Review Article

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The Challenges of Assessing Osteoarthritis and Postoperative Pain in Dogs

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Abstract. The challenge of measuring pain in veterinary medicine is compounded by the lack of fully validated, reliable methods to measure and assess pain in nonverbal patients. In human medicine, there are numerous, validated pain assessment tools (PATs) for assessing various, specific types of pain. The advances in human medicine pain management and numerous validated pain scales should serve as incentives and templates to facilitate similar advances in the development of validated PATs for use in dogs (and other species). The limited number of canine PATs constrains our ability to adequately and reliably assess pain. Improving the ability to quantify osteoarthritis and postoperative pain in dogs would enhance the development of analgesics for animals, advance the management of animal pain, facilitate the use of animal pain models in preclinical trials for human analgesics, and provide insight into the quantification of pain responses in humans who lack the ability to adequately communicate. This review describes the need for practical, valid, and reliable PATs for use in veterinary patients and discusses some currently available PATs commonly used to evaluate acute and chronic pain in dogs.

KEY WORDS: pain assessment; veterinary pain scales.

INTRODUCTION

The majority of literature pertaining to the assessment of pain in dogs deals with the evaluation of postoperative (POP) pain and osteoarthritis (OA) pain. The currently approved drugs for treating pain in dogs reflect this fact, as the three common indications are for the control of postoperative pain, the control of pain associated with osteoarthritis, and for the control of dental pain. Although there are many types of pain, this article focuses on the pain assessment tools (PATs) used to assess POP (acute) pain and OA (chronic) pain. Discussion of the many types of pain and the physiologic mechanisms of pain are outside the scope of this article. Importantly, regardless of the type of pain being considered, veterinary pain assessments must be made in the absence of the communication skills of the patient.

The article compares some of the commonly used PATs used in veterinary medicine to the multitude of validated pain scales developed on the human side. Although this article focuses on the dog, it is important to improve the ability to recognize pain and to measure pain intensity in all veterinary species. The development of reliable, validated veterinary PATs can greatly contribute to analgesic drug development. Advances in the development of veterinary PATs could facilitate pain management options in animals, the use of

animal pain models in human preclinical studies, and could provide insight into potential paths for quantifying pain responses in nonverbal humans.

PAIN AND THE CHALLENGES OF ASSESSING PAIN IN VETERINARY MEDICINE

The International Association for the Study of Pain (IASP) defines pain as an unpleasant sensory and emotional experience associated with actual or potential tissue damage. In addition, the IASP states that the inability to communicate verbally does not negate the possibility that an individual is experiencing pain and is in need of pain relieving treatment (1). Being unable to express pain is an issue that pertains not only to animals but also to children (infants), the cognitively impaired and comatose patients (2–5). Therefore, as stated by Lord Kelvin in 1883, the ability to effectively treat pain (both in the animal and human patient) is dependent on how well pain can be measured (6).

Pain is not an uncommon occurrence in veterinary patients. Millions of dogs and cats are spayed and castrated each year, approximately 20% of the canine population will have chronic pain associated with osteoarthritis (7), and approximately 4 million dogs annually are diagnosed with cancer (8). The need to manage surgical pain may be obvious; however, there is also the need to alleviate the pain and suffering that may go unrecognized in chronic conditions (e.g., OA, cancer). Veterinary medicine strives to effectively recognize, measure, and manage pain as part of ongoing efforts to address the issue of quality of life in companion animals. As interest in the understanding of animal pain has

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increased over the last two decades so too has research in managing animal pain. In this regard, numerous scientific articles have discussed the importance of pain management and many veterinary organizations have adopted official position statements on the need to alleviate animal pain and suffering (9,10,14,16–18).

Pain is subjective, dynamic, and multidimensional. Pain dimensions include the physiologic aspect, sensory (quality and intensity of pain), cognitive, behavioral, affective (mood, socialization), and social/cultural aspects. There are varying types of pain in humans and animals such as neuropathic (*e.g.*, post-amputation pain and postherpetic neuralgia [people]), maladaptive, dysfunctional, nociceptive, and inflammatory pain (surgical tissue damage). Additionally, pain may be of short duration (postoperative pain that resolves) or long term; superficial or deep, and somatic or visceral (*e.g.*, inflammatory bowel syndrome) in origin. The different mechanisms and manifestations of pain are complex; and unlike humans, animals cannot be comforted by the knowledge that pain will subside or improve. Therefore, creating a means by which to quantify pain is complicated, often involving the use of different PATs for assessing different types of pain and different dimensions of pain.

Although neurophysiologic research to characterize nociception and pain perception has advanced the understanding of animal pain, the ability to recognize and measure pain remains a fundamental obstacle to effectively managing pain (11). Assessing pain in animals is complicated by survival characteristics; dog and cats mask their pain as a protective mechanism, such as a dog experiencing pain may still wag its tail (12). Nevertheless, along with a thorough veterinary examination to locate, characterize, and diagnose the type of pain, the absence of normal behavior is often the best indication of pain in dogs. The latter is complicated by changes in a dog's normal behaviors that can be influenced by an altered environment, such as being in the hospital. Additionally, there are species, age- and breed-related differences to be considered where some dog breeds tend to be more stoic or more vocal.

Most human patients can describe their pain and intensity of pain. In veterinary medicine, accurately assessing pain is challenging as animals cannot communicate their perception or intensity of pain. Therefore, when direct communication is not feasible, an understanding of what constitutes “normal” animal/human behavior in the individual patient is an essential consideration. The activities and demeanor of the dog are commonly assessed to determine an overall interpretation of pain (similar to human patient global assessments). In this regard, assessing pain in dogs is similar to assessing pain in neonates, the cognitively impaired or nonverbal humans where the assessment of pain depends upon observer interpretation. Indicators of pain may be subtle and nonspecific (*e.g.*, inappetence, quiet demeanor) and therefore, may be overlooked by the observer, especially if the observer is unfamiliar with the animal (*e.g.*, a cageside assessment of a pet in a hospital setting).

Usually, pain assessments are based on the knowledge of an animal's “normal” *versus* “abnormal” behaviors (*e.g.*, the presence of lameness, slow gait, and a reluctance to perform activities typical of that dog). In infants, children, and animals, such assessments can be very challenging because

they depend upon the assessments of the parent or the pet owner. In this regard, qualitative similarities have been described between the pain assessments of pet owners and those of a parent or caregiver (13,14). Because of their inherent knowledge of what constitutes “normal” behavior for that individual, pet owner input is invaluable, especially as it pertains to chronic OA pain (14,15). Behavioral changes can be species-specific, injury-specific and influenced by the environment, or the time of day (16,17). Therefore, the home environment offers a comfortable setting for evaluating a pet's behaviors as compared to the challenge of determining if anxiety and stress are pain-related behaviors or related to the hospital setting (15).

Although owner evaluations are subject to the placebo effect, owners succeed in offering insight into the dog's behaviors in a natural setting, such as going up or down stairs, eating, grooming, ability to jump in the car, difficulty in rising, and inappropriate urination or defecation (18). For this reason, clinical effectiveness studies used to seek regulatory approval of new animal drugs for the control of pain associated with OA in dogs (19–22) have commonly included owner evaluations, which utilizes “actual conditions of use” (how the drug will be used in the general, target population).

THE NEED FOR VALIDATED PAIN ASSESSMENT TOOLS

Evidence-based pain management is dependent upon the ability to detect pain in dogs, and if affected, distinguish change in their mobility, daily activities, and normal behaviors *via* validated, sensitive pain assessment tools. In this regard, validated pain scales offer reliable methods for veterinarians/owners to assess pain and quantify changes in pain intensity. Due to the subjective and observational nature of many PATs, validated and reliable pain scales are essential to assure the usefulness of the measure to indicate pain or predict a dog's function or quality of life. Validated PATs offer the ability to repeatedly measure pain outcomes in the individual patient and across groups (*e.g.*, dogs with OA pain compared to dogs without OA pain). The use of validated PATs can provide the basis by which the effectiveness of pain therapies and new animal analgesics could be determined.

The subjective nature of assessing pain in dogs makes obtaining useful, reliable, nonbiased, and repeatable data difficult. It is essential to have scoring methods that allow for reduced variability between various users and across multiple hospital settings. Veterinary medicine needs well-defined, standardized specific outcome measures for acute and chronic pain; whereby the subjective scoring scale correlates to an objective measurement with established clinical relevance.

Psychometric instruments like health-related quality of life (HRQOL) questionnaires are PATs created by people and interpreted by people. A HRQOL questionnaire, although subjective, provides a way for the person most familiar with the pet (*e.g.*, the owner) to provide insight into the dog's abilities in the home environment, once the owner is educated on the use of the PAT. Therefore, PATs should possess the important psychometric properties of validity and reliability in order for a pain measurement to accurately quantify pain. For example, a quality of life (QOL) questionnaire should utilize words that are clear and commonly

interpreted across owners. In order to demonstrate that a PAT actually measures the pain variable(s) described, multiple studies and multiple users are needed to ensure that the scale can be successfully used in a clinical setting. Various PATs differ in the specific signs and types of tools used to generate the pain assessment. There are different levels of measuring pain when considering the abilities of a PAT: (1) the absence or presence of pain, (2) quantifying the severity of pain, and (3) and establishing equal intervals used to distinguish between each measured value (23). Not one ideal PAT exists for use in assessing all types of pain. However, ideal PAT characteristics include: the ability to detect change (sensitive), ease of scoring or administration, applicability across multiple languages, ease of data interpretation, and the need for minimal (or inexpensive) equipment to facilitate their use in a veterinary practice setting.

Furthermore, the PAT should demonstrate evidence of repeatability/reliability, responsiveness, and content (face) validity, construct validity, and criterion validity. Responsiveness is the ability to detect change over time and reliability means the scale lacks measurement error, has internal consistency, and intra- and inter-observer reliability (24). Internal consistency is essential when the scale utilizes a sum of categories to provide a total score (25). Additionally, a fully validated PAT for use in dogs would demonstrate that a measure assesses a specific domain or construct (construct validity), comprehensively captures the clinically relevant aspects of that type of pain (content validity), and correlates with another accepted, external measurement of the same type of pain (criterion validity) (26).

All PATs have inherent advantages and disadvantages, and no single PAT can measure and evaluate all dimensions (*e.g.*, pain intensity, behavior changes, quality of life, and functional ability) of a specific type of pain (*e.g.*, POP pain OA pain). In veterinary medicine, there is no gold standard for assessing acute or chronic pain or response to pain treatment. However, the use of a validated PAT that measures one or more clinically relevant pain dimension can offer potentially far greater insight into pain management and drug effectiveness than those obtained when using scales that have not demonstrated the significance of the measured outcome. Without validation, a PAT may only be measuring a preconceived concept of what pain looks like in dogs.

EXAMPLES OF VETERINARY AND HUMAN PAIN ASSESSMENT TOOLS

There are numerous PATs available in human medicine for use in assessing a variety of pain conditions (*e.g.*, OA, POP, cancer, neuropathic, and AIDs). Pain scales have also been developed to assess pain in the human fetus, infants, and children, and in cognitively impaired children and adults, and in disorders of consciousness (27,28). A recent literature review described over 80 different pain and HRQOL tools used in human medicine (29). A few examples of the variety of PATs used in human medicine are listed in Table I.

Standardized and validated human subjective scoring methods, such as the Likert (a unidimensional method;

Table I. Examples of the Variety of Human Pain Scales

McGill Pain Questionnaire
Rheumatoid Arthritis Severity Scale (RASS)
Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index
Lequesne Index (hip and knee versions)
Children's Hospital of Eastern Ontario Pain Scale
Douleur Neuropathique 4 (DN4)
Pain Assessment in Advanced Dementia (PAINAD)
Abbey Pain Scale (Abbey PS)
Discomfort Scale-Dementia of Alzheimer Type (DS-DAT)
Neonatal Infant Pain Scale
Wong-Baker Faces Pain Scale—Pediatric Use
Pediatric Outcomes Data Collection Instrument (PODCI)
Toddler–Preschooler Postoperative Pain Scale

commonly a 5-point scale) or Visual Analog Scoring (VAS; a 100 mm horizontal line anchored by descriptors “no pain” at one end and “worst pain” at the other) have been developed to “grade” one’s perceived level of pain (30). In human medicine, studies have demonstrated the reliable use of VAS scales in clinical settings. Thus, the VAS is often referred to as a “gold standard” method for assessing chronic and acute pain in humans and is a common research PAT (31,32). Additionally, human medicine has defined the change in VAS score that depicts the level at which human patients perceive adequate pain control, known as the minimum clinically important difference for pain intensity (33–35). For example in human OA clinical trials, commonly used criteria have been established for defining clinically relevant change in patients using VAS scores (36). The Osteoarthritis Research Society International response criteria use a 20% improvement in VAS score as a cutoff for clinically relevant improvement (high response) in a patient’s response (37). This allows each study participant to be individually determined as a treatment responder or not.

Similarly, veterinary medicine uses subjective methods such as the VAS, numerical rating scales (NRS), and simple descriptive scales (SDS). These are unidimensional methods that often rely on behavioral signs. Because subjective scales have the inherent risk for observer bias and lack sensitivity (38), VAS, NRS, and SDS are prone to interobserver variability, and erroneously imply that equal distances between scores on the scale denote equal distances in the dimension being measured (39).

Unfortunately, the degree of standardization and validation that has been reported for PATs in human medicine has not been established for those used in veterinary medicine. For example, in veterinary medicine, the criteria for what constitutes the minimum clinically important difference for pain intensity have not been established when using a VAS scale. Therefore, in clinical pain studies, VAS have not been used to determine each individual dog as a successful responder, as a clinically relevant change has not been established. Instead, most veterinary pain studies using a VAS compare mean differences in VAS values across treatment groups. This leads to a risk of small improvements in mean VAS scores between treatment groups that demonstrate statistical significance without a corresponding clinical relevance (40). In this regard, when group mean VAS scores are compared in veterinary studies, classification of each dog

as a treatment responder or nonresponder does not occur; hence, the failure to establish clinical relevance on an individual basis. NRS, while used to assess veterinary pain, are often not designed and validated to measure the psychological effects (the pain experience) such as anxiety, stress, or mood. Therefore, subjective NRS, which are unvalidated and lack sensitivity, may not provide a reliable outcome measure (41,42).

Veterinary assessments of OA pain commonly involve the use of a lameness score—where lameness refers to a deviation in the normal gait of an animal (43). An example of a veterinary SDS for assessing overall lameness (scored at a walk and a trot) might describe the patient at various time points as either: no lameness, mild lameness, moderate lameness, severe lameness, or exhibiting nonweight-bearing lameness. Using a SDS such as this may be useful in assessing acute pain associated with surgery; however, these lameness scores may not reflect the lameness typically seen in dogs with OA (*e.g.*, nonweight-bearing lameness is associated more readily with fractures than OA). Additionally, such lameness scales do not necessarily establish a correlation between the degree of lameness and severity of pain. Furthermore, studies have shown a lack of correlation between veterinary lameness assessments and owner assessment for OA (19,44).

Western Ontario and McMaster Universities Osteoarthritis Index

The measurement of pain and the evaluation of a patient’s functional capability are often interrelated when assessing pain. Due to the overlap in the measurement of function and the evaluation of pain, self-reported questionnaires were developed for use in human medicine. Examples include the Lequesne Index and the Western Ontario and McMaster Universities (WOMAC) Osteoarthritis Index used to assess chronic pain, function, and stiffness of the human knee and hip (45). The WOMAC Index is a patient-reported questionnaire utilizing 24 items grouped into three dimensions: pain, stiffness, and physical function (46). The WOMAC Index questionnaire comes in various formats (Likert, VAS, and NRS) (47). Similarly, the Lesquesne Index questionnaire is a composite measurement score of 11 items assessing pain in bed, morning stiffness, walking, standing 30 min, sitting for 2 h, maximum walking distance, use of a walking aid, putting socks on, picking an object up off the floor, doing stairs, and getting in and out of car (48).

In veterinary medicine, similar questionnaires have been used to evaluate pain, function, and QOL based on the observations of the veterinarian and/or owner (49). Lameness is often used as a measure of function and pain assessment; however, lameness is only one aspect of pain. Lameness may also be due to a mechanical deficit that may not be contributing to pain. Likewise, pain may affect a pet’s QOL, but it can be difficult to determine the effectiveness by which quality of life questionnaires measure pain.

Client-Specific Outcome Measures

The client-specific outcome measures (CSOM) is a questionnaire method for evaluating OA pain by assessing

the daily activities and specific activity impairments for an individual dog as identified by the owner. The process of determining the specific activity impairments to assess involves interviewing the owner and identifying behaviors and activities that have changed for the dog. Examples may include: playing with other animals, difficulty moving after rest, difficulty moving after major activity, trotting, urination, getting in and out of the car, and jumping onto furniture. When using a CSOM, the individual dog acts as his own control (comparing before and after pain medication administration). Owners specifically indicate both places and times when they observe impaired activities, *e.g.*, “climbing stairs last thing at night” or “getting in and out of the minivan in the morning”. Owners then rate the degree of impairment. Use of this method has demonstrated that owners were able to assess differences in their pet’s mobility when an analgesic was administered compared to a placebo (50). The use of CSOM has been shown to be a sensitive method for use in the pain management of dogs (51).

Canine Brief Pain Inventory

Another veterinary-developed questionnaire is the Canine Brief Pain Inventory (CBPI). This owner-completed questionnaire developed to measure OA pain, has also been used to measure cancer pain in dogs (18,52,53). The CBPI questionnaire asks owners to: (1) rate the dog’s pain at its worst, its least, on average, and at the current moment and (2) rate the dog’s activity level and quality of life. The CBPI provides a useful means to evaluate pain in an individual dog and can discern differences between normal and OA dogs.

The CBPI is similar to the Brief Pain Inventory (BPI) used in humans (see Table II), the latter having been validated in multiple languages (54,55). The BPI is a reliable, valid, multidimensional pain index for measuring human OA

Table II. Comparison of the Canine Brief Pain Inventory to the Brief Pain Inventory

CBPI (canine) (53)	BPI (human) (56)
Owner (proxy) assessment	Self-assessment
2 Factors	2 Factors
Pain severity	Pain intensity
Interference with function	Interference with function
11-Item questionnaire	11-Item questionnaire
Pain	Pain
1. Worst pain	1. Pain now
2. Least pain	2. Average pain
3. Average pain	3. Worst pain
4. Current pain	4. Least pain
Function	Function
5. General activity	5. General activity
6. Enjoyment of life	6. Mood
7. Ability to rise to standing	7. Walking ability
8. Ability to walk	8. Normal work
9. Ability to run	9. Relations with other people
10. Ability to climb stairs	10. Sleep
11. Quality of life	11. Enjoyment of life
Evaluated for use in dogs with OA and bone cancer (53)	Evaluated for use in humans with OA (56), chronic nonmalignant pain (55), cerebral palsy (57), and cancer pain (58)

and cancer pain as a patient self-assessment tool based on the factors of severity of pain and impact of pain. It includes 11 numeric ratings to evaluate activity, pain intensity, mood, work life, relationships, sleep, and quality of life. Similarly, the pet owner-completed CBPI is based on ten questions aimed at quantifying the severity of pain and how that pain interferes with the dog's normal activities. Although the CBPI has not currently been validated against an objective measurement, the ability of the CBPI to detect a significant difference in scores between dogs receiving a nonsteroidal antiinflammatory drug or a placebo treatment has been demonstrated (18).

Helsinki Chronic Pain Index

The Helsinki Chronic Pain Index (HCPI) was developed as a multifactorial, descriptive questionnaire for assessing chronic pain in dogs. The HCPI is an owner-completed PAT which is based on 11 questions tested in dogs with radiographic and clinical signs of OA (59). Within the HCPI, the answers to each question are based on a five-point descriptive scale. Owners assess their dog's attitude; level of play; willingness to walk, trot, and jump; vocalization; ease of lying down and standing, and activity level after rest and following exercise. In a study using 61 client-owned dogs, the owner-completed questionnaire was compared to the owner's assessment of lameness using the combination of a VAS and their assessment of their pet's overall QOL (59). Psychometric testing of the HCPI (in Finnish language) to evaluate reliability and content validity has also been studied (14,59).

Glasgow University Veterinary School Questionnaire

The Glasgow University Veterinary School Questionnaire (GUVQuest) is a questionnaire for use in dogs with chronic OA pain to measure the affective responses of dogs. The GUVQuest is based on 12 weighted factors and the relationship of these factors to behavioral domains such as activity, comfort, appetite, extroversion-introversion, aggression, anxiety, alertness, dependence, contentment, agitation, posture and mobility, and compulsion. Studies evaluating content and construct validity have demonstrated that the GUVQuest is a useful method that discriminately measures chronic pain due to canine degenerative joint disease (60,61).

Liverpool Osteoarthritis Clinical Metrology Instrument

The Liverpool Osteoarthritis clinical metrology instrument is an additional PAT for use in evaluating dogs with elbow OA. The questionnaire included three main groups of questions covering an overall assessment by the owner of the activity patterns, wellbeing, and function of the dog (62).

Glasgow Composite Measures Pain Scale

Veterinary questionnaires have also been developed for assessing acute postoperative pain (POP). The Glasgow Composite Measures Pain Scale (GCMPS) is a multidimensional, subjective pain scale for use in dogs to assess acute pain in a

hospital setting. The GCMPS was developed at the University of Glasgow and incorporates an observer assessment of the dog while in the cage, upon opening the cage (to assess the dog's ability to rise and walk), upon surgical site palpation, and an overall pain assessment. The scale was developed using the same psychometric methodology as that employed in the McGill Pain Questionnaire for human medicine, providing a composite score based on seven behavioral categories (see Table III) with precise definitions of the descriptors (63,64). The GCMPS is divided into equal intervals, thereby enabling the severity of pain to be quantified based on a total score of the equally weighted categories (interval weighted) (65). The scale enables the practitioner to assess acute pain associated with multiple types of orthopedic and soft tissue surgical procedures and various medical conditions (65).

Glasgow Short Form

To increase the practicality of the GCMPS in a clinical setting, a shortened form was developed. The simplified Short

Table III. Comparison of the McGill Short Form Questionnaire and the GCMPS-SF

McGill Short Form (64)	Glasgow CMPS-SF (67)
Total of 15 descriptors	Total of 7 categories
11 Sensory descriptors and 4 affective descriptors (each individually ranked on intensity as: none, mild, moderate, or severe)	Based on observations of the dog's behavior
Throbbing	Demeanor
Shooting	Aggressive, depressed
Stabbing	Uninterested
Sharp	Nervous, anxious, fearful
Cramping	Posture
Gnawing	Rigid
Hot-burning	Hunched
	Normal
Aching	Comfort
Heavy	Uncomfortable
	Comfortable
Tender	Vocalization
Splitting	Cry
Tiring, exhausting	Groan
Sickening	Scream
Fearful	Quiet
Punishing, cruel	Attention to surgical wound
A Present Pain Intensity (6 points, NRS of no pain, mild, discomforting, distressing, horrible, excruciating).	Chewing
A VAS scale (100 mm line anchored by "no pain" or "worst possible pain")	Licking, looking, rubbing
	Ignoring
	Mobility
	Refuses to move
	Stiff
	Slow, reluctant
	Lame
	Normal
	Response to touch
	Cry
	Flinch
	Snap
	Growl, guard
	Do nothing

Form uses substitution of a rank instead of calculated interval weights, thus becoming a behavioral NRS that utilizes psychometric principles and interval level scaling (66). The Glasgow Short Form (CMPS-SF) is a questionnaire based on five sets of behavioral categories that evaluate the dog's spontaneous behavior, interactive assessment of mobility and response to touch, and the observer's overall impression of the dog's posture and activity.

The Short Form has been tested at multiple university veterinary hospital settings, resulting in consistent statistical differences in scores across multiple hospital sites (66,67). The use of this scale facilitates comparison of scores across time and across different clinical investigator/hospital sites, as well as a means to quantify individual pain and assess pain management.

This scoring system provides a clear, repeatable format that the observer may use to identify specific behaviors using set definitions, thereby reducing bias, interpretation, and interobserver variability. In addition to its use as a means to quantify individual pain and assess pain management, the CMPS-SF provides an intervention score, which defines when additional analgesia should be considered (66). Furthermore, since each individual composite score enables the veterinarian to determine if analgesia was sufficient on a single-patient basis (rather than providing a mean change in score across treatment groups); the CMPS-SF can be of value as a tool for evaluating the effectiveness of a new drug product in a postoperative setting. As the CMPS-SF is used in more clinical studies, the generalizability and validity under actual conditions of use will be further elucidated. A comparison of the McGill Short Form and the CMPS-SF is represented in Table III.

University of Melbourne Pain Scale

The University of Melbourne Pain Scale, used to assess POP in dogs, is based on the assessment of six categories (68). The categories include objective physiological data (e.g., respiratory rate, heart rate, pupil dilation, salivation, and rectal temperature), response to palpation, activity, mental status, posture, and vocalization. Each of these six categories is further divided into subcategories that are assigned individual numerical weights. The physiologic assessments are based on the differences between presurgical and postoperative values.

When assessing a dog's postoperative pain, the observer chooses the most applicable single descriptor for each of the six categories. Similar to the Children's Hospital of Eastern Ontario Pain scale developed by McGrath *et al.* 1985 (69), each descriptor has a numeric score. The physiological data descriptors include defined ranges for increases in heart rate and respiratory rate with higher scores being assigned to larger increases in postoperative heart and respiratory rates compared to presurgical values. However, this assigned scoring assumes that the increases in these physiologic parameters are specific and direct indicators of pain intensity, which is a correlation that has not been established in dogs (70,71).

Objective physiologic measurements such as increases in heart rate and respiratory rate, increased mean arterial blood pressure and pupil dilation, and increased plasma cortisol

concentrations have not been demonstrated as sensitive demarcations between nonpainful and painful animals (dogs and cats) as a means to assess severity of pain (70–72). These changes in physiologic measurements are not specific pain indicators and may also be associated with physical exertion, fever, and anxiety (73). Similarly, although increased changes in physiological parameters have been shown in children in pain, no correlation in children between improved pain scores and changes in respiratory rates, heart rates, or blood pressure has been demonstrated (74).

Various levels of validation testing have been researched for the function and/or QOL questionnaires discussed. For example, the content validity, reliability, and responsiveness of the CBPI and HCPI have been evaluated (18,52,59) and the content and criterion validity, responsiveness, and reliability of the Liverpool Osteoarthritis questionnaire have been studied (59). Additional work is needed to continue validation of the PATs used in veterinary medicine to determine their reliability and responsiveness when used in other studies, by individuals not familiar with the development of the tool, and when used in various languages to improve their comprehensive use.

Gait Analysis

In addition to the subjective PATs and the objective physiological parameters noted, other objective methods have been used to facilitate the assessment of pain in dogs and to aid in the validation of subjective measures. Gait analysis is commonly used in research settings as an objective methodology to evaluate limb motion. Force plates, pressure sensitive walkways, treadmills, and digital optoelectronic systems have led to advancements in canine gait analysis research (75–77).

Force plates are a non-invasive method for objectively evaluating lameness in dogs. A force plate can evaluate the degree of canine lameness through the use of a computerized sensor plate that monitors dog movements for repeated measures of ground reaction forces (kinetic data). Multiple passes across the force plate are required in order to measure various ground reaction forces from all four feet (78). Pressure mat walkways provide objective visual graphics of the distribution of individual paw pressure as the dog walks across pressure sensors in the mat (spatiotemporal gait analysis; kinetic data) (79). The advantage to using a pressure mat walkway is that it enables the investigator to obtain data from all four feet without the need for repetitive passes (77,80). Force plate data have been used in assessing gait and time to return to normal function of the affected limb following surgery in dogs (82). Studies have also demonstrated the use of force plate and kinematic data to evaluate gait in OA dogs (75,83,84).

Although gait analysis offers repeatable, objective methods to obtain quantitative measurements of limb use (85), force plate data may be difficult to interpret in the presence of multiple arthritic joints. In the presence of multiple limb involvement, force plate data can help in the detection of changes in lameness but not stiffness. Furthermore, these objective measures cannot provide information on the pet's ability to jump/rise, activity level, reluctance to

run, play, aggression, or its withdrawn behavior (75). This can be a limitation of gait analysis when assessing pain since the dog may have limb pain but not show limb disuse. The dog may redistribute gait forces to compensate for the lameness (86). Additionally, changes in limb use may not denote pain or intensity.

To date, incremental improvements in dog gait measures (e.g., peak vertical force and vertical impulse) that correspond to a clinically recognizable improvement in the individual patient have not been established. Many interrelated measurements may be evaluated during gait analysis, but not one measurement provides a complete description of gait (81,87,88). Force plate data may show subtle changes that are not noticed clinically (83). Conversely, a positive response to treatment using clinical assessment without a corresponding treatment effect in force plate analysis has also been shown (89). Studies have concurrently assessed musculoskeletal pain using various subjective lameness scales and force plate data. However, there is lack of agreement among study findings on a correlation between force plate data and subjective lameness scores, likely due to the differences in what these tools are measuring (90–92).

Although commonly used in research and referral facilities, gait analysis instrumentation is often not practical as a clinical diagnostic tool in most veterinary hospitals due to expense, space requirements, equipment maintenance, and the need for technically trained personnel. Variables associated with gait analysis data include the need for repetitive passes, use of multiple handlers, interday comparisons, the different types of equipment used, and the size and velocity of the dog (77,79,93,94).

Accelerometers

Other objective methods used in veterinary research include the use of non-invasive, portable accelerometers. The use of accelerometers and pedometers in human research is in its infancy (95,96). Recent advancements in technology have led to the development of inexpensive, miniature accelerometers (97). An advantage to utilizing such equipment in the assessment of chronic pain in dogs is its potential to objectively evaluate active movement in the home environment, facilitating the generation of reliable mobility information. Osteoarthritis studies have incorporated the use of a small, sensitive, and omnidirectional accelerometer to measure daily activity in dogs (17,98). However, before these quantitative devices can be used in clinical veterinary studies to evaluate analgesics, additional research is needed to assess their performance across breeds and ages of dogs, to establish a correlation between activity and pain, and determine what degree of increased activity translates into a clinically relevant, significant improvement in pain.

Additional research is needed to establish a correlation between force plate data and subjective pain evaluations. Additionally, veterinary medicine could benefit from establishing criterion validity of HRQOL questionnaires by use of objective measurement tools, such as gait analysis and activity monitors (88). Clearly, continued research that explores the correlations between function and QOL questionnaires, gait analysis, and activity monitor data is needed to advance the development of reliable PATs.

REGULATORY PERSPECTIVE

Pain management is critical to animal welfare and to the availability of safe and effective pain medications for use in animals is crucial to protecting the health of animals. The development of these therapies is necessary to enhance pain management for various types of pain (e.g., postoperative pain, chronic conditions) in pets and farm animals.

For a drug to be approved by the Center for Veterinary Medicine (Food and Drug Administration) for use to control pain in dogs, a drug company is required, among other things, to demonstrate substantial evidence of effectiveness in the target population under sections 512(d)(1)(E) and (d)(3) of the Federal Food Drug and Cosmetic Act. Substantial evidence of effectiveness for new animal drugs is defined in Title 21, section 514.4, of the Code of Federal Regulations (21 CFR §514.4). Drug companies are required to submit effectiveness data that is generated from well-controlled studies in order to distinguish the effect of the new animal drug from other influences, such as spontaneous change in the course of the disease, normal animal production performance, or biased observation (21 CFR §514.117(a)). Data submitted in support of substantial evidence of effectiveness for a new animal pain drug must permit qualified experts to conclude that a pain drug will have the effect it purports or is represented to have under the conditions of use suggested in labeling (21 CFR §514.4(b)(3)(i)(C)).

One or more adequate and well-controlled studies are required to establish substantial evidence and provide inferential value that a new animal drug is effective. The effectiveness study is intended to demonstrate that the drug is effective for the intended use and associated conditions of use (21 CFR §514.4(b)(2)). The study should be of sufficient quality to permit qualified experts to determine that the parameters selected for measuring (pain) and the measured responses reliably reflect the effectiveness of the drug, and to determine that the study results are likely to be repeatable and that valid inferences can be drawn to the target population (21 CFR §514.4(b)(3)). The effectiveness study is typically a multicenter, multi-investigator design intended to evaluate the product in an environment that represents the broader population, thus providing the best prediction of how the drug will perform once approved. New drug approval is based on, among other factors, controlled evidence demonstrating effectiveness and an overall risk–benefit assessment.

In human OA drug trials, valid OA measurements are critical to good trial design (99). Hopefully, the development of validated PATs will provide valid osteoarthritis and postoperative pain measurements for use in assessing new veterinary drugs. Unfortunately, there is no consensus in veterinary medicine on the amount of pain relief that is considered clinically significant (that correlates to a clinically significant improvement) (100). Many types of pain scales are used for assessing pain; both objective and subjective scales have degrees of variability and sensitivity, thus not one scale acts as an all-encompassing PAT. Ideally, a PAT's measurement properties should be established prior to use in clinical drug trials in support of approval (99).

CONCLUSION

Validated pain scales that demonstrate reliability and responsiveness are essential to the recognition and

management of pain in dogs. There is a need for standardization or consensus on the degree of reduction/increase that would be considered clinically significant when using individual pain scales for assessing pain in dogs. Advances in animal pain management could benefit from the collaboration of pharmaceutical industry, academia, veterinary practice, and drug regulatory authorities *via* a pain consortium to promote this area of veterinary medicine.

While veterinary pain assessment is advancing, ongoing studies are needed to investigate the use of PATs and to establish correlations between objective and subjective measurements. Practical, repeatable PATs are necessary for evaluating clinically significant changes. Ultimately, such reliable, valid PATs would greatly facilitate the assessment of animal pain, aid veterinarian decisions regarding therapeutic interventions, and support the development of new animal drugs for the control of pain and the use of the dog as a naturally occurring pain model for the development of new human pain therapeutics. The recent advancements in the development of acute and chronic pain assessment tools for use in dogs will hopefully lead to the development of similar PATs for use in cats, horses, and farm animals.

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