ASSESSING AND MANAGING CHRONIC PAIN IN CATS

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**Introduction**

In humans, chronic pain has been defined in different ways. One approach is to link it to time; for example, “any pain that lasts more than 3-6 months”, but is this set timeline relevant in veterinary species with different life expectancies? Pain that “persists beyond the normal tissue healing time” is another definition. This latter definition indicates that a clear demarcation between acute and chronic pain does not always exist and that they may be on a continuum.\(^1\) A person or an animal may have “chronic pain” but no clear inciting cause can be identified. It makes sense that if we understand the underlying cause of the patient’s pain our treatment plan can be specific and targeted. Based on the concept of treating the underlying cause, Woolf proposed that the two terms, *adaptive* and *maladaptive* be used to describe pain.\(^1\)

**Adaptive pain**

Adaptive pain includes nociceptive and inflammatory pain. Nociceptive pain is activated by high threshold noxious stimuli (e.g. heat) and is a protective mechanism; it may or may not result in tissue damage but is essential for survival. Tissue damage (e.g. a surgical incision) results in inflammatory pain with local tissue becoming more sensitive to stimuli. Inflammatory pain is considered adaptive because it serves a purpose by helping the animal protect itself against further injury. It is usually easy to identify the cause of adaptive pain and normally it is reversible or self-limiting.

**Maladaptive pain**

Maladaptive pain is not protective, it has no biological value, and should be considered a disease rather than a symptom. It results from changes in pain processing systems and can be separated into two types:

1. *Neuropathic pain*; this is a result of obvious neural tissue damage (central or peripheral; it is important to acknowledge that one cause is surgical trauma).
2. *Functional pain*; no neural damage or inflammation is present, but the driving force for pain is a malfunction or dysfunction in the nociceptive system.

In maladaptive pain there is amplification and facilitation of “pain traffic” and increased sensitivity to stimuli. Pain can be spontaneous due to generation of nociceptive input from the central nervous system itself. Other things that contribute to maladaptive pain are an imbalance between inhibitory and excitatory nociceptive input, altered descending inhibition and decreased activation of endogenous analgesic systems and spontaneous ectopic discharge from injured nerves. Another term that is important to the concept of maladaptive pain is *central plasticity* which is initiated through cellular wind-up. *Wind-up* is defined as a neuron’s increased response and output following identical, repeated stimuli. The term central plasticity refers to an autonomous global response that continues after the stimulus stops, or which is sustained by low level nociceptor input in the periphery.\(^2\) Because some processing systems are down-regulated the term central plasticity is more descriptive than central sensitization. The result of these changes is hyperalgesia or allodynia and expansion of the receptive field of neurons.\(^3\)
Examples of maladaptive pain
An obvious example of neuropathic pain is a nerve sheath tumor. Surgery causes nerve damage and if healing is abnormal, or acute pain management is inadequate this may lead to persistent postsurgical pain which is a long-term and maladaptive condition; this is seen in some cats after onychectomy. An example of functional pain in humans is fibromyalgia. Although the term is new to veterinary medicine cats with orofacial pain syndrome may have functional pain. In many long-term painful conditions in cats, there is a complex combination and overlap of adaptive and maladaptive pain. It is likely that with each disease and even in each individual, different neurobiological processes will be at play and vary over time, making treatment challenging and the response to analgesics unpredictable. The list of conditions with a pain component known to affect the wellbeing of cats over long periods is extensive and includes, but is not limited to, neoplasia, degenerative joint disease, dental and oral disease, inflammatory bowel disease, persistent post-surgical pain and non-healing wounds.

Assessment tools
Owner evaluations are very important in the assessment of long-term pain because owners know their cat best and spend the most time with them and can assess behaviors that cannot be observed during a clinic visit (e.g. using a litter box, interaction with other people and pets in the household). In addition, there is a possibility that when in stressful environment stress induced analgesia may occur. There is a growing understanding of behaviors that may be related to musculoskeletal disease in cats, but one assessment tool may not be applicable to all cats due to different lifestyles (e.g. indoor versus outdoor). The pain scales for cats with DJD include the Feline Musculoskeletal Pain Index (FMPI)\(^4\), the Client Specific Outcomes Measure (CSOM)\(^5\), the Montreal Instrument for Cat Arthritis Testing (MI-CAT)\(^6\) and the Owner Behaviour Watch (OBW).\(^7\) The FMPI and CSOM are questionnaire based and completed by the owner. The OBW asks owners to assess their cat within 4 major domains: general activity, mobility, temperament and grooming.\(^7\) The MI-CAT is designed for veterinarians and includes assessment of movement and posture and has been tested using mechanical threshold testing (von Frey), activity monitors (accelerometers) in a research setting. Because of the difficulty of performing a complete orthopedic examination and observing a cat’s normal activity in a consulting room, it is extremely helpful to ask owners to capture video clips of their cats in their own home environment. Objective measures of movement can be captured using activity monitors attached to cat’s collars or harnesses; these “Feline Fitbits” are sensitive to changes in acceleration and can identify cats with DJD from normal cats and the impact of treatment.\(^8\)

Quantitative Sensory Testing (QST)
Ideally, we need to test the somatosensory system to determine the degree of malfunction present and to direct our treatment plan. QST measures the frequency or intensity of different stimuli required to elicit a response by the patient. The stimuli used include mechanical, heat, cold and vibration, and are widely used in humans. When central plasticity has occurred changes in sensation to these stimuli can be measured. QST is in its infancy in veterinary medicine, however by using mechanical sub-threshold repetitive stimuli, Guillot and colleagues could discriminate cats with osteoarthritis from non-affected cats.\(^9\)

Quality of Life Scores
Assumptions on what constitutes a good Quality of Life (QoL) for a patient should be made carefully; it was assumed that cats with DJD or OA would have a diminished QoL and this would be primarily linked to mobility impairment; however owners ranked that 60% of things their cat did are “inactive” things that do not require normal mobility. Pain may only be one component of what is affecting a cat’s quality of life. A large percentage of cats with DJD also have chronic kidney disease. Because many cats often have several comorbidities, an overall health related QoL (HRQoL) may be more valuable. The CHEW questionnaire is one approach but still requires testing as a screening tool. An on-line tool which assesses the emotional and physical impacts of disease is available from Newmetrica (HRQL Instrument for Cats: www.newmetrica.com).

**Cognitive Function Testing**
Cognitive dysfunction (CD) or decline is reported in humans with maladaptive pain. CD is recognized in cats, usually senior or geriatric cats that are also likely to have a maladaptive pain condition such as DJD, therefore cognitive function testing is something we should consider in this population. This is an interesting area of future research as we still have a lot of dots to connect.

**Management of maladaptive pain**
Maladaptive pain is complex, exists in a continuum and is seldom static (good days and bad days). A combination of inflammatory and maladaptive pain is often present. It is now recognized that in humans, osteoarthritis has a component of neuropathic and functional pain which explains the clinical signs in many patients. Clear communication with the client is essential at the outset of a treatment plan. The owner must understand that comfort but not cure is the goal in many cases and that it is rare to achieve complete resolution of clinical signs of pain and it is helpful to describe maladaptive pain as a disease in itself. Treatment requires a committed and compliant owner and the financial, and emotional cost, and time investment required should not be under-estimated. Quality of Life assessments are essential as is a discussion of euthanasia when suffering can no longer be relieved. These discussions should start early and revisited during treatment. Assessments over time are vital to ensure adequate treatment and a good QoL.

**Approach to Treatment**
Identifying the source and cause of pain is not always easy and often the first treatment plan is a “best guess”. A short analgesic trial can be used to gauge the response to a specific drug before long-term planning. This “trial and error” approach is what leads to disappointment and frustration, as the first plan does not always reap the desired results. A multimodal approach is required with the following owner and cat factors considered:

1. Drug burden (how many drugs and how often?)
2. Ease of administration (palatability, owner’s skill)
3. The cat’s tolerance to drugs and their administration
   Note: drug, and caregiver aversion is a possible outcome of drug treatment.
4. Access to, and the cat’s tolerance to non-drug therapies (is there a rehabilitation center nearby?)

**Pharmacologic Therapy - Primary Analgesics**
Nonsteroidal anti-inflammatory drugs (NSAIDs) are the primary class of drug used to manage OA/DJD in all species. We have less experience and fewer choices with chronic use of NSAIDs in cats than we do in other companion animals. Meloxicam has efficacy in cats with DJD based on different methods of evaluation. Many older cats with DJD also have chronic kidney disease, however studies show that, with caution, these cats can still benefit from NSAID administration and studies report the use of meloxicam in this population. For an concise open access discussion of this topic see the reference by Monteiro and others. In a euvoletic state, renal perfusion is not prostaglandin (PG) dependent but in the face of hypovolemia or hypotension, vasodilatory PGs are important for maintaining perfusion. The owner and veterinarian should work together to find the lowest effective dose for each individual patient; in countries where it is authorized, the label dose of meloxicam is 0.05 mg/kg orally, once daily but many cats do well on doses of 0.01-0.03 mg/kg. Robenacoxib has been studied in cats with DJD, with and without kidney disease, over a 28-day period with no reported adverse effects. This drug has recently received authorization for “treatment of pain and inflammation associated with chronic musculoskeletal disorders” in cats by the European Medicines Agency.

Other Analgesic Drugs
Tramadol has undergone pharmacokinetic and efficacy studies in laboratory cats and client owned cats. Although deemed efficacious in these studies, palatability and adverse side effects including, sedation, dysphoria, diarrhea and inappetence is a major drawback for clinical use. Gabapentin is frequently prescribed by veterinarians, yet the efficacy of gabapentin has only recently been reported in a small group of cats. Treatment was associated with improvement in activities that owners had identified as being impaired, but based on activity monitors overall activity levels were lower when cats were receiving gabapentin compared to placebo treatment. Sedation was the most common side effect.

Non-drug Treatments
Some of the commercially available “joint diets” that contain the omega-3 fatty acids eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), green-lipped mussel extract and glucosamine/chondroitin sulfate are beneficial. Physical rehabilitation modalities include but are not limited to laser therapy, electrical stimulation, passive range of motion exercises, massage, trigger point therapy and therapeutic exercise. Acupuncture is now a respected component of treatment in human pain clinics. Although there is a need for well controlled clinical studies using these techniques there is general agreement that many cats greatly benefit from these therapies, especially when an integrative approach is used. Many owners want to be part of the treatment plan for their cat and we can teach them how to perform some therapies. Cats with impaired movement will need assistance with some “every day” activities. These include but are not limited to:

- Accessing elevated places – use steps, chairs and boxes to make this easier
- Eating and drinking – elevate food and water bowls
- Using a litter-box – ensure this is “easy entry” with a low access point
- Doing their “favorite thing” – this will be different for each cat
- Grooming – owners can assist with this

Emerging modalities for maladaptive pain
There has been a huge growth in the use of monoclonal antibodies to treat numerous diseases in humans and this has spilled over into veterinary medicine. Neutralizing antibodies to nerve growth factor (NGF) provide pain relief in humans, rodent models and dogs and cats with osteoarthritis.23 A new class of drugs called the piprants are being widely studied and one such drug, grapiprant, is now available for the treatment of osteoarthritis associated pain in dogs. Grapiprant is a selective antagonist of the EP4 receptor, one of the four prostaglandin E2 (PGE2) receptor subtypes. There are likely to be fewer unwanted side-effects with this class of drug because the COX-1 and COX-2 pathways are not affected and the safety data in cats including when given at high doses encouraging.24

Maladaptive pain is common on cats, but progress has been made in understanding its etiology, raising awareness and developing new targeted therapies and treatment modalities.

References


