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Editorial

Introduction

The Association of Veterinary Anaesthetists' Spring Meeting 2017 took the theme 'Chronic Pain' and, to mark the occasion, the editors of *Veterinary Anaesthesia and Analgesia* (VAA) suggested publishing an online supplement. The brief was to compile a selection of papers published in VAA, relating to the assessment of chronic pain.

Chronic pain is more than persistent acute pain. Whereas acute pain can be considered 'adaptive', enabling an animal to avoid further injury and promote healing, chronic pain is 'maladaptive' and there is no benefit to the animal. Chronic pain has been described as a disease condition (Siddall & Cousins 2004), with changes to the structure and function of the peripheral and central sensory nervous systems. There is no single step marking the transition from acute to chronic pain, and the process is considered a continuum. For a review of the mechanisms involved, see Kuner & Flor (2017).

At first glance, selecting a portfolio of manuscripts published in VAA and relevant to chronic pain appeared to present a challenge. VAA has a long history of publishing clinical research, but much of the archive content relates to anaesthesia, acute pain and the assessment of analgesics. However, on browsing the VAA archive, one discovers a number of early papers acting as 'signposts', reviewing the body of knowledge at the time of writing and recognizing fertile areas for research.

One such review (Molony 1984) was published a month after central sensitization was first reported by Woolf (1983). Molony described pain as being more than nociception and discussed the sensory, emotional and cognitive contributions to the pain experience. Subjective methods of pain assessment were discussed where inferences were drawn from observing animals' behaviour, but the author noted the need for valid assessment tools in nonverbal humans and animals. The relative merits and flaws of different objective parameters to assess pain were also outlined, e.g. physiological data, posture, vocalizing, changes in cognition and motor skills. This manuscript provided our inspiration to find papers published in VAA addressing some of those questions posed by Molony and summarizing the current state of veterinary chronic pain assessment and treatment.

Assessment of chronic pain

Livingston (1994) reviewed developments in the understanding of pain mechanisms, from nociception, the 'gate theory', the discovery of descending inhibitory mechanisms and neuronal plasticity and the difficulties of pain assessment in animals. The current view of pain assessment in people focuses on a convergence of biologic, behavioural, and self-report measures. In people, the 'gold standard' for assessment is self-report, or 'pain is what the patient says that it is and exists whenever he or she says it does' (McCaffery & Pasero 1999). Yeates (2015) reviewed some of the challenges in this process of subjective appraisal of pain or quality of life (QoL) in animals, but many pain assessment tools have been developed and validated, based on the premise that in veterinary species 'pain is what the patient expresses that it is'. Although the use of pain assessment tools to identify acute pain (e.g. Reid et al., 2005) is well established in small animal practice, there are potential obstacles to their widespread use. For example, Catanzaro et al. (2016) reported that 74% of surveyed Italian veterinarians did not use pain scoring, possibly due to the lack of time, or perhaps the assessment tools were not regarded as easy to use in the clinical setting. The development of online tools, used by owners in their homes, may increase compliance and usefulness of QoL data (Reid et al., 2018).

Supraspinal influences and behavioural assessment

Emotional and cognitive influences on pain affect the perception of pain and pain assessment in people and animals. Väisänen et al. (2005) showed physiological and behavioural parameters in healthy dogs could be affected by apprehension and stress in the clinical environment, reducing the validity of their measurement as a means of assessing pain. Further evidence for the supraspinal effect on pain was reported by Nalon et al. (2016), who proposed that mechanical nociceptive thresholds in sows were reduced by hunger. Pain has also been assessed in horses by identifying abnormal behaviours (Price et al., 2003) and also alterations in facial symmetry (Gleerup et al., 2015).

Gait and mobility

Assessment of mobility and gait can inform clinicians whether a treatment is effective, for example the use of accelerometers to measure activity in cats (Lascelles et al., 2008) and force-plate analysis to assess gait, as a method of assessing pain relief in elderly cats with osteoarthritis (Monteiro et al., 2016).

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Quantitative sensory testing

Quantitative sensory testing (QST) is a validated noninvasive psychophysical tool that was developed to assess human responses to painless or painful stimuli. QST results in man reflect the functionality of, not structural changes to, the nervous system (Backonja et al., 2013). In an attempt to objectively investigate the functionality of the nervous system, QST and other objective measurements have begun to be investigated in domestic species. Knazovicky et al. (2017) sought to broaden the knowledge base relating to QST in dogs, investigating aspects of clinical feasibility. Unfortunately, despite a well-designed study, cognizant of the limitations of the technique in human practice (Maier et al., 2014), QST took 3–4 hours to perform and values showed some variability over time. Backonja et al. (2013) recommended that investigators performing QST should undergo rigorous training to improve inter-observer reliability and reduce bias. Sanchis-Mora et al. (2017) were recently able to undertake patient assessment within 90 minutes and found repeatability, but their results apply only to pain-free dogs. Thus, the introduction of QST into clinical practice as a reliable tool remains an aspiration, but is not currently a practical reality.

Advanced imaging

Alongside this patient-centred approach, neuroscience has asked the question, 'Can we image pain?' (Tracey 2008). Researchers are beginning to use blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) to explore this possibility; BOLD indirectly measures blood flow via blood oxygenation, and local metabolic changes due to increased neuronal activity (Hare et al., 1998).

Wager et al. (2013) published a controversial study entitled 'An fMRI-based neurologic signature of physical pain'. The authors described a neurologic signature that discriminates between the sensations of painful heat and nonpainful heat, is specific to physical pain and is responsive to the analgesic agent remifentanil. They concluded that fMRI could be used to assess noxious heat-related pain in healthy people, but more work is needed to see whether this 'signature' could be used to identify clinical pain.

Such advances in fMRI based imaging have brought to the fore the issue of whether there are brain biomarkers of pain that can be used to diagnose and verify the presence of chronic pain; a so-called 'painometer', an objective test of pain based on brain imaging, is currently being sought (Davis 2016). However, recent work showed the complexity of the issue; using direct intracerebral recordings in people, Liberati et al. (2016) identified similar responses in the insula following both painful and nonpainful stimuli. The use of fMRI imaging of brain activity in dogs is at an early stage; for a review, see Cook et al. (2016).

Treatment of chronic pain

VAA has published reviews of established evidence-based treatments for chronic pain, for example the clinical use of non-steroidal anti-inflammatory drugs in cats and dogs (Lascelles et al., 2007; KuKanich et al., 2012). Researchers have also published work describing a range of treatments across a variety of veterinary species including hens (Nasr et al., 2015), cattle (Bergadano et al., 2006) and goats (Cui et al., 2017).

Various authors have also described the veterinary use of drugs widely used to treat chronic pain in human medicine. The efficacy of tramadol has been reported in the laboratory setting (Kögel et al., 2014) and clinical management of cancer pain (Flôr et al., 2013). Another work reported a lack of additional benefit when tramadol was co-administered with meloxicam to treat osteoarthritis related pain in cats (Monteiro et al., 2016). A case report described the use of amantadine in a mechanism-based treatment for neuropathic pain (Madden et al., 2014). However, a case report by Clark et al. (2017) serves as a caution that lack of formal drug licensing also carries the risk of unexpected adverse effects. Another important aspect to consider with unlicensed drugs is whether owners can give informed consent, unless all the potential treatment risks are discussed.

The future

There is no doubt the application of new technologies in research will augment the discovery of pain mechanisms, but is there a temptation to focus on pixels, rather than the whole animal? Molony (1984) saw the need to progress from the fine detail of pain neurophysiology, calling for a more 'holistic' approach to assessment of animals' pain. The past three decades have seen many papers in VAA addressing some of these research areas, and this online VAA Supplement summarizes the progress made in meeting Molony's goals. The assessment of pain in the research setting has advanced from the factors affecting nociception, to QST and the discovery of pain mechanisms involved in central sensitization in veterinary species.

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