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Transcranial magnetic motor evoked potentials in Great Danes with and without clinical signs of cervical spondylomyelopathy: Association with neurological findings and magnetic resonance imaging

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ABSTRACT

Transcranial magnetic motor evoked potentials (TMMEPs) assess the functional integrity of the descending motor pathways, which are typically compromised in canine cervical spondylomyelopathy (CSM). The objective of this prospective study was to establish the reference ranges of TMMEP latency and amplitude in clinically normal (control) Great Danes (GDs), compare TMMEPs obtained in GDs with and without CSM, and determine whether there is any association between TMMEP data and severity of neurological signs or magnetic resonance imaging (MRI) findings. Twenty-nine client-owned GDs were enrolled (15 controls, 14 CSM-affected). All dogs underwent TMMEPs under sedation, and latencies and amplitudes were recorded from the extensor carpi radialis (ECR) and cranial tibial (CT) muscles. MRI of the cervical vertebral column was performed to evaluate the presence and severity of spinal cord (SC) compression, and the presence of SC signal changes.

ECR and CT latencies were significantly longer in CSM-affected than control GDs. No significant differences between groups were found for amplitudes or neuronal path lengths. For the CT TMMEPs, CSM-affected GDs with moderate and severe clinical signs had significantly longer latencies than those with mild clinical signs. Significantly longer CT latencies were found in dogs with moderate and severe SC compression compared with dogs with mild compression. CT TMMEPs could not be recorded in 7/9 CSM-affected GDs with SC signal changes. These results provide a reference range for TMMEPs of clinically normal GDs. The use of TMMEPs is a valid ancillary test to assess the integrity of motor pathways in GDs with CSM.

Introduction

The use of transcranial magnetic motor evoked potentials (TMMEPs) was first described in humans in 1985 (Barker et al., 1985). To obtain TMMEPs, a magnetic stimulator and a coil are used to apply a brief magnetic field to the motor cortex, which generates a recordable motor evoked potential in the contralateral appendicular muscles (Nollet et al., 2003). This technique provides a non-invasive method for assessing descending motor pathway function (Barker et al., 1985; Di Lazzaro et al., 1999).

In humans, TMMEPs have been used to evaluate the functionality of the motor pathways in cervical spondylotic myelopathy, which is a common cause of chronic compressive cervical myelopathy similar to canine cervical spondylomyelopathy (CSM) (Di Lazzaro et al., 1999; Lo, 2007; da Costa, 2010). Magnetic resonance imaging (MRI) is typically used to diagnose this human disease and define the compressive sites, but it cannot provide information about spinal cord (SC) functionality (Capone et al., 2013). In this human condition, TMMEPs can be used to detect preclinical myelopathy, monitor disease progression by obtaining serial recordings, and monitor SC function during surgery (Travlos et al., 1992; Lo et al., 2004, 2006; Capone et al., 2013).

The use of TMMEPs has been reported in horses and dogs with cervical SC disease (Nollet et al., 2002; Poma et al., 2002; da Costa et al., 2006; De Decker et al., 2011). In CSM-affected Doberman Pinschers, TMMEP latencies were increased when compared with clinically normal Dobermans, and correlated with the severity of neurological signs and MRI findings in affected dogs (da Costa et al., 2006; De Decker et al., 2011). Great Danes (GDs) are also frequently affected by CSM (da Costa, 2010). However, no study has reported TMMEPs values in clinically normal GDs or investigated its use in GDs with CSM. In humans and horses, TMMEP latencies are influenced by body size (Chu, 1989; Nollet et al., 2004). GDs are

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larger than Doberman Pinschers; thus, TMMEPs reference ranges obtained in Doberman Pinschers may not apply to GDs.

The purpose of this study was to establish the reference ranges of TMMEP latency and amplitude in clinically normal GDs, compare TMMEPs obtained in GDs with and without clinical signs of CSM, and determine whether there is any association between TMMEP data, severity of neurological signs, and MRI findings. We hypothesized that differences would be identified in the TMMEP latencies between clinically normal and CSM-affected GDs, but no amplitude differences would be identified between groups, similar to what has been previously reported in a TMMEP study performed in Dobermans with and without CSM (da Costa et al., 2006). We also hypothesized that TMMEP latencies would be longer in the CSM-affected GDs with more severe clinical signs and SC compression.

Materials and methods

Animals

The study was conducted in accordance with the guidelines and with the approval of The Ohio State University Clinical Research Advisory Committee and the Institutional Animal Care and Use Committee (2011A00000027). Written owner consent was obtained prior to study enrollment. Two groups of client-owned GDs were prospectively enrolled between April 2011 and October 2012. The first group included 15 clinically normal (control) GDs based on a normal neurological examination and no history of neurological disease. Only GDs ≥ 1 year of age were eligible for enrollment as control dogs. The second group included 14 GDs with clinical signs and neurological examination consistent with CSM and diagnostic confirmation via MRI. The time of onset of signs was recorded. A video of the gait of all CSM-affected dogs was obtained at the time of enrollment. All GDs were examined by the two investigators, and underwent TMMEPs and MRI of the cervical vertebral column.

Gait grading

The video material was reviewed at a later time by one investigator (PMV) to assign a neurological grade to each CSM-affected GD. At least 2 min of video material were available for all dogs. The gait was graded from 0 to 3 for each thoracic and pelvic limb as follows: grade 0, normal limb; grade 1, abnormal use of the limb <40% of the steps; grade 2, abnormal use of the limb between 40% and 70% of the steps, and grade 3, abnormal use of the limb >70% of the steps. Signs of both paresis/weakness (i.e., knuckling, scuffing, dragging) and/or ataxia/incoordination (inconsistent limb/foot placement) were considered as an abnormal use of the limb. If the grade assigned to the right and left thoracic limbs differed, the worse grade (from 0 to 3) was used as the overall grading for that pair of limbs. The same process was followed for the pelvic limb gait grading.

The thoracic limb grade (from 0 to 3) and the pelvic limb grade (from 0 to 3) were summed for each dog, producing an overall final gait grade ranging from 1 to 6 (no CSM-affected dog had four limbs characterized as normal, thus no overall final grade of 0 was possible). For the purpose of statistical analysis to investigate associations between disease severity based on gait grading and the TMMEPs, the overall final gait grades 1 and 2 were grouped and categorized as mild, grades 3 and 4 were categorized as moderate, and grades 5 and 6 were categorized as severe.

TMMEPs

Dogs were sedated with hydromorphone (0.05–0.1 mg/kg intravenously [IV]) and dexmedetomidine (4–8 μg/kg IV). The dogs were positioned in lateral recumbency. The technique of TMMEPs acquisition was based on previous studies (da Costa et al., 2006; De Decker et al., 2011). Transcranial magnetic stimulation was performed using a magnetic stimulator (Cadwell Sierra Wave, Cadwell Laboratories) and a 9.0 cm circular coil (Magstim, The Magstim Company) capable of producing a peak magnetic field of 2.0 Tesla at the coil surface. Supramaximal stimulus intensity (100% stimulus) was delivered by the magnetic coil held tangentially to the skull, with the center of the coil over the skull lateral to the vertex. The coil was kept in close contact with the skin, and the current flow within the coil ran in a clockwise direction. Four individual stimulations were delivered over the motor cortex before repeating the procedure on the opposite side.

Recordings of TMMEPs were obtained by use of an electromyography (Cadwell Sierra Wave, Cadwell Laboratories). Disposable13-mm non-insulated, stainless steel needles were used as the recording (active), reference, and ground electrodes (Technomed Europe, Medical Accessories). The recording electrode was inserted in the muscle belly of both the extensor carpi radialis (ECR) and cranial tibial (CT) muscles. The reference electrode was positioned subcutaneously 1 cm distal to the active electrode. The ground electrode was placed subcutaneously in the dorsal aspect of the cranial thoracic region. The recording electrode was connected to the negative input of the preamplifier, thus negativity of the recording electrode with respect to the reference electrode caused an upward deflection of the trace.

The TMMEPs were recorded from the right and left limbs after stimulating the respective contralateral cortex. The recorded TMMEP waveforms were displayed on the oscilloscope screen and saved. The total recording time was 100 ms. The low and high frequency filters were set at 30 Hz and 10 kHz, respectively. The sensitivity was set at 1000 μV/division for all recordings.

The latencies and amplitudes were measured using the manually directed cursors on the oscilloscope. Onset latencies were measured in ms and calculated as the interval from the onset of the stimulus to the onset of the response. Peak-to-peak amplitudes were measured in microvolts and calculated from the peak of the negative wave to the nadir of the first positive wave. When measuring latencies and amplitudes, the gain was adjusted as needed to optimize the visualization of waves and the manual placing of cursors to obtain latency and amplitude data. The neuronal path length of each dog was measured using a tape from the site of the transcranial magnetic stimulation to the active electrode located within the ECR and CT muscles contralateral to the stimulated site.

MRI

All dogs underwent MRI of the cervical vertebral column under general anesthesia with a 3.0 Tesla magnet (Achieva, Philips Healthcare) and a surface coil. Dogs were positioned in dorsal recumbency. Turbo spin-echo sagittal and transverse T2-weighted images (WI) were obtained and used to determine the sites of SC compression. Seven intervertebral spaces (C2-3 to T1-2) were imaged and five transverse slices obtained for every intervertebral space. All MRI studies were evaluated by one investigator (PMV) using dedicated software (E-Film Merge Healthcare). Spinal cord compression was graded as previously described (da Costa et al., 2012): mild (<25% reduction in the SC diameter), moderate (25–50% reduction), and severe (>50% reduction in the SC diameter). If more than one type of SC compression was present in the same dog, the most severe type of compression was used for statistical analysis. Sites of SC signal changes, defined as SC hyperintensity on T2-weighted images, were also recorded.

Statistical methods

For all TMMEP variables (latency, amplitude, and neuronal path length for the ECR and CT muscles), values recorded in each dog for left and right limbs were averaged to obtain a single value for each variable and dog. A random-effects linear regression model was used to compare the TMMEP variables between control and CSM-affected GDs, and to investigate associations between TMMEP latencies and amplitudes with the neurological status and MRI findings in CSM-affected GDs. Adjustments were made for age, gender, and weight. The P values were adjusted by Holm's procedure to conserve the type I error at 0.05. Significance was set at $P < 0.05$. Analyses were performed by use of computer software (Stata v.12.1, Stata Corporation).

Results

Clinical data and MRI findings

The clinically normal GDs included seven females (six spayed, one intact) and eight males (seven neutered, one intact). Their median age at the time of enrollment was 2.3 years (range, 1–6.4 years). The median weight was 52 kg (range, 40.5–73 kg). All clinically normal GDs had a normal neurological examination. The CSM-affected GDs included two spayed females, 11 neutered males, and one intact male. Their median age at the time of enrollment was 4.2 years (range, 1–7.2 years). The median weight was 57.5 kg (range, 45–79.3 kg). The reported median age at the onset of signs of CSM was 1.6 years (range, 0.4–4.2 years). The clinical signs had been present for a mean time of 1.6 years (range, 0.2–5 years) before enrollment. Thirteen out of the 14 CSM-affected dogs showed ambulatory tetraparesis with proprioceptive ataxia of all limbs, and one showed a hypertonic thoracic limb gait with ambulatory paraparesis and proprioceptive ataxia of the pelvic limbs. All CSM-affected GDs had delayed postural reactions involving all limbs, and five had mild neck pain.

Gait grading yielded the following results: grade 1, $n = 1$; grade 2, $n = 3$; grade 3, $n = 1$; grade 4, $n = 3$; grade 5, $n = 1$; grade 6, $n = 5$. For statistical analysis, four dogs were considered to have mild signs (grades 1–2), four had moderate signs (grades 3–4), and six had severe signs (grades 5–6). Overall, 43 sites of SC compression were

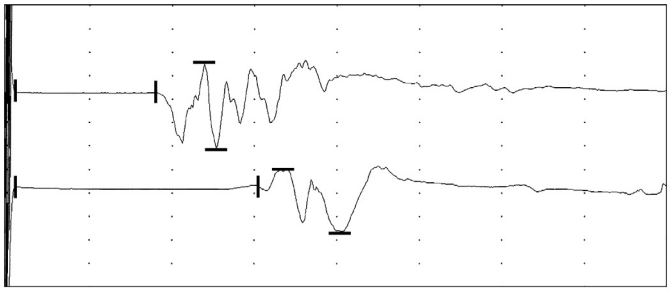

Fig. 1. Transcranial magnetic motor evoked potential (TMMEP) recorded from the left extensor carpi radialis muscle (upper trace) and left cranial tibial muscle (lower trace) from a clinically normal Great Dane. Vertical bars indicate distance from the stimulus artifact to the onset of the response (onset latency). Horizontal bars indicate peak-to-peak amplitude. Sensitivity: 1000 μV/division. Distance between dotted lines: 10 ms.

recorded in the CSM-affected GDs. Based on the severity of the SC compression, one dog was classified as having mild compression, three had moderate compression, and 10 had severe compression. Fourteen sites of SC hyperintensity were recorded in 9 CSM-affected GDs.

TMMEPs and associations with neurological signs and MRI findings

The TMMEPs waveform appeared polyphasic in all GDs, regardless of their clinical status (Figs. 1 and 2). In 8/14 CSM-affected GDs, TMMEPs could not be recorded in either pelvic limb. In an additional three CSM-affected GDs, TMMEPs were recordable only in one pelvic limb (Fig. 3). In the remaining three affected GDs, TMMEPs were recordable in both pelvic limbs. The TMMEPs were recordable in the thoracic limbs for all CSM-affected GDs and in all four limbs for all control GDs. Mean values for latencies, amplitudes, and neuronal path lengths for control and CSM-affected GDs were calculated (Table 1). Extensor carpi radialis and CT latencies were significantly longer for CSM-affected GDs when compared with control GDs. No significant differences between groups were found for amplitudes or neuronal path lengths.

In the CSM-affected GDs, ECR mean latencies progressively increased with severity of neurological signs (Table 2). However, only the comparison of ECR latencies between CSM-affected GDs with mild and severe signs yielded significant differences. Extensor carpi radialis amplitudes were significantly different in dogs with moderate signs when compared with those that had mild signs. For the

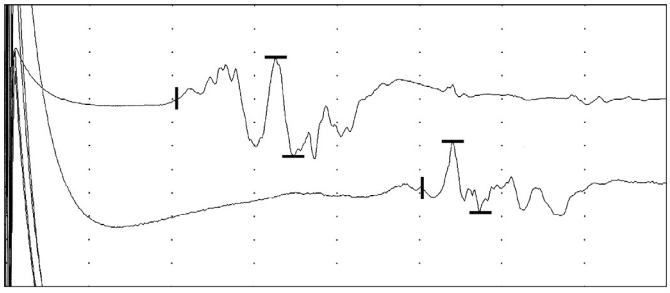

Fig. 2. Transcranial magnetic motor evoked potential (TMMEP) recorded from the right extensor carpi radialis muscle (upper trace) and left cranial tibial muscle (lower trace) from a CSM-affected Great Dane with mild clinical signs. Vertical bars indicate onset latency. Horizontal bars indicate peak-to-peak amplitude. Sensitivity: 1000 μV/division for extensor carpi radialis muscle, and 200 μV/division for cranial tibial muscle. Distance between dotted lines: 10 ms. Note the polyphasic configuration of both traces and the increased onset latencies when compared to the traces in Fig. 1, especially for the cranial tibial TMMEPs.

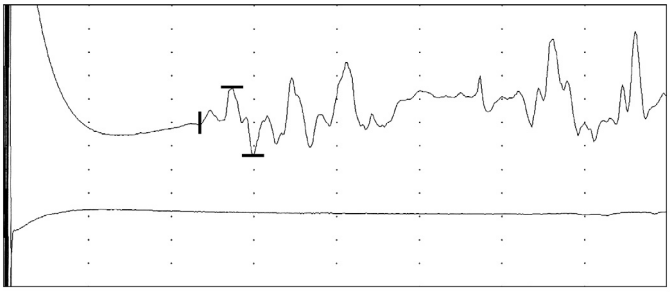

Fig. 3. Transcranial magnetic motor evoked potential (TMMEP) recorded from the right extensor carpi radialis muscle (upper trace) and left cranial tibial muscle (lower trace) from a CSM-affected Great Dane with moderate clinical signs. Vertical bar indicates onset latency. Horizontal bars indicate peak-to-peak amplitude. Sensitivity: 500 μV/division. Distance between dotted lines: 10 ms. Note the marked polyphasic configuration in the extensor carpi radialis TMMEPs and the increased onset latency when compared to Fig. 1. No TMMEPs could be obtained from the cranial tibial muscle in this CSM-affected dog.

CT TMMEPs, CSM-affected GDs with moderate and severe clinical signs had significantly longer latencies that those with mild signs (Table 2).

For the ECR TMMEPs, there were no significant associations between latencies or amplitudes and severity of SC compression recorded on MRI (Table 3). The degree of SC compression did show a significant association with CT latencies, with longer latencies in affected GDs with moderate and severe SC compression, compared with dogs that had mild SC compression (Table 3). Out of the nine CSM-affected GDs with SC signal changes, two had recordable TMMEPs in one pelvic limb, and 7/9 had no recordable TMMEPs on either pelvic limb. No SC signal changes were present in 3/3 CSM-affected GDs with recordable TMMEPs from both pelvic limbs, in 1/3 CSM-affected GDs with recordable TMMEPs from one pelvic limb, and in 1/8 CSM-affected GD with no recordable TMMEPs from either pelvic limb. No significant associations were found between ECR latencies ($P = 0.463$) or CT latencies ($P = 0.999$), and the presence of SC signal changes in the CSM-affected GDs.

Discussion

The present study provides reference ranges for TMMEP latencies and amplitudes in clinically normal GDs. We also found that CSM-affected GDs had significantly longer TMMEP latencies for the ECR and CT muscles when compared with control GDs. Moreover, CT latencies were significantly associated with the severity of neurological signs and SC compression in CSM-affected GDs. The results are in agreement with two previous studies performed on Doberman Pinschers with and without signs of CSM, which also reported that CT latencies were significantly different between groups, and correlated with the degree of neurological signs and severity of SC compression (da Costa et al., 2006; De Decker et al., 2011).

The ECR latencies yielded conflicting results in Doberman Pinschers with and without signs of CSM. One study reported no differences between clinically normal and CSM-affected Dobermans Pinschers, whereas another study did report significant differences between the two groups (da Costa et al., 2006; De Decker et al., 2011). Our study did show significantly longer ECR latencies in CSM-affected GDs when compared with control GDs. However, the onset latencies for the ECR and CT muscles obtained in both clinically normal and CSM-affected GDs were longer than the equivalent latencies in normal and CSM-affected Doberman Pinschers.

GDs are larger and taller than Doberman Pinschers, with a mean neuronal path length of 106.7 cm for the ECR muscle and 167.5 cm for the CT muscle in normal GDs, when compared to a mean neuronal path length of 78.4 cm and 124.9 cm in normal Dobermans,

Table 1
Mean onset latencies, peak-to-peak amplitudes, and neuronal path lengths for transcranial magnetic motor evoked potentials (TMMEPs) recorded from the extensor carpi radialis muscle (ECRM) and cranial tibial muscle (CTM) in clinically normal (control) Great Danes (GDs) and GDs with clinical signs of cervical spondylomyelopathy (CSM).

Variable	Muscle	Control[a]	CSM-affected[b]	*P*
Latency (ms)	ECRM	18.1 (14.4–21.8)	25.3 (22.4–28.3)	0.006[c]
	CTM	29.6 (25.9–33.3)	46.4 (42.4–50.3)	<0.001[c]
Amplitude (μV)	ECRM	2910 (1978–3842)	2504 (1745–3263)	0.760
	CTM	1617 (685–2549)	599 (–583–1782)	0.331
Neuronal path length (cm)	ECRM	106.7 (102.8–110.5)	101.7 (98.6–104.9)	0.110
	CTM	167.5 (163.6–171.4)	170.2 (165.2–175.2)	0.629

Data are presented as means (95% confidence interval).
[a] TMMEPs were recordable from all four limbs in all 15 clinically normal GDs enrolled.
[b] TMMEPs were recordable from the ECRM in all 14 CSM-affected GDs enrolled. In 8/14 affected GDs, TMMEPs could not be recorded from either pelvic limb. TMMEPs were recordable from the CTM of both pelvic limbs and one pelvic limb in 3/14 and 3/14 of affected GDs, respectively.
[c] Indicates statistical significance, $P < 0.05$.

respectively (da Costa et al., 2006). A longer neuronal path length means that the impulse will need to travel a larger distance before reaching the muscle and generating a motor evoked potential; thus, yielding longer latencies. The influence of body size on TMMEP latencies has also been reported in humans and horses (Chu, 1989; Nollet et al., 2004). These results indicate that reference ranges for TMMEP latency will likely be different across dog breeds with different body sizes.

Overall, TMMEP amplitudes were markedly variable for both control and CSM-affected GDs, showing a high degree of overlap between groups and no significant differences. In humans, TMMEP amplitudes are reported to be extremely variable even within the same individual (Eisen and Shtybel, 1990). Amplitudes also showed more variability and appeared less reliable than TMMEP latencies in dogs and horses (Nollet et al., 2002; da Costa et al., 2006).

In this study, no TMMEPs could be elicited from the pelvic limbs in several of the CSM-affected GDs, whereas pelvic limb TMMEPs were recordable from all control GDs. Similar findings have been reported in human cervical spondylotic myelopathy (Tavy et al., 1994; Lo et al., 2004, 2007). One study reported absent TMMEPs in 34/141 (24.1%) people with cervical spondylotic myelopathy of varying severities (Lo et al., 2004). Similarly, absent pelvic limb TMMEPs have been reported in CSM-affected Doberman Pinschers and horses with cervical myelopathy (Nollet et al., 2002; De Decker et al., 2011). The reason behind this phenomenon is not well understood; however, experimental studies of SC injury in humans and animals have suggested that the propagating impulse, albeit present in the SC distal to the lesion, may not be strong enough to increase the postsynaptic membrane potential of the motor neuron to its threshold; thus, no impulse will be present in the peripheral nerve and muscle from

Table 2
Association between mean onset latencies (in ms) and peak-to-peak amplitudes (in μV) for transcranial magnetic motor evoked potentials (TMMEPs) recorded from the extensor carpi radialis muscle (ECRM) and cranial tibial muscle (CTM) and the severity of neurological signs in 14 Great Danes with cervical spondylomyelopathy.

Severity of signs	ECRM latency	ECRM amplitude	CTM latency	CTM amplitude
Mild ($n = 4$, $n = 2$)[a]	21.9 (17.7–26.1)	3939 (2716–5162)	37.6 (33.1–42.2)	2046 (360–3733)
Moderate ($n = 4$, $n = 2$)[a]	24.1 (19.8–28.4)	1245 (1.3–2490)	50.2 (44.9–55.5)	970 (–1,419–3360)
Severe ($n = 6$, $n = 2$)[a]	28.5 (25.1–31.8)	2299 (1334–3263)	51.9 (48–55.8)	284 (–2053–1484)
Mild vs. moderate[b]	0.489	0.010[c]	0.001[c]	0.478
Mild vs. severe[b]	0.042[c]	0.069	<0.001[c]	0.193
Moderate vs. severe[b]	0.253	0.206	0.618	0.808

Data are presented as mean (95% confidence interval).
[a] n = number of affected dogs categorized as having mild, moderate, and severe signs. For a given severity of neurological signs, the first n indicates the number of recordable TMMEPs from the ECRM, and the second n indicates the number of recordable TMMEPs from the CTM in the affected dogs.
[b] P values based on a linear regression model adjusted for age, gender, and weight.
[c] Indicates statistical significance, $P < 0.05$.

Table 3
Association between mean onset latencies (in ms) and peak-to-peak amplitudes (in μV) for transcranial magnetic motor evoked potentials (TMMEPs) recorded from the extensor carpi radialis muscle (ECRM) and cranial tibial muscle (CTM) and the severity of spinal cord compression recorded on MRI in 14 Great Danes with clinical signs of cervical spondylomyelopathy.

Severity of signs	ECRM latency	ECRM amplitude	CTM latency	CTM amplitude
Mild ($n = 1$, $n = 1$)[a]	18.8 (9.4–28.2)	5114 (2766–7462)	31.9 (22.4–41.3)	3502 (1155–5849)
Moderate ($n = 3$, $n = 1$)[a]	24.6 (18.9–30.2)	2161 (752–3570)	49 (42.5–55.6)	1665 (–852–4181)
Severe ($n = 10$, $n = 4$)[a]	26.6 (23.4–29.7)	2154 (1366–2941)	48.8 (45.2–52.5)	320 (–1069–1710)
Mild vs. moderate[b]	0.622	0.073	0.007[c]	0.570
Mild vs. severe[b]	0.387	0.061	0.003[c]	0.064
Moderate vs. severe[b]	0.563	0.993	0.956	0.353

Data are presented as means (95% confidence interval).
[a] n = number of affected dogs categorized as having mild, moderate, and severe spinal cord compression. For a given severity of spinal cord compression, the first n indicates the number of recordable TMMEPs from the ECRM, and the second n indicates the number of recordable TMMEPs from the CTM in the affected dogs. When $n = 1$, the mean and 95% confidence interval presented is the result of the eight TMMEPs (four from the right side, four from the left side) recorded for that given dog from either the ECRM or the CTM.
[b] P values based on a linear regression model adjusted for age, gender, and weight.
[c] Indicates statistical significance, $P < 0.05$.

which the TMMEP recordings are obtained (Konrad et al., 1987; Owen et al., 1989; Kraus et al., 1990; Nollet et al., 2002).

Moreover, no pelvic limb TMMEPs could be recorded in 7/9 CSM-affected GDs showing SC signal changes. Even if no statistical significant associations were found between the presence of SC signal changes and TMMEP latencies, the difficulty in recording TMMEPs from this subset of CSM-affected GDs is consistent with studies investigating the use of TMMEPs in people with cervical spondylotic myelopathy and SC signal changes (Lo et al., 2004). In one study, no TMMEPs could be recorded in 24/36 (67%) people with cervical spondylotic myelopathy and hyperintense T2-weighted SC signal changes, whereas absent TMMEPs were only found in 10/77 (13%) subjects with cervical SC compression but without SC signal changes (Lo et al., 2004). In this study, CSM-affected dogs with more severe SC compression and dogs with the presence of SC signal changes showed lack of recordable pelvic limb TMMEPs more often than those dogs with milder SC compression and normal SC signal. Hence, the lack of recordable pelvic limb TMMEPs suggests more severe SC involvement.

A limitation of our study is its small sample size. However, this was a prospective study with limited funds and time for subject enrollment. The prospective nature of this investigation allowed us to use a constant sedation protocol and TMMEP technique for all dogs enrolled. Various sedation protocols have been used to obtain TMMEPS in dogs (Sylvestre et al., 1992; Van Ham et al., 1994; Van Soens et al., 2009). We used a combination of an α_2-adrenergic agonist (dexmedetomidine) and an opioid (hydromorphone). Combined sedation protocols achieve better levels of sedation to obtain TMMEPs in dogs, and α_2-adrenergic agonists originate more profound sedation than other drugs (Van Ham et al., 1994; Van Soens et al., 2009). One study reported that a combination of medetomidine and methadone yielded longer TMMEP latencies and smaller amplitudes in dogs (Van Ham et al., 1994). In contrast, a more recent study compared the effects of medetomidine and acepromazine/methadone on canine TMMEPs and found no differences in latencies and/or amplitudes between the two protocols, concluding that both sedation protocols were equally valid and that the previously reported effects of α_2-adrenergic agonists on TMMEPs were probably due to the higher doses used in the first study (Van Soens et al., 2009). The dose of dexmedetomidine used in our study was similar to the medetomidine dose administered in this latter study by Van Soens et al. (2009).

While MRI of the cervical vertebral column is necessary to confirm the presence, extent, and location of SC compressive sites in CSM-affected GDs, the significant TMMEP latency differences found in this study between clinically normal and CSM-affected GDs, suggest that TMMEPs could be used as an initial screening test in GDs with clinical signs consistent with CSM before MRI is pursued. The use of TMMEPs can offer functional information about the status of the SC motor pathways, which cannot be obtained from the advanced imaging modalities routinely used to diagnose CSM. In CSM-affected dogs treated surgically, TMMEPs could be used as an objective outcome measure of the functionality of the SC motor pathways before and after surgery is pursued.

Conclusions

We report reference ranges for TMMEP latencies and amplitudes for clinically normal GDs. Both ECR and CT TMMEP latencies helped differentiate between control and CSM-affected GDs. In CSM-affected GDs, CT TMMEP latencies were significantly associated with the degree of neurological signs and the severity of SC compression on MRI. The use of TMMEPs is a valid ancillary test to assess the integrity of motor pathways in CSM-affected GDs.

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organizations that could inappropriately influence or bias the content of the paper.

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