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von Frey anesthesiometry to assess sensory impairment after acute spinal cord injury caused by thoracolumbar intervertebral disc extrusion in dogs

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ABSTRACT

Sensory threshold (ST) was measured using an electric von Frey anesthesiometer (VFA) in all limbs of 20 normal dogs and 29 dogs with acute thoracolumbar spinal cord injury (SCI) caused by spontaneous intervertebral disc extrusion. ST values were measured at three separate time points in normal dogs and on days 3, 10 and 30 following decompressive surgery in dogs with SCI. ST values were compared between groups and correlated with locomotor recovery in SCI-affected dogs.

ST values were significantly higher (consistent with hypoalgesia) in the pelvic limbs of SCI-affected dogs at day 3, day 10 and day 30 when compared to normal dogs ($P < 0.05$), while no significant difference in thoracic limb ST values was observed between groups. A progressive decrease in pelvic limb ST values occurred in SCI-affected dogs over time, consistent with improvement toward normal sensation or development of allodynia. This finding correlated inversely with locomotor score at 3 and 10 days after surgery. A significant decline in ST values across testing sessions was observed for all limbs of normal and SCI-affected dogs and may be related to patient acclimation, operator training effect, or effect of analgesic medications. This study supports the feasibility of VFA to assess differences in ST between normal and SCI-affected dogs. However, future studies must focus on techniques to minimize or compensate for clinical, environmental and behavioral factors which may impact ST values in the clinical setting.

Introduction

Acute spinal cord injury (SCI) is a common neurological problem in dogs (Olby et al., 2003). Despite the prognostic significance of diminished conscious pain perception in canine SCI, routine clinical evaluation of dogs with SCI has historically focused on locomotor scoring and only a crude assessment of the 'presence' or 'absence' of a behavioral response to a painful stimulus (Olby et al., 2001; Levine et al., 2009; Lascelles, 2013). Abnormalities in sensory processing such as allodynia and hyperesthesia are reported in up to 90% of human patients after SCI (Boldt et al., 2014). Sensory abnormalities have yet to be thoroughly explored in dogs with SCI, despite being repeatedly documented in rodent models of SCI and in the human clinical setting (Lindsey et al., 2000; Hayes et al., 2002; Carlton et al., 2009; Felix and Widerstrom-Noga, 2009; Densmore et al., 2010; Hoschouer et al., 2010).

Recent studies suggest that an electronic von Frey anesthesiometer (VFA) may prove useful in dogs as an objective mechanical quantitative sensory test (QST) (Moore et al., 2013; Briley et al., 2014). This technique has been used previously to assess hyperalgesia in dogs with orthopedic disease (Brydges et al., 2012), anti-nociceptive effects of analgesics (KuKanich et al., 2005a, 2005b; KuKanich and Papich, 2011), and to evaluate sensory threshold (ST) in a small number of dogs with acute SCI (Moore et al., 2013). ST in these studies has been defined as the strength of mechanical stimulus required to produce a conscious behavioral response to that stimulus. When assessing patients with SCI, increases in ST above baseline are generally interpreted to represent hypoalgesia while decreases in ST below baseline are representative of allodynia or hyperesthesia (Detloff et al., 2010; Moore et al., 2013).

The goal of our study was to explore the feasibility of VFA to measure differences in ST values between normal dogs and dogs with acute thoracolumbar SCI caused by intervertebral disc extrusion (IVDE) in the clinical setting. We also aimed to document how ST values changed in SCI-affected dogs over a 30-day period of neurological recovery. We hypothesized that pelvic limb ST values would differ between normal dogs and those with thoracolumbar SCI, while thoracic limb ST values would not. Based on our previous work, we also hypothesized that pelvic limb ST values in SCI-affected dogs would have an inverse correlation with improving locomotor scores, consistent with recovery of sensory function in the weeks following SCI.

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Materials and methods

The study was approved by the Ohio State University (OSU) Clinical Research Advisory Committee and the Institutional Animal Care and Use Committee (2012A00000149). Written owner consent was obtained prior to study enrollment.

Normal dogs

Twenty apparently healthy adult dogs were recruited from the OSU Veterinary Medical Center. Dogs had no prior history of neurological or orthopedic disease and were of a small breed (≤20 kg). All dogs were assessed to be neurologically and orthopedically normal based on examination by two of the investigators (RBS and SAM), with the exception that valgus and varus conformational limb abnormalities typical for chondrodystrophic breeds were considered acceptable for enrollment to facilitate generalization of our results across a realistic clinical population.

An electronic VFA device (IITC) was used for ST measurement in all four limbs. This device is composed of a load cell, a recording device, a handle, and a rigid 0.8 mm diameter plastic disposable tip. The one used for this study measured, stored and digitally displayed the maximum force applied to the limb between 0.1 and 1000 g during a test.

ST testing was performed in a quiet room with minimal traffic, as previously described (Moore et al., 2013). Testing order of the limbs was decided by a coin toss and recorded. Dogs were positioned in lateral recumbency and maintained in this position using minimal restraint. They were placed in left lateral recumbency for testing of the right-sided limbs and vice versa. The limb being tested was allowed to rest on the floor in a neutral position. For the pelvic limbs, the electronic VFA probe was applied perpendicular to the dorsal surface of the metatarsus, halfway between the tarsometatarsal and metatarsophalangeal joints between digits IV and V; this region lies within the cutaneous autonomous zone of the fibular branch of the sciatic nerve. For thoracic limbs, the electronic VFA probe was applied perpendicular to the dorsal surface of metacarpus, halfway between the carpometacarpal and metacarpophalangeal joints between digits IV and V; this region lies within the cutaneous autonomous zone of the radial nerve.

Dogs were prevented from visualizing the device during application to ensure behavioral responses were due to tactile stimulation (Detloff et al., 2010). Steady, progressively increasing pressure was applied until the dog displayed a behavioral response to the stimulus, regarded as a conscious response such as vocalization, or lip licking. This response generally occurred in conjunction with withdrawal of the limb, but not in all cases. Immediate withdrawal of the limb upon application of the probe before application of pressure was considered a reflexive movement or a product of proprioceptive input rather than a conscious response to tactile stimulus and was discarded and the stimulus repeated after 1 min (Kloos et al., 2005; KuKanich et al., 2005a; Detloff et al., 2010).

The evaluator (RBS) was blinded to the pressure readings obtained during testing. The minimum pressure required to elicit a behavioral response was recorded. The test was repeated five times in each limb, with each test separated by 1 min to avoid windup, ST decay, and hypersensitization (KuKanich et al., 2005b; Detloff et al., 2010, 2012). The highest and lowest ST values were excluded and the three middle values averaged to assign a single ST value to each limb (Moore et al., 2013). ST testing was repeated three times at least 48 h apart in all normal dogs.

Affected dogs

Twenty-nine adult dogs with acute T3-L3 myelopathy caused by IVDE were consecutively and prospectively enrolled from the general patient population at OSU Veterinary Medical Center. Dogs were eligible for enrollment if diagnostic testing (CT, CT and myelogram, or MRI) confirmed IVDE, and they weighed ≤20 kg. A subjective assessment of intact conscious response to pain stimulus, as assessed by both the attending clinician and the investigators, was required for enrollment. All dogs underwent surgical decompression for their IVDE. ST testing of all four limbs using the technique described above was performed at three time points: 3, 10 and 30 days after surgery. Each affected dog was also assigned a locomotor score by the investigators using the Olby Spinal Cord Injury Scale (OSCIS) (Olby et al., 2001) at each time point. Analgesic and/or anti-inflammatory medications were prescribed for all patients during the perioperative period with dosing at the discretion of the attending clinician. All medications that the subjects were receiving at the time of testing were recorded.

Statistics

Summary statistics including mean and standard error of the mean (SEM), or median and range where appropriate, are reported for clinical data on all dogs, and for ST values for all testing sessions. Normality of data was verified by the Anderson–Darling method. Data for ST values were compared across three testing sessions in normal dogs and in SCI-affected dogs using a mixed effect model, incorporating repeated measures for each subject (Verbeke and Molenberghs, 2000). Spearman correlations were calculated to assess the relationship between ST values and locomotor scores in SCI-affected dogs. A P-value of <0.05 was considered significant for all analyses. Analyses were conducted using SAS software.

Results

Normal dogs

Normal dogs ranged in age from 8 months to 6.5 years (median 3 years) and weighed between 3.7 kg and 17.2 kg (median 9.4 kg). There were eight spayed females and 12 castrated males. Breeds were as follows: mixed breed dogs (6), Dachshund (4), Miniature Schnauzer (2), Sealyham terrier (2), Beagle (1), Bichon frise (1), Cocker spaniel (1), Pembroke Welsh corgi (1), Miniature Pinscher (1), and Shih Tzu (1). Time period between testing sessions for each dog ranged from 2 to 27 days (median 6 days).

Affected dogs

A total of 29 dogs with acute SCI caused by IVDE were enrolled. Dogs ranged in age from 2 to 11 years (median 5 years) and weighed between 3.9 kg and 17.0 kg (median 8.0 kg). There were 14 spayed females, 13 castrated males, and two intact males. Breeds were as follows: Dachshund (12), mixed breed dogs (6), French bulldog (4), Beagle (2), Pembroke Welsh corgi (2), Shih Tzu (2), and Cocker spaniel (1).

All dogs underwent decompressive hemilaminectomy or pediculectomy at one or multiple sites between T10–11 and L3–4 intervertebral disc spaces, with or without one or more lateral disc fenestrations dependent on imaging results and discretion of the surgeon. Postoperative analgesic dosage and type was dependent on the surgeon's preference but included a fentanyl constant rate infusion for 12–24 h post-operatively, a fentanyl patch placed immediately post-operatively, and combinations of tramadol, gabapentin, methocarbamol, or diazepam. Post-operative anti-inflammatory therapy generally included tapering anti-inflammatory doses of prednisone or a non-steroidal anti-inflammatory drug (NSAID). The medication doses, frequency of administration, and number of total medications were recorded for each dog at each session.

von Frey anesthesiometry sensory threshold (ST) values of normal dogs

Mean ST values for normal dogs across three testing sessions are summarized in Table 1. Mean ± SEM sensory threshold values in grams for normal dogs across three testing sessions were as follows: 161.9 ± 14.8, 128.4 ± 11.7, 102.7 ± 10.0 (left thoracic limb – LTL); 145.7 ± 9.8, 116.5 ± 11.9, 94.8 ± 8.0 (left pelvic limb – LPL); 147.1 ± 11.6, 127.1 ± 9.0, 116.7 ± 9.0 (right thoracic limb – RTL); 142.8 ± 12.6, 121.4 ± 10.5, 100.6 ± 9.3 (right pelvic limb – RPL). A significant difference was not identified between ST values obtained from the LTL, RTL, LPL, and RPL of normal dogs between sessions 1 and 2 ($P = 0.18$, 0.43, 0.25, 0.39, respectively) or between sessions 2 and 3 ($P = 0.31$, 0.68, 0.39, 0.41). When comparing sessions 1 and 3, a significant decrease in session 3 was noted in ST values for the LTL ($P = 0.02$) and LPL ($P = 0.04$).

ST values differ in the pelvic limbs between normal and SCI-affected dogs

ST values obtained from SCI-affected dogs at three time points after injury are summarized in Table 2. Mean ± SEM sensory threshold values in grams for SCI-affected dogs at days 3,10, and 30 after surgery were as follows: 199.0 ± 15.6, 156.3 ± 12.0, 148.3 ± 10.1 (LTL); 349.6 ± 27.1, 254.7 ± 23.9, 205.6 ± 18.1 (LPL); 196.9 ± 20.2, 151.9 ± 11.7, 163.4 ± 11.0 (RTL); 356.9 ± 31.6, 235.6 ± 22.9, 214.5 ± 16.2 (RPL). ST values from the limbs of normal dogs at session 1 were compared to ST values from SCI-affected dogs at days 3, 10, and 30 (Fig. 1). ST values derived from session 1 were used for comparison as they