describe the ischemic penumbra during vasoocclussive stroke, in which areas of the brain are electrically quiescent but have not yet lost ion gradients and membrane stability.[12] The increase in interstitial K^+ levels occurs in three phases: an initial slow rise to levels of approximately 10 mM; a rapid second increase in potassium levels from 10 mM to 60 mM; and a third slow increase from 60 mM toward

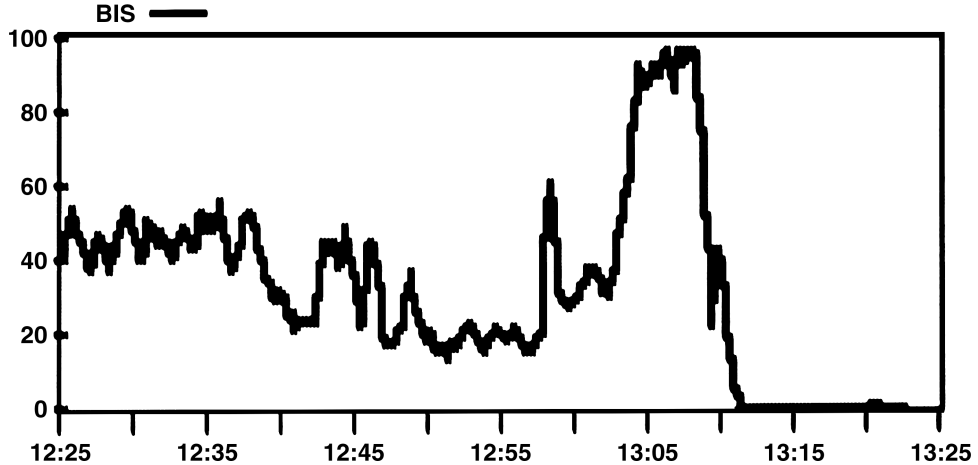

FIG. 3. BIS tracing of patient number 3.

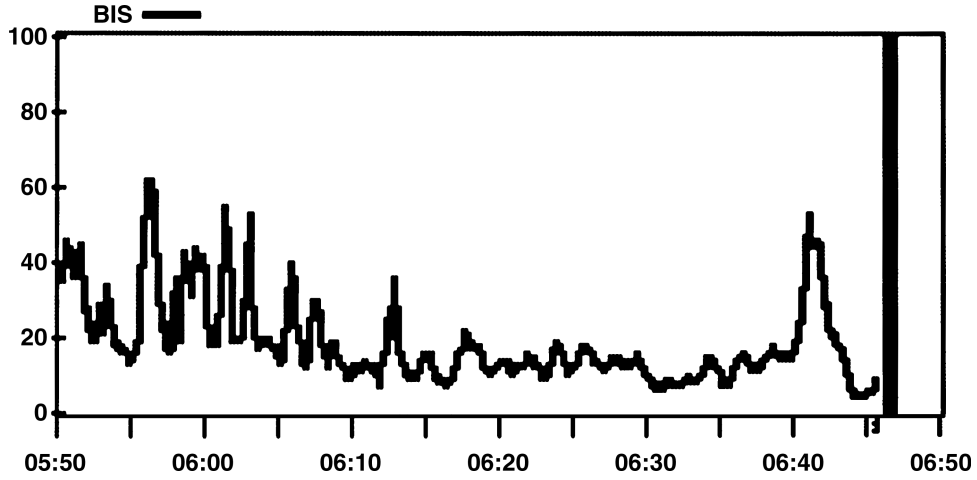

FIG. 4. BIS tracing of patient number 4.

80 mM.[11] The rapid second phase increase in potassium levels occurs several minutes after the onset of ischemia and the loss of electrical activity. Along with this second phase, an anoxic depolarization occurs as the cellular ion gradient disappears. This anoxic depolarization is seen as a fast negative deflection in the local electrical potential, with an amplitude of roughly 20 mV.[11] This anoxic depolarization has been described in experimental models focusing on the microlevel with ion-sensitive microelectrodes. We found no description of surface EEG changes during this anoxic depolarization in our review of the literature.

Significance

As Figures 1–7 show, the shape and duration of the BIS/PSI spike are variable with no discernable signature. The most consistent feature of the spikes are a steep slope up and down, and elevated difference in signal as compared to the immediate previous baseline. These spikes are temporally associated with the loss of measurable blood pressure, and immediately after the spike, the BIS/PSI signal drop to zero and the patient is soon pronounced dead. The BIS spikes last for a few minutes at maximum, but usually last between 30–180 seconds.

We offer two potential hypotheses for this observed phenomenon.

First, some form of electrical interference affects the algorithm and creates the observed spikes. Given that this has been shown in two different devices using different algorithmns, and that the raw EEG signal shows high-frequency EEG waves, we think that this possibility is unlikely. However, in the one previous case report of EMG causing an increased signal, the patient was not moving, and the artifact was attenuated with the administration of atracurium.[8] We speculate that if there were high-frequency EMG activity that was not strong enough to cause movement, but enough to generate electrical activity, this could be the source of this EEG signal surge. The consistent timing of the surge in so many patients is not easily explained by this mechanism.

Second, as the brain reaches a critical level of hypoxia, the Na-K potential is lost by large numbers of neurons, and this

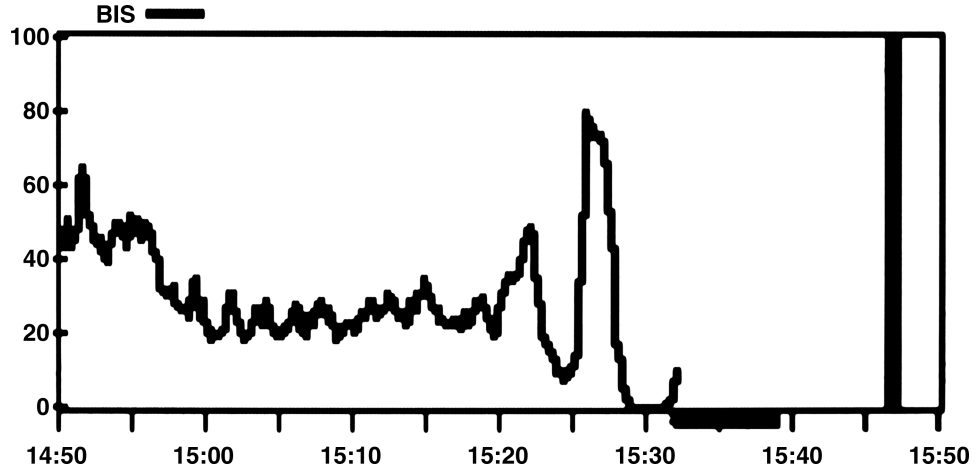

FIG. 5. BIS tracing of patient number 5.

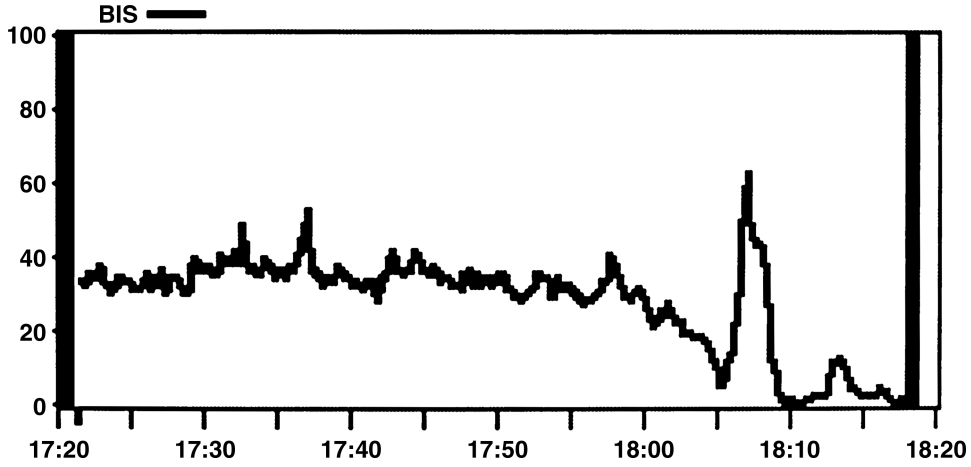

FIG. 6. BIS tracing of patient number 6.

loss of electrical potential causes a cascade of electrical activity. This activity creates high frequency EEG current and rapidly dissipates as the cells lose their resting potential. We speculate that in those patients who suffer cardiac arrest who are successfully revived, they may recall the images and memories triggered by this cascade. We offer this as a potential explanation for the clarity in which many patients have "out of body experiences" when successfully revived from a near death event.

Near death experiences have been documented by a large number of people.[14] Interestingly, these descriptions tend to have a similar theme in that the recollection is vivid and detailed. The nature of these experiences often invokes a spiritual or divine explanation, a topic well beyond the scope of this report. Nonetheless, the end of life is a poorly studied area of clinical medicine and deserves more attention. Whether this observation is meaningful will be determined by future investigation. For the palliative care medicine practitioner, we believe that these observations may be useful. In our critical care practice, we spend a significant amount of time with grieving families. In these interactions, we have found that the idea that "something" happens at the time of death to be comforting to the families. Given that we know so little about this observation, we are careful not to make any definitive statements or assertions. However, this notion of an electrical signal that can be objectively measured at or near the time of death has been a source a comfort to many of the families of those patients who succumb in the ICU.

Limitations

The limitations of this case series are numerous. One, we did not have full EEGs placed on these patients to understand the full dimensions of these observations. Two, we cannot rule out the possibility of other types of artifact or signal that might be responsible for these BIS/PSI spikes. Our conclusion that this spike may explain "near death" experience is totally speculative. Nonetheless, the rather consistent timing of the spikes is curious and appears to be physiologic.

Conclusions and Future Research

Formal 24-lead EEG studies in patients who are dying should be conducted. If these EEG studies confirm our initial observations, then advanced studies of the brain using positron emission tomography (PET) scanning and functional magnetic resonance imaging (fMRI) should be conducted in order to further investigate this phenomenon. Our knowledge of what occurs in the brain of patients when they die is extremely limited and warrants extensive further study. Perhaps Shakespeare said is best when Hamlet opined: ". . . ay, there's the rub, For in that sleep of death what dreams may come." (*Hamlet*, Act III, Scene I)

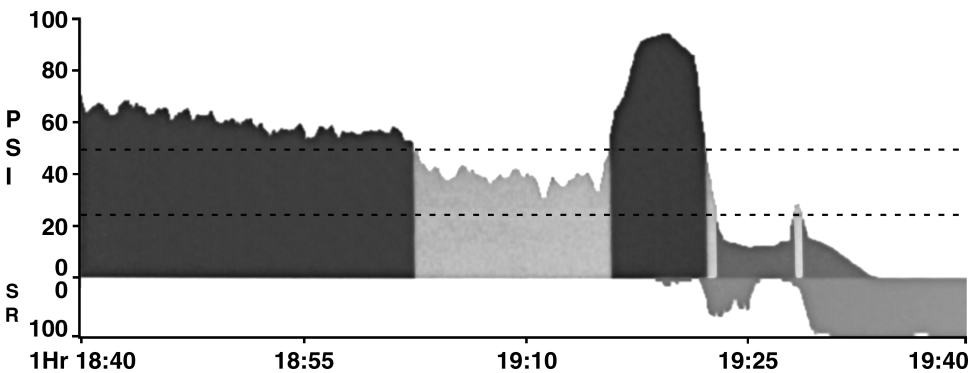

FIG. 7. SEDline tracing of patient number 7.

Author Disclosure Statement

No competing financial interests exist.

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