

## Electroencephalogram of Healthy Horses During Inhaled Anesthesia

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**Background:** Previous study of the diagnostic validity of electroencephalography (EEG) to detect abnormalities in equine cerebral cortical function relied on the administration of various drugs for sedation, induction, and maintenance of general anesthesia but used identical criteria to interpret recordings.

**Objectives:** To determine the effects of 2 inhalation anesthetics on the EEG of healthy horses.

**Animals:** Six healthy horses.

**Methods:** Prospective study. After the sole administration of one of either isoflurane or halothane at 1.2, 1.4, and 1.6 times the minimum alveolar concentration, EEG was recorded during controlled ventilation, spontaneous ventilation, and nerve stimulation.

**Results:** Burst suppression was observed with isoflurane, along with EEG events that resembled epileptiform discharges. Halothane results were variable between horses, with epileptiform-like discharges and bursts of theta, alpha, and beta recorded intermittently. One horse died and 2 were euthanized as the result of anesthesia-related complications.

**Conclusions and Clinical Importance:** The results of this study indicate that the effects of halothane and isoflurane on EEG activity in the normal horse can be quite variable, even when used in the absence of other drugs. It is recommended that equine EEG be performed without the use of these inhalation anesthetics and that general anesthesia be induced and maintained by other contemporary means.

**Key words:** Halothane; Isoflurane; Epilepsy; Seizures; Equine.

In the late 19th century, Richard Caton discovered the presence of ongoing electrical activity in the brain by using a galvanometer to record from rabbits, cats, and monkeys.<sup>1</sup> Over 50 years later, Hans Berger reported his findings on the study of human electroencephalography (EEG).<sup>2</sup> Shortly thereafter, Gibbs, et al.<sup>3</sup> described the classic 3 Hz spike-and-wave EEG pattern associated with petit mal (absence) epilepsy. Since then, numerous epileptic syndromes in humans have been described and characterized, based, in part, on specific EEG criteria.<sup>4</sup>

An attempt has been made to classify epilepsy in horses.<sup>5</sup> With the exceptions of juvenile idiopathic epilepsy of Egyptian Arabians<sup>6</sup> and lavender foal syndrome

### Abbreviations:

|      |                                   |
|------|-----------------------------------|
| BIS  | bispectral index                  |
| EEG  | electroencephalography            |
| EOG  | electrooculogram                  |
| MAC  | minimum alveolar concentration    |
| qEEG | quantitative electroencephalogram |

of Arabians,<sup>7</sup> only broad categories of epilepsy have been described in horses.<sup>5</sup> The majority of EEG recordings (56 of 63) performed on horses in that report were done under general anesthesia. Electroencephalography recorded during chemical restraint were deemed inconclusive because of the presence of muscle artifact or “chemical- or age-induced alterations in background pattern.”<sup>5</sup> The authors described the use of a variety of agents (xylazine, guaifenesin, thiopental sodium, thiamylal sodium, ketamine, halothane, and isoflurane) in an earlier, related, publication on equine EEG.<sup>8</sup> They claimed to be able to distinguish pathologic slowing of background activity from anesthesia-induced slowing but there was no mention of the criteria used to differentiate the two. In addition, their findings were based, in part, on EEG semi-quantitative data (a score calculated by assigning variable values to frequency, amplitude, asymmetry, and paroxysmal activity data measured from segments of the recording). Their hypothesis was that 8–13 Hz activity (which they referred to as an “alpha rhythm” [a pattern recognized in human but not veterinary EEG]) at an amplitude between 25 and 50  $\mu$ V without the presence of asymmetry and paroxysmal discharges was normal and anything outside this range was abnormal. This type of analysis is not utilized in human epileptology.<sup>9</sup> It appears to be adapted from the use of quantitative electroencephalogram (qEEG) for scoring stages of sleep, as the authors’ cite sleep medicine references, not those applicable to epilepsy monitoring.<sup>10–12</sup>

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Submitted June 19, 2015; Revised July 23, 2015; Accepted August 5, 2015.

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DOI: 10.1111/jvim.13613

This study was designed to determine whether general anesthesia might produce EEG findings in normal horses that could complicate the interpretation of those recordings. Without clearly defining the background activity and transient events that are considered normal in this species, accurate interpretation of EEG findings recorded from neurologically compromised animals is impossible. The goal was to study the effects of inhalant anesthetics alone on the EEG without the influence of sedatives or induction agents. Data were analyzed visually and quantitatively. This study was performed under tightly controlled conditions to insure that all data obtained were representative of each anesthetic dose (expressed as a multiple of the minimum alveolar concentration or MAC) for every horse. Although applicable to the monitoring of equine anesthesia, the focus of this segment of the study was to determine whether the practice of obtaining clinical EEG recordings using general anesthesia is a valid method or if alternative techniques should be considered the standard of care.

### Materials and Methods

These are described elsewhere.<sup>13</sup> In brief, horses were anesthetized with either one of two inhalation agents, halothane or isoflurane in a cross-over design (with the exception of one horse that was humanely euthanized after complications from the first anesthesia session). They were instrumented with EEG, electrooculogram (EOG), electromyogram, electrocardiogram, and bispectral index (BIS) electrodes as previously described.<sup>13</sup> The right carotid artery was catheterized to allow sampling for an assortment of hematological tests. Multiple physiological measurements were monitored throughout each recording session using equipment that was calibrated over the range of anesthetic doses studied for each anesthetic employed. Randomized multiples of MAC (1.2, 1.4 and 1.6) were employed. Each contained a period of controlled ventilation, spontaneous ventilation, and peroneal nerve stimulation. Four consecutive 10 second epochs of recording were selected and analyzed from each condition at each MAC multiple. Standard quantitative EEG values (power in each frequency band, total power, BIS, median frequency, spectral edge [95%], and suppression ratio) were calculated and examined statistically.

Additional analyses for this report consisted of reviewing each epoch for the presence of epileptiform-like discharges. These included spikes (duration of <70 msec), sharp waves (70 to <200 msec) and spike-and-slow waves (a spike followed by a wave

with a duration of >200 msec). Segments were scored as + for present in EEG channels, – for absent from all channels, and o as present in EOG channels only. Horse #1 for isoflurane and horse #5 for halothane did not have stimulation segments. Horse #6 lacked all isoflurane data.

### Results

Findings were variable between horses and between epochs in individual horses. Isoflurane and halothane recordings shared the presence of frontal sharp waves and generalized slowing of background activity, however, there were several differences between agents. Isoflurane was associated with burst suppression patterns in all horses at 1.4 and 1.6 MAC and one horse at 1.2 MAC but no such pattern was observed with halothane. Total power with isoflurane was twice that of halothane and the greater power was apparent in all but the  $\gamma$  (>30 Hz) frequency band (which was minimal in both). Intermittent bursts of  $\alpha$  (8 to <13 Hz),  $\theta$  (4 to <8 Hz), and  $\beta$  (13 to <30 Hz) activity were seen with halothane only. Quantitative data did not provide information that could be useful in monitoring anesthesia. Statistical significance was attained for some variables (BIS for isoflurane and median frequency for halothane) which were the reverse of what was expected (values increased at higher MAC levels).

Analysis of epileptiform-like discharges revealed that these were present in all epochs in every horse (at all MAC levels and conditions) for isoflurane and were variable for halothane (Table 1). Their appearance was periodic with isoflurane (Fig 1), intermittent with halothane (Fig 2). They were present in most epochs in one horse administered halothane, whereas, in the other horses they were often present only in the EOG channels or they disappeared entirely, particularly during stimulation segments. Nystagmus and muscle artifact would frequently replace the discharges, especially in one horse.

### Discussion

Considerable variability in EEG findings exists between normal horses at the same level of general anesthesia (as measured by MAC).<sup>13</sup> In addition, the EEG is dynamic in the same horse even under constant

**Table 1.** Epileptiform-like discharge percentages obtained from scoring the 10 second epochs for all horses.

| MAC Conditions | 1.2   |       |       | 1.4   |       |       | 1.6   |       |       |
|----------------|-------|-------|-------|-------|-------|-------|-------|-------|-------|
|                | CV    | SV    | ST    | CV    | SV    | ST    | CV    | SV    | ST    |
| Isoflurane (%) |       |       |       |       |       |       |       |       |       |
| +              | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| –              | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| o              | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     | 0     |
| Halothane (%)  |       |       |       |       |       |       |       |       |       |
| +              | 50.0  | 66.7  | 20.0  | 75.0  | 83.3  | 25.0  | 75.0  | 66.7  | 30.0  |
| –              | 33.3  | 25.0  | 75.0  | 8.3   | 12.5  | 65.0  | 8.3   | 29.2  | 65.0  |
| o              | 16.7  | 8.3   | 5.0   | 16.7  | 4.2   | 10.0  | 16.7  | 4.2   | 5.0   |

+ denotes discharges were present, – denotes the absence of discharges and o denotes that the discharges were seen in the electrooculogram channels only. These data are shown for isoflurane and halothane at each minimum alveolar concentration (MAC) level (1.2, 1.4 and 1.6) under each condition, CV = controlled ventilation, SV = spontaneous ventilation, and ST = peroneal nerve stimulation.

conditions. Events resembling epileptiform discharges, were observed with isoflurane (Fig 1) and were present with halothane (Fig 2). With the exception of these events and the generalized slowing of background activity, halothane findings were different from those of isoflurane. Burst suppression was not associated with halothane anesthesia but bursts of activity in the alpha, theta, and beta frequency ranges were observed. Depending on sample selection, the inclusion of these bursts could have profound effects on quantitative analyses in individual horses. Furthermore, the total power (and amplitude) associated with halothane was much lower (half) than that of isoflurane.<sup>13-15</sup> Therefore, applying the same EEG interpretation criteria, based on frequency and power (or amplitude) data, and the presence of paroxysmal (epileptiform-like) events, to recordings performed using different agents in an attempt to diagnose cerebral dysfunction is not valid.<sup>8</sup> Assuming that one frequency band is more normal than another, particularly during inhalation anesthesia, (where an increase in slow [ $\delta$ , >0 to <4 Hz] activity is expected) is not supported by evidence.

In human medicine, visual inspection of the EEG by highly trained electroencephalographers is still consid-

ered the "gold standard" when assessing cerebral cortical function.<sup>9,16</sup> Adjunct information obtained via qEEG, such as spectral analysis data, automated event detection, dipole localization methodology, and topographic mapping, can also be beneficial but is not meant to take the place of visual examination of the raw data (traditional EEG interpretation). Differences in the anatomy of the cranial vault between humans and animals will likely render some forms of qEEG analyses of limited value in veterinary medicine (at least in recordings made from electrodes on the scalp). Nuwer warned that the use of statistical differences in qEEG values between patient populations does not necessarily imply that abnormalities exist and that this application may lead to the erroneous diagnoses of numerous false-positives.<sup>9</sup>

Recording duration is a factor in obtaining diagnostic EEG from human epilepsy patients. Even for a recording with a minimum duration of 30 minutes, including hyperventilation and photic stimulation (2 activation techniques used to increase the diagnostic yield [chance of obtaining epileptiform discharges in the EEG]), the odds are roughly 50% that abnormalities will be detected. These odds increase to 85% if a period of



**Fig 1.** Sharp waves (blue ovals) and spikes (red boxes) in an epoch from horse #2 during isoflurane anesthesia at 1.6 times minimum alveolar concentration with controlled ventilation. Similar discharges are often recorded from epileptic patients. Note: These events were also recorded by the electrooculogram (EOG) channels below. Gain calibration is shown for electroencephalography and EOG tracings only, others vary. The squaring off of some events denotes they are outside the dynamic range of the amplifiers.

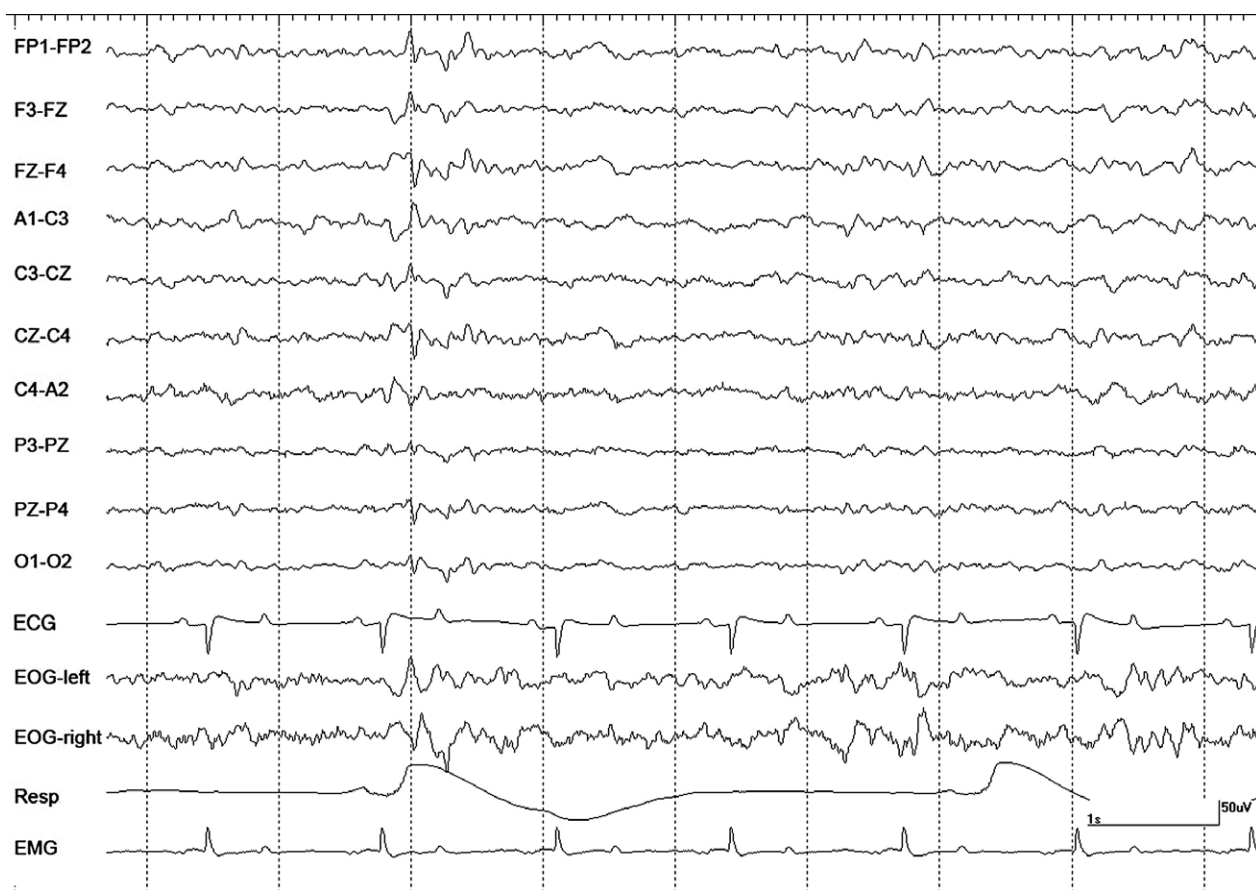


Fig 2. Sharp waves in an epoch from horse #1 during halothane anesthesia at 1.4 times minimum alveolar concentration during spontaneous ventilation. Gain calibration is shown for electroencephalography and electrooculogram tracings only, others vary.

sleep is included in the EEG.<sup>17</sup> Ambulatory<sup>18</sup> or long-term monitoring of EEG, preferably with video to better identify artifact and to correlate findings with clinical signs,<sup>19</sup> would be beneficial in this species. Although it is possible to instrument and record EEG in horses without the use of sedation,<sup>19</sup> it is not always practical in the clinical setting. By applying techniques similar to those described in the previous publications<sup>19,20</sup> it is possible to combine the use of sedation to record a standard EEG in the horse's stall while continuing to record as drug effects dissipate, thereby also performing long-term monitoring over several hours, or even days (D.C.W., personal observation). Attempts to improve the diagnostic yield by increasing the duration of a recording using isoflurane anesthesia might impact cerebral perfusion,<sup>21</sup> potentially worsening a horse's neurologic status and further complicating interpretation of the EEG.

A higher morbidity and mortality is associated with general anesthesia in the horse as compared to other species.<sup>22</sup> Although this study was designed to be non-terminal, one horse died and 2 were euthanized because of complications of anesthesia. The first was a case of malignant hyperthermia,<sup>23</sup> the second suffered a complete luxation of the metatarsophalangeal joint during recovery and the third developed a severe bilateral

triceps myopathy. All were Quarter horse geldings that had undergone halothane anesthesia.

Because of the confounding factors of epileptiform-like activity seen in healthy horses' EEG during anesthesia, the variability in EEG features between anesthetics, the uncertainty in the effects of other agents used for premedication and induction (and the duration of their effects), coupled with the inherent risk of general anesthesia in horses, the use of general anesthesia for clinical EEG recording is discouraged. Safer alternatives with fewer variables exist and should be utilized.

### Acknowledgments

This research was funded by the Center for Equine Health with funds provided by the Oak Tree Racing Association, the State of California Pari-Mutuel Fund and contributions by Private Donors. It was also supported by the Clinical Electrophysiology Laboratory at the William R. Pritchard Veterinary Medical Teaching Hospital. The authors thank Mr. Vince Long, Mr. Ramon Cervantes, Mr. Don Hermes, Mr. Richard Morgan, Dr. Ayako Imai and Mr. John Doval, for technical assistance. We also thank Aspect Medical Systems for their generous loan of a BIS monitor. Submitted in partial satisfaction of the requirements for the

degree of Doctor of Philosophy in Comparative Pathology in the Office of Graduate Studies of the University of California, Davis.

*Conflict of Interest Declaration:* Authors disclose no conflict of interest.

*Off-label Antimicrobial Declaration:* Authors declare no off-label use of antimicrobials.

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