Title
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Permalink
https://escholarship.org/uc/item/7371m0c9

Journal
Journal of veterinary internal medicine, 30(1)

ISSN
0891-6640

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Publication Date
2016

DOI
10.1111/jvim.13613

Peer reviewed
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.1 Over 50 years later, Hans Berger reported his findings on the study of human electroencephalography (EEG).2 Shortly thereafter, Gibbs, et al.3 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.4

An attempt has been made to classify epilepsy in horses.5 With the exceptions of juvenile idiopathic epilepsy of Egyptian Arabians6 and lavender foal syndrome of Arabians,7 only broad categories of epilepsy have been described in horses.8 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.”5 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.8 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 µV 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.9 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.10–12

Abbreviations:
BIS  bispectral index
EEG  electroencephalography
EOG  electrooculogram
MAC  minimum alveolar concentration
qEEG  quantitative electroencephalogram
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. 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. 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 are described elsewhere. Considerable variability in EEG findings exists between normal horses at the same level of general anesthesia (as measured by MAC). In addition, the EEG is dynamic in the same horse even under constant conditions. 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). In addition, the EEG is dynamic in the same horse even under constant conditions.

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

| MAC Conditions | 1.2          | 1.4          | 1.6          |
|----------------|--------------|--------------|--------------|
| Isoflurane (%) | CV | SV | ST | CV | SV | ST | CV | SV | ST |
| –              | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 | 100.0 |
| o              | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Halothane (%)  | CV | SV | ST | CV | SV | ST | CV | SV | ST |
| +              | 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. 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. Assuming that one frequency band is more normal than another, particularly during inhalation anesthesia, (where an increase in slow [δ, >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 considered the “gold standard” when assessing cerebral cortical function. 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.

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.
Sleep is included in the EEG. Ambulatory or long-term monitoring of EEG, preferably with video to better identify artifact and to correlate findings with clinical signs, would be beneficial in this species. Although it is possible to instrument and record EEG in horses without the use of sedation, it is not always practical in the clinical setting. By applying techniques similar to those described in the previous publications, 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, 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. 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, 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.

References

1. Caton R. The electric currents of the brain. Br Med J 1875; 2:278.
2. Berger H. Über das elektrenkephalogramm des menschen. Arch Psychiatr Nervenkr 1929;87:527–570.
3. Gibbs FA, Davis H, Lennox WG. The electroencephalogram in epilepsy and in conditions of impaired consciousness. Arch Neurol Psychiatry 1935;34:1133–1148.
4. Berg AT, Berkovic SF, Brodie MJ, et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on classification and terminology, 2005–2009. Epilepsia 2010;51:676–685.
5. LaCombe VA, Mayes M, Mosseri S, et al. Epilepsy in horses: Aetiological classification and predictive factors. Equine Vet J 2012;44:646–651.
6. Aleman M, Gray LC, Williams DC, et al. Juvenile idiopathic epilepsy in Egyptian Arabian foals: 22 cases (1985–2005). J Vet Intern Med 2006;20:1443–1449.
7. Page P, Parker R, Harper C, et al. Clinical, clinicopathologic, postmortem examination findings and familial history of 3 Arabians with lavender foal syndrome. J Vet Intern Med 2006;20:1491–1494.
8. Lacombe VA, Podell M, Furr M, et al. Diagnostic validity of electroencephalography in equine intracranial disorders. J Vet Intern Med 2001;15:385–393.
9. Nuwer MR. Assessing digital and quantitative EEG in clinical settings. J Clin Neurophysiol 1998;15:458–463.
10. Balzamo E, VanBeers P, Lagarde D. Scoring of sleep and wakefulness by behavioural analysis from video recordings in the rhesus monkeys: Comparisons with conventional EEG analysis. Electroencephalogr Clin Neurophysiol 1998;106:206–212.
11. MacLean AW, Lue F, Moldofsky H. The reliability of visual scoring of alpha EEG activity during sleep. Sleep 1995;18:565–569.
12. Drane DB, Martin WB, Viglione SS. The application of pattern recognition techniques to the scoring of EEG sleep patterns. Electroencephalogr Clin Neurophysiol 1971;30:94–95.
13. Williams DC, Brosnan RJ, Fletcher DJ, et al. Qualitative and quantitative characteristics of the electroencephalogram in normal horses following anesthetic administration: – Implications for anesthesia monitoring. J Vet Intern Med in progress.
14. Otto K, Short CE. Cerebral responses in horses to halothane and isoflurane anesthesia: EEG power spectrum analysis and differences in arteriovenous oxygen content. Vet Anaesth Analg 1991;18(Suppl. 1):85–99.
15. Ekström PM, Short CE, Geimer TR. Electroencephalography of detomidine-ketamine-halothane and detomidine-ketamine-isoflurane anesthetized horses during orthopedic surgery: A comparison. Vet Surg 1993;22:414–418.
16. Duffy FH, Hughes JR, Miranda F, et al. Status of quantitative EEG (QEEG) in clinical practice, 1994. Clin Electroencephalogr 1994;25:vi–xxii.
17. Binnie CD, Stefan H. Modern electroencephalography: Its role in epilepsy management. Clin Neurophysiol 1999;110:1671–1697.
18. Wijnberg ID, van der Ree M, van Someren P. The applicability of ambulatory electroencephalography (AEEG) in healthy horses and horses with abnormal behaviour or clinical signs of epilepsy. Vet Q 2013;33:121–131.
19. Williams DC, Aleman M, Holliday TA, et al. Qualitative and quantitative characteristics of the electroencephalogram in normal horses during spontaneous drowsiness and sleep. J Vet Intern Med 2008;22:630–638.
20. Williams DC, Aleman M, Tharp B, et al. Qualitative and quantitative characteristics of the electroencephalogram in normal horses following sedative administration. J Vet Intern Med 2012;26:645–653.
21. Brosnan RJ, Steffey EP, LeCouteur RA, et al. Effects of duration of isoflurane anesthesia and mode of ventilation on intracranial and cerebral perfusion pressures in horses. Am J Vet Res 2003;64:1444–1448.
22. Wagner AE. Complications in equine anesthesia. Vet Clin North Am Equine Pract 2009;24:735–752.
23. Aleman M, Brosnan RJ, Williams DC, et al. Malignant hyperthermia in a horse anesthetized with halothane. J Vet Intern Med 2005;19:363–367.