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Short Communication

Effect of Xylazine, Detomidine, and Detomidine–Butorphanol Combination on Latencies of Peaks I–V of Brainstem Auditory–Evoked Responses in Horses

Ezio Bianchi*, Fabio Leonardi, Stefano Zanichelli, Alberto Sabbioni, Maurizio Dondi, Silvia Natella, Mario Angelone

Department of Veterinary Science, University of Parma, Parma, Italy

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ABSTRACT

Literature reports on the effect of sedative and anesthetic drugs on the first five peaks of brainstem auditory–evoked responses (BAERs) are somehow contradictory. In particular, no data are available on the effect of sedatives on BAER in horses. The objective of the study was to evaluate the influence of sedation with xylazine, detomidine, and detomidine–butorphanol combination on latencies of BAER peaks in horses. The absolute peak latencies of waves I, II, III, and V and interpeak latencies (IPLs) I–III, III–V, and I–V obtained in nine Bardigiano horses without sedation and with each of the sedation protocols were statistically compared. A statistically significant ($P < .05$) increase of the latency of wave III and of the IPL I–III was present in horses sedated with detomidine compared with the subjects not sedated or sedated with xylazine. An effect of detomidine on conduction time along the auditory pathway is suspected. These results must be taken into account when using α2-agonists with greater affinity for specific receptors, such as detomidine, for sedation of animals undergoing BAER for clinical or research purposes.

1. Introduction

Brainstem auditory–evoked responses (BAERs) are far-field potentials produced from structures in the auditory pathway within 10 ms of an acoustic stimulus [1]. Because the first description of BAER in humans of Kiang in 1961, many studies have been performed in humans and animals to report methodological aspects and clinical applications of the test [1–5]. Brainstem auditory–evoked response is an important part of the diagnostic evaluation of horses with suspected hearing loss and vestibular and diffuse or multifocal brain lesions [6]. Literature reports on the effect of sedative and anesthetic drugs on BAER are somehow contradictory. Therapeutic doses of central nervous system (CNS) depressant drugs are traditionally considered unable to significantly affect the first five peaks of BAER tracing [7,8]. Nevertheless, several studies over the last decades have reported a statistically significant effect of some drugs such as diazepam and ketamine on latencies of peaks I–V of BAER in humans, cats, and laboratory animals [9–13]. Although most of the studies assessing BAER in horses have been performed under sedation [4,6,14,15], none have assessed the effect of sedative drugs on this diagnostic procedure. To establish the effect of some sedatives commonly used in practice on BAER, we compared the values obtained in nine Bardigiano horses without sedation and using xylazine, detomidine, and detomidine–butorphanol.

* Corresponding author at: Ezio Bianchi, Department of Veterinary Science, University of Parma, Via del Taglio, 7, 43125 Parma, Italy.
E-mail address: ezio.bianchi@unipr.it (E. Bianchi).

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2. Materials and Methods

2.1. Horses

Nine female Bardigiano horses judged clinically healthy (ASA I) based on medical history and physical examination were randomly chosen. All the mares were docile and presumed to have normal hearing based on their alerting responses to sound and normal movement of head or ears toward the source of sounds.

2.2. Sedative Protocols

The tests were performed in a quiet stall, with an environmental temperature of 24°C. Their mean weight (±standard deviation [SD]) was 394 ± 16 kg (range, 350–400 kg) and mean age (±SD) was 21 ± 6 years (range, 7–26). Brainstem auditory–evoked responses were obtained in three different times, with a recovery period between sedations of 4 weeks. The first time the BAERs were obtained before and after sedation with xylazine (Megaxilor; BIO 98, Milan, Italy), 0.29 mg/kg IV. Brainstem auditory–evoked responses were then repeated for the second time after sedation with detomidine (Domosedan; Orion Corporation, Espoo, Finland), 10 μg/kg IV, and for the third time after sedation with detomidine, 6 mcg/kg IV, in combination with butorphanol (Nargesic; ACME, Cavriago [Reggio Emilia], Italy), 6 μg/kg IV. Animals were fasted for 12 hours with free access to water before sedation. The level of sedation was scored using defined criteria: 0 = no sedation, 1 = mild sedation, 2 = moderate sedation, and 3 = deep sedation [16]. The tests were started when the desired level of sedation (score 2) was reached.

2.3. Brainstem Auditory–Evoked Responses

Acoustic stimuli (clicks) were produced by delivering electrical square waves of 0.1 ms to an insert earphone connected with polyvinyl chloride eartips (0.30-ms delay; intra-auricular headset; VIASYS HealthCare, Old Woking, Surrey, UK). The earphones were inserted as deep as possible into the external auditory canal and supported in place by a piece of foam. In all the horses, only one ear (the left one) was tested each time. Rarefaction stimuli with a rate of 10.3 Hz and an intensity of 100 dB normal hearing level were used. A contralateral wide band noise, 30 dB below the click stimulus intensity, was delivered to the untested ear (right ear). An electrodiagnostic system (Myoquick; Micromed, Mogliano Veneto [Treviso] Italy) was used for recordings. The signal was amplified and filtered with a bandwidth from 100 to 3,000 Hz. With an analysis time of 10 ms, 500–1,000 sweeps were averaged for each trial. Automatic artifact rejection was used. To assess waveform consistency, two trials were performed every time on each subject. Recording electrodes were 25-mm stainless steel subdermal needles with the non-inverting input of the amplifier inserted at the vertex and the inverting input of the amplifier inserted at the ipsilateral mastoid. The ground needle electrode was placed over the external occipital protuberance. For each test, rectal temperature was measured immediately before the first trial, between the first and the second trials, and after the second trial. To exclude partially deaf horses or a malposition of earphones, only tracings that had a wave I with an amplitude of >0.5 μV and an absolute latency of <1.6 ms were included in the study. Absolute latencies of peaks I, II, III, when present IV, and V, and I–III, III–V, and I–V interpeak latencies (IPLs) were recorded in all the tracings obtained. No correction was made for the auditory stimulus delay within the eartips.

2.4. Statistical Analysis

Data were analyzed by the procedure GLM (SAS, 2008; User's Guide: Statistics, version 9.2, SAS Institute Inc, Cary, NC) by means of a model with group (four levels) as a fixed model and age of the mare (years) as a covariate. Least squares means are reported in Table 1, and differences among factor levels were considered significant for $P < .05$.

3. Results

All subjects remained quiet during the procedure, including those performed without sedation. Brainstem auditory–evoked responses could be recorded every time, in all the horses. A moderate sedation (score 2) was achieved with all the sedative protocols. Waves I, II, III, and V were clearly visible in all the recordings, and wave IV was present only occasionally and therefore was not included in the statistical evaluation (Fig. 1). For each test, the two trials

Table 1
Effect of the sedative protocols on waves I–V of BAER.

Waves and IPL	Awake	Detomidine	Detomidine/Butorphanol	Xylazine	Age[c]	RSE	R^2
Wave I (ms), mean (SD)	1.502 (0.05)	1.541 (0.05)	1.534 (0.19)	1.495 (0.05)	−0.005[$]	0.100	0.116
Wave II (ms), mean (SD)	2.624 (0.14)	2.765 (0.23)	2.741 (0.24)	2.654 (0.17)	0.009[$]	0.187	0.187
Wave III (ms), mean (SD)	3.685[a] (0.26)	4.033[b] (0.23)	3.888[ab] (0.25)	3.732[a] (0.27)	−0.004	0.249	0.258
Wave V (ms), mean (SD)	4.499 (0.29)	4.825 (0.35)	4.724 (0.32)	4.603 (0.3)	−0.012	0.300	0.197
IPL I–III (ms), mean (SD)	2.183[a] (0.26)	2.492[b] (0.24)	2.354[ab] (0.24)	2.237[a] (0.25)	0.000	0.247	0.209
IPL III–V (ms), mean (SD)	0.814 (0.1)	0.792 (0.26)	0.836 (0.17)	0.871 (0.13)	−0.008	0.182	0.101
IPL I–V (ms), mean (SD)	2.997 (0.28)	3.284 (0.35)	3.190 (0.31)	3.108 (0.3)	−0.008	0.305	0.134

Abbreviations: BAER, brainstem auditory–evoked response; IPL, interpeak latency; RSE, residual standard error.
Least squares means (M) of absolute latencies and interpeak latency and standard deviations (SD) of horses evaluated in this study are reported.
[a,b]Different letters on the same row indicate a significance level of $P < .05$.
[$]$P < .10$.
[c] Linear regression coefficient with the age of the mare (years).