Received: 16 January 2019 | Accepted: 11 July 2019

DOI: 10.1111/jvim.15576

STANDARD ARTICLE

Journal of Veterinary Internal Medicine Open Access

ACVIM American College of Veterinary Internal Medicine

Determination of magnetic motor evoked potential latency time cutoff values for detection of spinal cord dysfunction in horses

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Abstract

Background: Transcranial magnetic stimulation (TMS) and recording of magnetic motor evoked potentials (MMEP) can detect neurological dysfunction in horses but cutoff values based on confirmed spinal cord dysfunction are lacking.

Objectives: To determine latency time cutoff for neurological dysfunction.

Animals: Five control horses and 17 horses with proprioceptive ataxia.

Methods: Case-control study with receiver operating characteristic curve analysis, based on diagnostic imaging, TMS, and histopathological findings. Horses were included if all 3 examinations were performed.

Results: Diagnostic imaging and histopathology did not show abnormalities in the control group but confirmed spinal cord compression in 14 of 17 ataxic horses. In the remaining 3 horses, histopathological lesions were mild to severe, but diagnostic imaging did not confirm spinal cord compression. In control horses, latency time values of thoracic and pelvic limbs were significantly lower than in ataxic horses (20 ± 1 vs 34 ± 16 milliseconds, $P = .05$; and 39 ± 1 vs 78 ± 26 milliseconds, $P = .004$). Optimal cutoff values to detect spinal cord dysfunction were 22 milliseconds (sensitivity [95% CI interval], 88% [73%-100%]; specificity, 100% [100%-100%]) in thoracic and 40 milliseconds (sensitivity, 94% [83%-100%]; specificity, 100% [100%-100%]) in pelvic limbs. To detect spinal cord dysfunction caused by compression, the optimal cutoff for thoracic limbs remained 22 milliseconds, while it increased to 43 milliseconds in pelvic limbs (sensitivity, 100% [100%-100%]; specificity, 100% [100%-100%] for thoracic and pelvic limbs).

Abbreviations: CI, confidence interval; CVM, cervical vertebral malformation; EDM/NAD, equine degenerative myeloencephalopathy or equine degenerative myeloencephalopathy and neuroaxonal dystrophy; EPM, equine protozoal myeloencephalitis; MMEP, magnetic motor evoked potentials; MRI, magnetic resonance imaging; TMS, transcranial magnetic stimulation.

Conclusions and Clinical Importance: Magnetic motor evoked potential analysis using these cutoff values is a promising diagnostic tool for spinal cord dysfunction diagnosis in horses.

KEYWORDS
ataxia, cervical radiographs, cervical vertebral malformation, myelogram, transcranial magnetic stimulation

1 | INTRODUCTION

In Warmblood horses,[1-4] Tennessee walking horses,[3,4] and Thoroughbreds,[3-5] spinal cord disease is common. Major causes include cervical vertebral malformation/malarticulation (CVM), equine degenerative myeloencephalopathy or equine degenerative myeloencephalopathy and neuroaxonal dystrophy (EDM/NAD), equine protozoal myeloencephalitis (EPM), and trauma.[6] Equine protozoal myeloencephalitis and EDM/NAD are important causes in the United States,[7] but worldwide, the most common cause probably is CVM. A correct diagnosis of the exact etiology of ataxia is important, as different causes imply different treatment options and prognosis. However, diagnosis of the specific etiology remains challenging, and the use of a combination of diagnostic techniques is necessary.

Because of the size of the horses, the spinal canal can be difficult to evaluate in detail, especially in the thoracic and lumbar region. Furthermore, sensitivities (43%-85%) and specificities (70%-78%) of plain radiographs or myelograms are too low for adequate diagnosis of spinal cord compression,[3,8] and variation between measurements and observers can result in discrepancies in diagnosis.[9] Therefore, the diagnosis of CVM must be confirmed postmortem by histopathology.

A supplementary, noninvasive diagnostic test for CVM could be transcranial magnetic stimulation (TMS) with recording of magnetic motor evoked potentials (MMEP). Transcranial magnetic stimulation is standardized in horses using a 70 mm round coil to produce a maximal output of 4 T on the upper medial forehead of the horse.[10] The magnetic stimulation excites the descending motor tracts, and the resulting muscle contraction (MMEP) is registered at the tibialis cranialis in the pelvic and the extensor carpi radialis muscle in the thoracic limbs.[10-12] The time between stimulation and muscle contraction is called the latency time and is the most important variable. The peak-to-peak amplitude of MMEP is a second variable, but shows a lot of variation, even in normal horses[11-13] and is therefore more difficult to use in practice. Left or right side measurements, coil current,[10,11] sex, age,[11] sedation with detomidine and an opioid,[13] and the surface of needle electrode recordings[12] do not have a significant influence on MMEP latency time. Weight, wither height, and length do influence latency time in normal horses.

Transcranial magnetic stimulation assesses the conduction through the descending pathways and thus the motor function of the spinal cord. The proprioceptive, ascending pathways cannot be evaluated with TMS, but in cases showing proprioceptive ataxia, often both ascending (proprioceptive) and descending (motor) pathways are affected. Therefore, TMS can be helpful in these cases, having prolonged latency times.[14,15] In horses with thoracic or thoracolumbar pathology, only pelvic limb MMEP are abnormal.[14] In cases with cervical spinal cord disease, both thoracic and pelvic MMEP values are clearly prolonged.[14,15] Latency times in ataxic horses range from 28 to more than 200 milliseconds in the thoracic and from 53 to more than 200 milliseconds in the pelvic limbs,[14,15] but in most of these studies, there is no confirmation of the exact etiology by histopathology or diagnostic imaging. In dogs, there is a correlation between the severity of the neurological deficits and MMEP latency time.[16-18] In cases with mild or subclinical neurological deficits, latency times might be only slightly prolonged. Therefore, reliable cutoff values are required to help clinicians declare an animal healthy or affected. However, in horses, no cutoff values have been determined. Therefore, the objective of this study was to determine MMEP latency time cutoff values for detection of spinal cord dysfunction in horses with determination of the cause of spinal cord dysfunction through diagnostic imaging and histopathology.

2 | MATERIALS AND METHODS

2.1 | Horses

Twenty-two horses, 17 cases with proprioceptive ataxia and 5 control horses, were included in this study. All horses were presented at the faculty of Veterinary Medicine between 2008 and 2017. All were clinically evaluated by a veterinarian with more than 3 years of experience in neurological examinations, and afterward, TMS-MMEP, diagnostic imaging, and histopathology were performed. The 5 control horses (2 female, 3 male castrated) had a median age of 7 (range 5-19) years and a mean weight of 550 (437-655) kg. None of the control horses had abnormalities detected during neurological examination. The group of ataxic horses included 8 intact males, 4 females, and 5 castrated males. Their median age was 4 (0.5-20) years, their mean bodyweight 426 (180-572) kg. All ataxic horses had normal mentation, no cranial nerve deficits, and blindfolding did not trigger a head tilt. They showed a mean grade of ataxia of 3.6/5 (range 1-5).[19] Except horse 12, all horses showed ataxia in both thoracic and pelvic limbs, suggesting a cervical spinal cord dysfunction. Horse 12 showed a severe ataxia in only the pelvic limbs. A T3-L3 myelopathy was suspected.

2.2 | TMS with MMEP recording

For TMS-MMEP, the procedure described by Rijckaert et al[12] was followed. Each horse was sedated with a combination of detomidine (12 μg/kg body weight; Domidine, Eurovet Animal Health, Bladel, The Netherlands) and butorphanol (12 μg/kg body weight, Dolorex, MSD Animal Health, Boxmeer, The Netherlands). A magnetic stimulator (Magstim 200; The Magstim Company Ltd, Whitland, United Kingdom) and a round 70 mm coil were used to generate a maximal magnetic field of 4 T at the coil surface. The coil was centered over the forehead and maximal stimulus intensity (100%) was applied.[11] A standard electromyograph (Medelec Sapphire; Medelec Ltd, Surrey, United Kingdom) recorded the muscle responses from the tibialis cranialis and the extensor carpi radialis muscle through intramuscular needle (25 mm monopolar, disposable, insulated, stainless steel needle; TECA Corporation, Pleasantville, New York) or adhesive surface electrodes (Skintact FS50; Skintact, Innsbruck, Austria). These electrode types do not have an important influence on latency time.[12] One limb at a time was tested, starting at the left pelvic limb, going to the right pelvic, left thoracic, and finally right thoracic limb.[12] For each limb, 4 sequential muscle responses were recorded. For each elicited MMEP, latency time, which is the time interval between the trigger and the first deflection from the baseline, was measured in milliseconds. For each horse, 1 mean latency time was calculated for the thoracic limbs (mean of 8 thoracic measurements, 4 left and 4 right) and 1 mean latency time for the pelvic limbs (mean of 8 pelvic measurements). All MMEP measurements were performed by 1 blinded operator.

2.3 | Diagnostic imaging

For all horses, lateral radiographs of the cervical vertebrae were made from the occiput to the first thoracic vertebra with a ceiling mounted Phillips X-Ray tube (80 kW). Output parameters varied from 70 kV/25 mAs for the cranial cervical vertebrae to 90 kV/90 mAs for C7-T1. A CR system (Agfa DXM) was used with a grid. All radiographs were anonymized and evaluated for any abnormalities by a blinded, board-certified radiologist. Additionally, the intravertebral and intervertebral sagittal diameter ratios of the vertebral canal were measured at each cervical vertebra.[20] For both ratios, a cutoff value of 0.485 was used to distinguish between a normal and a narrowed vertebral canal resulting in spinal cord compression.[20]

If horses had signs of proprioceptive ataxia on the clinical examination, but standard lateral radiographs did not reveal any abnormalities explaining the clinical signs, additional imaging was performed. This included additional radiographic projections such as oblique and ventrodorsal views, a myelogram, or a combination of both. Myelograms were performed under general anesthesia (triple drip with ketamine, guaiacol glyceryl ether, and detomidine or isoflurane inhalation anesthesia) with injection of iodinated contrast medium (Omnipaque 350, 0,2 mL/kg, diluted 30%) in the subarachnoid space. A similar volume of cerebrospinal fluid was withdrawn from the subarachnoid space before injection of the contrast medium. To visualize dynamic spinal cord compression, radiographs were taken with the neck in neutral, flexed, and extended position. Compression sites were identified by more than 50% reduction of the dorsal contrast column or more than 20% reduction of the dural diameter.[21]

2.4 | Histology

All horses were necropsied immediately after euthanasia to minimize postmortem artifacts. Samples of the cerebrum (3 samples of the rostral, middle, and caudal part bilaterally), cerebellum (1 sample, cerebellum-pontine area), brainstem (1 sample, medulla oblongata), cervical (7 samples at the level of the dorsal roots, C1-C7), thoracic (2 samples at the level of the dorsal roots, T2-T3 and T7-T8), lumbar (2 samples at the level of the dorsal roots, L1-L2 and L4-L5), spinal cord and cauda equina (1 sample) were fixed in a phosphate-buffered formaldehyde solution and embedded in paraffin wax. Four micrometer thick sections were stained with hematoxylin and eosin. T-lymphocytes were visualized using a polyclonal rabbit anti-CD3 antibody (Dako, Glostrup, Denmark). All tissues were immunolabeled with anti-synaptophysin to show degenerating neurons (Dako). A standard avidin-biotin complex method with diaminobenzidine as chromogen was used for visualization (Envision, Dako). All sections were assessed blinded by a board-certified veterinary pathologist for inflammatory, degenerative, or neoplastic changes. The presence of T-lymphocytes in the parenchyma and meninges was evaluated with grade 0 representing no infiltration, grade 1 mild, grade 2 moderate, and grade 3 severe infiltration. Also the degree of neuronal and axonal degeneration (spheroids) was scored with grade 0 representing no degeneration, grade 1 mild, grade 2 moderate, and grade 3 severe degeneration. T-lymphocytes infiltration or degree of degeneration was called mild if there were locally a few lymphocytes or spheroids visible, moderate if they were visible locally but in large numbers, and severe if they were present in large numbers on different sites through the nervous tissue.

2.5 | Statistical analysis

For each series of 8 stimulations, the mean value was calculated and entered as elementary unit to the dataset. To determine the possible significant weight and age differences in case and control animals, analysis of variance was used. The outcome variable of interest was latency time, which was first checked for a normal distribution.

Analysis of variance was used to assess the effect of control/ataxic horse on latency time values. A separate model was built for the thoracic and pelvic limbs. To determine the optimal cutoff latency time to differentiate an ataxic horse from a control animal, receiver operating curves were made, separately for thoracic and pelvic limbs. The Youden's index (sensitivity + specificity − 1) was calculated to determine optimal cutoff values. Sensitivity, specificity, and their 95% confidence intervals (CIs) were determined. All analyses were done in IBM SPPS, version 25, and WINEPISCOPE 2.0.

3 | RESULTS

None of the control horses had abnormalities on plain radiographs, and all intervertebral and intravertebral ratios were above cutoff values. None of these horses showed important degenerative or inflammatory changes on histopathology.

In 14 of 17 horses with C1-T2 myelopathy, diagnostic imaging supported spinal cord compression and Wallerian degeneration was confirmed on histopathology. Seven horses had indications of spinal cord compression on cervical radiographs. Two of them were suspected to have a neoplastic lesion as they showed severe osteolysis of the vertebral body. The other 5 had at least 1 cervical site with an intravertebral or intervertebral ratio below 0.485. In the other 7 horses, additional radiographs or myelogram were required for diagnosis as cervical radiographs were normal. In 6 of these horses, the myelogram suggested cervical spinal cord compression. In the other horse, radiographs of the thoracic part of the spine revealed a severe vertebral malformation of T8-T9. The vertebral bodies were shorter compared with surrounding vertebrae, wedge shaped, and displaced dorsally. On histopathology, clear degenerative and inflammatory changes were seen. Only the pelvic limb latency times of this horse were included further in the study. The remaining 3 of 17 ataxic horses had normal cervical radiographs and myelogram. No radiographs of thoracic or lumbar region were taken. On histopathology, 1 of these horses showed only mild degenerative and inflammatory lesions, another only showed a moderate mononuclear inflammation, and the third had moderate degenerative lesions at the level of the cervical spinal cord.

There was no significant difference in age between both groups, but ataxic horses had a significantly (P = .02) lower weight than control horses. Mean ± SD latency time in normal horses was 20 ± 1 milliseconds in thoracic limbs and 39 ± 1 milliseconds in pelvic limbs. Mean ± SD latency time values for the ataxic horses were 34 ± 16 milliseconds in the thoracic limbs and 78 ± 26 milliseconds in the pelvic limbs. Latency time values from both thoracic (the thoracic latency time value of the horse with the thoracic lesion was not included) and pelvic limbs were significantly different from those in the control horses (P = .05 and P = .004, respectively).

Figure 1 shows the receiver operating characteristic (ROC) curves for thoracic and pelvic limb latency times based on 21 and all 22 horses, respectively. The optimal cutoff values for latency time to detect spinal cord dysfunction in ataxic horses were 22 milliseconds (sensitivity [95% CI interval], 88% [73%-100%]; specificity [95% CI interval], 100% [100%-100%]) in thoracic and 40 milliseconds (sensitivity, 94% [83%-100%]; specificity, 100% [100%-100%]) in pelvic limbs. If the 2 ataxic horses without clear compression of the spinal cord (only inflammatory or very mild degenerative lesions) were excluded, the optimal cutoff value for the thoracic limbs remained 22 milliseconds, but the sensitivity and specificity increased to 100% (100%-100%) each. The suggested optimal cutoff value for the pelvic limbs, however, was 43 milliseconds with an increase in sensitivity as consequence (sensitivity, 100% [100%-100%]; specificity, 100% [100%-100%]).

4 | DISCUSSION

This study determined cutoff values of MMEP latency time for spinal cord dysfunction in horses, confirmed by narrowing of the vertebral canal on diagnostic imaging and inflammatory or degenerative lesions on histopathology. There were a number of limitations. First, the weight of the control horses differed significantly from the ataxic horses. Although weight is excluded in multivariable analysis because of the strong correlation with wither height, a significant influence of

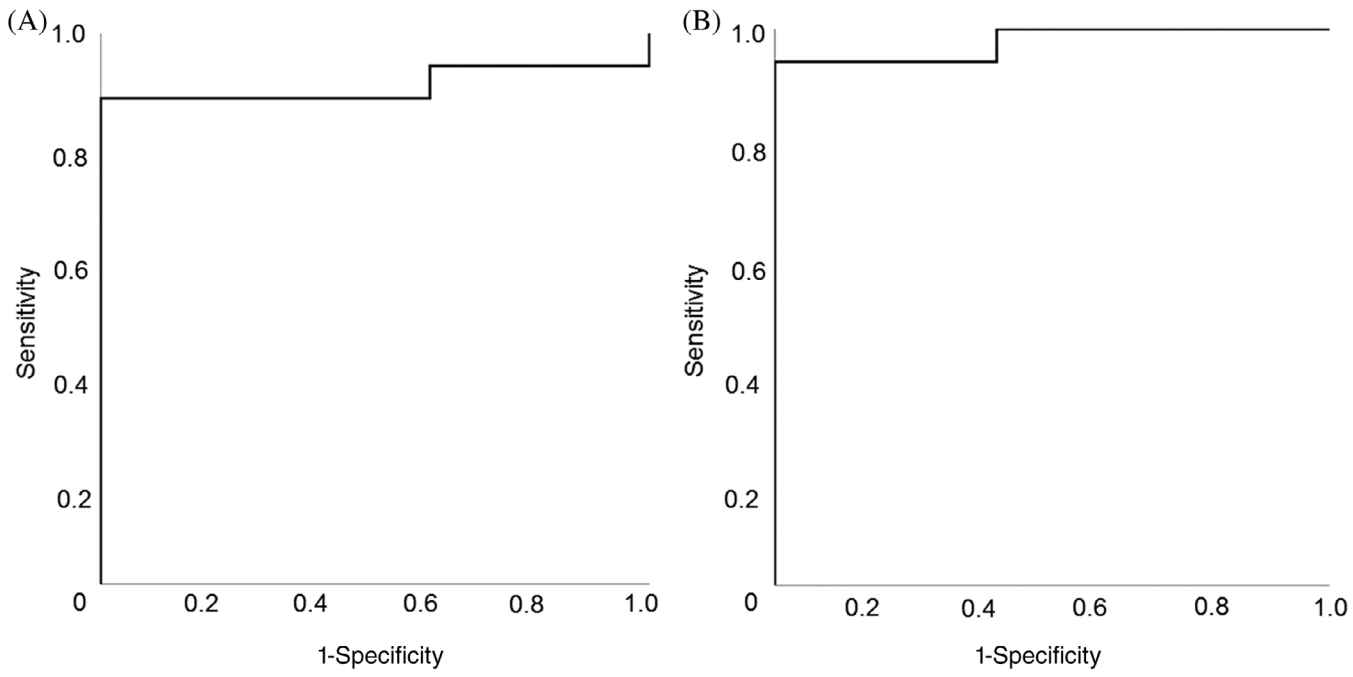

FIGURE 1 Receiver operating characteristic curves for thoracic (left) and pelvic (right) limb latency times based on 22 horses

weight on latency time in univariate analysis is found.[11] So, the weight difference in the present study could have an influence on MMEP results. However, as the weight of the ataxic horses is lower, they are probably smaller, and a shorter latency time would be expected compared to the heavier, and probably taller, control horses.

Secondly, the present calculations were made on only 5 control horses, but differences between groups were significant. Furthermore, the variation in latency time between the different control animals is small, as we expected from former MMEP research in larger numbers of healthy horses.[11,12] So, because of ethical reasons, the number of controls was kept as low as possible. The fact that all control horses were adult while in the ataxic group also young horses were included neither should be an issue, as age does not have a significant influence on latency time in horses.[11] A more important problem is that the ataxic horses had a high grade of ataxia (mean 3.6/5). In these obviously ataxic horses, TMS might be unnecessary. Transcranial magnetic stimulation is especially useful in the subtle cases, where additional confirmation of neurological dysfunction is wanted. In the present study, however, only 1 horse with a grade 1 and no horses with a grade 2 were included. Therefore, the present cutoff values need to be validated in future TMS studies on larger numbers of horses, including cases with subtle signs of proprioceptive ataxia.

Third, not all horses, and none of the control horses, were examined by myelography. In the ataxic horses without myelogram, cervical radiographs already indicated spinal cord compression which was confirmed by histopathology. In the control horses, it is unlikely that a myelogram would have shown spinal cord compression, as histopathology did not reveal abnormalities.

Fourth, only lateral cervical radiographs were made and no attention was paid to enlargement of the caudal articular process joints. These enlarged joints do not necessarily result in spinal cord compression,[22] but in some cases they will.

Lastly, conclusions were made based on histopathology, which is not a perfect gold standard. Functional deficits can occur before histopathological changes can be found and influence of age and postmortem artifacts can impede interpretation. However, it is currently the most accurate and sensitive test available.[23,24]

With these limitations in mind, the present study defines clear cutoff values for thoracic and pelvic limb MMEP latency times, with a high sensitivity and specificity to diagnose spinal cord dysfunction in horses. The results are in line with a comparable study in Doberman Pinscher dogs where latency time cutoff values were calculated to discriminate between normal and affected animals, based on the findings of clinical examinations and MRI. Comparable to our results, in these dogs, the pelvic limb latency times had the highest sensitivity and overall MMEP sensitivities and specificities were high (about 90%).[25]

Similar to the horses in the present study, significantly different latency times were found in dogs with and without cervical spinal cord disease.[16-18,26] In these studies, MMEP results were always compared with MRI findings but there was no histopathological confirmation of spinal cord disease. Magnetic resonance imaging is a popular, noninvasive, and sensitive technique, although not all lesions on MRI cause functional deficits. In horses, MRI scanning facilities are not always available, and only postmortem cervical MRI studies have been published.[24,27,28] Postmortem MRI examinations seem to be more accurate than cervical radiographs to diagnose CVM,[28] but sensitivity and positive predictive values remain poor to moderate, compared to histopathological diagnosis.[24]

There was overall a good agreement between clinical examination, diagnostic imaging, and histopathology, but in 3 of 22 horses, there were contradictory results. Three ataxic cases were evaluated as normal on diagnostic imaging. This might be because there was no compression or because the compression was not diagnosed. False-negative results are possible in cases of lateral compression, enlarged articular process joints, or because of the low sensitivity of the used cutoff values. For the plain radiographs, 0.485 was used as the cutoff value for cervical vertebral sagittal ratios, but also 0.52 and 0.56 have been proposed in earlier research.[29] Logically, sensitivity to identify spinal cord compression will be higher using 0.52 and 0.56, but also the rate of false positives will increase. The same problem exists for myelography. Several cutoff values have been proposed, but it remains difficult to combine acceptable sensitivity and specificity in 1 number.[21]

On histopathology, the difference between controls and ataxic horses was apparent. Control horses had only mild degenerative or inflammatory lesions, possibly a consequence of age, whereas most ataxic horses had mild to moderate inflammatory changes and moderate to severe degenerative changes. Two ataxic horses did not have clear lesions of spinal cord compression. In these 2 horses, latency time values were only slightly increased. Horse 6 even had mean latency time values below the cutoff values. In combination with only a grade 1 ataxia, the question arises whether the horse did have a neurological problem or whether an orthopedic cause would be more likely. Nollet et al[30] suggested that TMS could help in differentiating between orthopedic and neurological causes of recumbence such as severe laminitis or physitis, but no data are available about more subtle cases. As no cases with clear orthopedic gait deficits were included in the study, no further conclusions can be made about this hypothesis. The other horse (horse 18) without clear signs of spinal cord compression had a thoracic latency time slightly above the threshold and moderate signs of inflammation in the spinal cord in combination with a grade 4 ataxia. Possibly, the proprioceptive ataxia was caused by another etiology than spinal cord compression (eg, EPM, EDM/NAD, or equine herpesvirus myeloencephalopathy). The present study confirms the test can detect spinal cord compression, but in the future, it might be interesting to evaluate the sensitivity in cases with an etiology of ataxia other than spinal cord compression too.

In conclusion, in the present study population, with a high prevalence of horses with a high grade of ataxia, 22 milliseconds for thoracic and 43 milliseconds for pelvic limbs were the optimal cutoff values to differentiate between horses with spinal cord dysfunction, caused by spinal cord compression, and neurologically healthy animals. With these threshold values for latency time, a much higher sensitivity and specificity than currently reported for cervical radiography were obtained. These results are promising and merit validation of these cutoffs on a larger data set, including animals with mild ataxia and gait deficits of orthopedic nature in future work.

CONFLICT OF INTEREST DECLARATION

Authors declare no conflict of interest.

OFF-LABEL ANTIMICROBIAL DECLARATION

Authors declare no off-label use of antimicrobials.

INSTITUTIONAL ANIMAL CARE AND USE COMMITTEE (IACUC) OR OTHER APPROVAL DECLARATION

The study was approved by the ethical committee of the faculty of veterinary medicine, Ghent University (EC2016/59).

HUMAN ETHICS APPROVAL DECLARATION

Authors declare human ethics approval was not needed for this study.

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REFERENCES

1. Szklarz M, Skalec A, Kirstein K, et al. Management of equine ataxia caused by cervical vertebral stenotic myelopathy: a European perspective 2010-2015. *Equine Vet Educ*. 2018;30:370-376.
2. Walmsley JR. Surgical treatment of cervical spinal cord compression in horses: a European experience. *Equine Vet Educ*. 2005;17:39-43.
3. Levine JM, Scrivani PV, Divers TJ, et al. Multicenter case-control study of signalment, diagnostic features, and outcome associated with cervical vertebral malformation-malarticulation in horses. *J Am Vet Med A*. 2010;237:812-822.
4. Levine JM, Ngheim PP, Levine GJ, Cohen ND. Associations of sex, breed, and age with cervical vertebral compressive myelopathy in horses: 811 cases (1974-2007). *J Am Vet Med A*. 2008;233:1453-1458.
5. Oswald J, Love S, Parkin TD, et al. Prevalence of cervical vertebral stenotic myelopathy in a population of thoroughbred horses. *Vet Rec*. 2010;166:82-83.
6. Nout YS, Reed SM. Cervical vertebral stenotic myelopathy. *Equine Vet Educ*. 2003;15:212-223.
7. Hamir AN, Moser G, Rupprecht CE. A five year (1985-1989) retrospective study of equine neurological diseases with special reference to rabies. *J Comp Pathol*. 1992;106:411-421.
8. Levine JM, Adam E, MacKay RJ, et al. Confirmed and presumptive cervical vertebral compressive myelopathy in older horses: a retrospective study (1992-2004). *J Vet Intern Med*. 2007;21:812-819.
9. Hughes KJ, Laidlaw EH, Reed SM, et al. Repeatability and intra- and inter-observer agreement of cervical vertebral sagittal diameter ratios in horses with neurological disease. *J Vet Intern Med*. 2014;28:1860-1870.
10. Nollet H, Van Ham L, Dewulf J, et al. Standardization of transcranial magnetic stimulation in the horse. *Vet J*. 2003;166:244-250.
11. Nollet H, Deprez R, Van Ham L, et al. Transcranial magnetic stimulation: normal values of magnetic motor evoked potentials in 84 normal horses and influence of height, weight, age and sex. *Equine Vet J*. 2004;36:51-57.
12. Rijckaert J, Pardon B, Ham LV, et al. Magnetic motor evoked potential recording in horses using intramuscular needle electrodes and surface electrodes. *J Equine Vet*. 2018;68:101-107.
13. Nollet H, Van Ham L, Gasthuys F, et al. Influence of detomidine and buprenorphine on motor-evoked potentials in horses. *Vet Rec*. 2003;152:534-537.
14. Nollet H, Van Ham L, Verschooten F, et al. Use of magnetic motor-evoked potentials in horses with bilateral hind limb ataxia. *Am J Vet Res*. 2003;64:1382-1386.
15. Nollet H, Deprez P, Van Ham L, et al. The use of magnetic motor evoked potentials in horses with cervical spinal cord disease. *Equine Vet J*. 2002;34:156-163.
16. Martin-Vaquero P, da Costa RC. Transcranial magnetic motor evoked potentials in great Danes with and without clinical signs of cervical spondylomyelopathy: association with neurological findings and magnetic resonance imaging. *Vet J*. 2014;201:327-332.
17. da Costa RC, Poma R, Parent JM, Partlow G, Monteith G. Correlation of motor evoked potentials with magnetic resonance imaging and neurologic findings in Doberman Pinschers with and without signs of cervical spondylomyelopathy. *Am J Vet Res*. 2006;67:1613-1620.
18. Poma R, Parent JM, Holmberg DL, Partlow GD, Monteith G, Sylvestre AM. Correlation between severity of clinical signs and motor evoked potentials after transcranial magnetic stimulation in large-breed dogs with cervical spinal cord disease. *J Am Vet Med A*. 2002;221:60-64.
19. Mayhew IG. *Large Animal Neurology—Neurological Evaluation Form*. 2nd ed. Chichester: Wiley-Blackwell; 2008:453.
20. Hahn CN, Handel I, Green SL, et al. Assessment of the utility of using intra- and intervertebral minimum sagittal diameter ratios in the diagnosis of cervical vertebral malformation in horses. *Vet Radiol Ultrasound*. 2008;49:1-6.
21. van Biervliet J, Scrivani PV, Divers TJ, Erb HN, de Lahunta A, Nixon A. Evaluation of decision criteria for detection of spinal cord compression based on cervical myelography in horses: 38 cases (1981-2001). *Equine Vet J*. 2004;36:14-20.
22. Down SS, Henson FM. Radiographic retrospective study of the caudal cervical articular process joints in the horse. *Equine Vet J*. 2009;41:518-524.
23. Van Biervliet J. An evidence-based approach to clinical questions in the practice of equine neurology. *Vet Clin N Am Equine Pract*. 2007;23:317-328.
24. Mitchell CW, Nykamp SG, Foster R, Cruz R, Montieth G. The use of magnetic resonance imaging in evaluating horses with spinal ataxia. *Vet Radiol Ultrasound*. 2012;53:613-620.
25. De Decker S, Van Soens I, Duchateau L, et al. Transcranial magnetic stimulation in Doberman pinschers with clinically relevant and clinically irrelevant spinal cord compression on magnetic resonance imaging. *J Am Vet Med A*. 2011;238:81-88.
26. Amendt HL, Siedenburg JS, Steffensen N, et al. Correlation between severity of clinical signs and transcranial magnetic motor evoked potentials in dogs with intervertebral disc herniation. *Vet J*. 2017;221:48-53.
27. Sleutjens J, Cooley AJ, Sampson SN, et al. The equine cervical spine: comparing MRI and contrast-enhanced CT images with anatomic slices in the sagittal, dorsal, and transverse plane. *Vet Q*. 2014;34:74-84.
28. Janes JG, Garrett KS, McQuerry KJ, et al. Comparison of magnetic resonance imaging with standing cervical radiographs for evaluation of vertebral canal stenosis in equine cervical stenotic myelopathy. *Equine Vet J*. 2014;46:681-686.

29. Moore BR, Reed SM, Biller DS, Kohn CW, Weisbrode SE. Assessment of vertebral canal diameter and bony malformations of the cervical part of the spine in horses with cervical stenotic myelopathy. *Am J Vet Res*. 1994;55:5-13.
30. Nollet H, Vanschandevijl K, Van Ham L, et al. Role of transcranial magnetic stimulation in differentiating motor nervous tract disorders from other causes of recumbency in four horses and one donkey. *Vet Rec*. 2005;157:656-658.

How to cite this article: Rijckaert J, Pardon B, Saey V, et al. Determination of magnetic motor evoked potential latency time cutoff values for detection of spinal cord dysfunction in horses. *J Vet Intern Med*. 2019;33:2312–2318. https://doi.org/10.1111/jvim.15576