THESIS

Sueyeon Kang

2023

Department and Clinic of Small Animal Internal Medicine
University of Veterinary Medicine Budapest

The Effects of Acupuncture on Pain Management for Canine Patients: A Review Based on Relevant Literature

By
Sueyeon Kang

Supervisor:
Eva Balogh, DVM, PhD

Budapest, Hungary
2023

1 TABLE OF CONTENTS

2 INTRODUCTION

Pain is one of the five aspects which characterize inflammation according to ancient medical physicians, the other four being redness, swelling, heat and loss of function.[1] Assessment and treatment of pain in human and veterinary patients is an essential part of treating diseases, as untreated pain can negatively affect the outcome of treatment, as well as the general well-being of the animal. Furthermore, untreated pain in chronic patients can lead to negative clinical consequences, such as immune suppression and increased risk of secondary diseases. In cats, management of pain can significantly benefit the patient's health, as inappetence, reduced caloric intake and cachexia caused by pain often puts the feline patient at risk of hepatic lipidosis which can be life threatening.[2]

The International Association for the Study of Pain defines pain as "an unpleasant sensory and emotional experience associated with actual or potential tissue damage, or described in terms of such damage".[3] It may be noted that pain is defined as an experience and not a sensation, implying that individuals may perceive a pain differently in terms of its nature and degree, even if the pain stimulus originated from the same source with the same intensity. This is because in humans and animals alike, pain is perceived as a final result of many coordinated neurological signals in the body, and encoding and modifying processes of the pain signals may differ greatly between individuals. Furthermore, part of the pain processing has affective-motivational aspects, which suggests its connection to emotion.[3] Therefore, it is essential to consider multiple facets of it when studying pain.

There are several treatment methods for pain available in the field of veterinary medicine. The most conventional methods are analgesic medications such as opioids, non-steroid anti-inflammatory drugs (NSAIDs) and steroids, which produce consistent and reliable results in patients. Alternative methods are also popular options, whether done alongside conventional treatments or on their own. Physiotherapy is one of the most popular alternative methods, which offers several possibilities to relieve pain like massage, heat treatment, electrical stimulation, laser treatment and many others. Controlled exercise may help reduce the

stiffness of the soft tissue, reducing pain in the area as a result. Homeopathy is also becoming an increasingly popular therapy option for pain management.

Acupuncture is another popular alternative method to conventional Western medicine for the treatment of pain, though some western practitioners are still doubtful of its effectiveness. However, there is increasing acknowledgement of its effects among Western practitioners, with many veterinary schools around the world having started teaching acupuncture courses. With the launch of the American Journal of Traditional Chinese Veterinary Medicine in 2006, there have been increasing number of attempts to research the effects of acupuncture. Acupuncture as a modality for treatment of pain, in particular, has been of great interest to many researchers, and many studies have effectively produced promising results. Acknowledging these results, the most recent canine and feline pain management guidelines developed by the World Small Animal Veterinary Association Pain Council lists acupuncture as a non-pharmaceutical treatment for small animal pain.[4]

Acupuncture involves using needles for stimulation of specific anatomical locations called acupoints, which are essentially concentrated regions of free nerve endings, lymphatics, small arterioles, venioles and mast cells.[5] These points represent areas of concentrated or blocked Qi, or blocked energy, according to the traditional Chinese theory. The acupoints are connected by channels of energy, known as meridians.[6] The system of acupoints and meridians is illustrated in **Figure 1.**

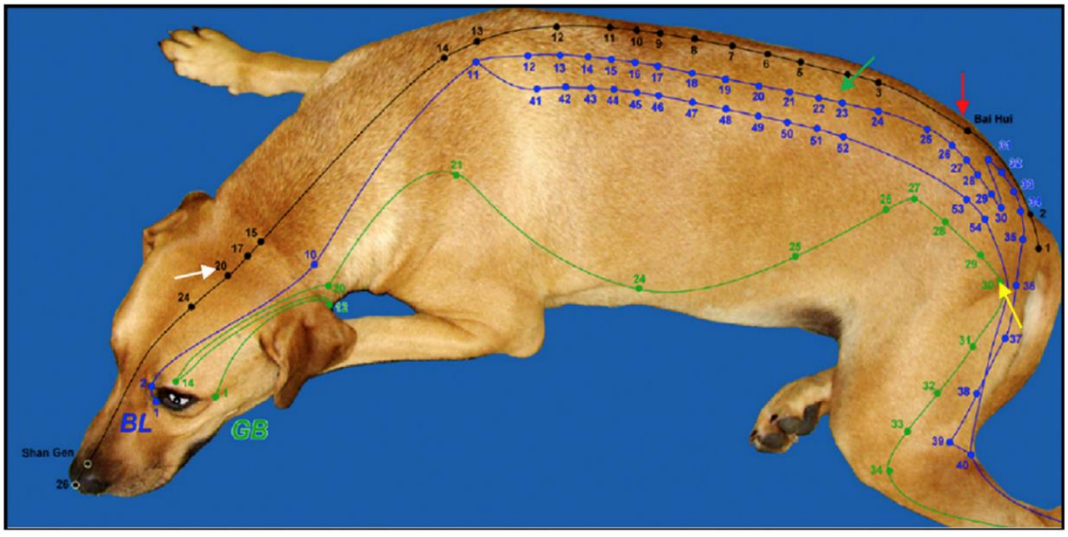

Figure 1. Meridians with acupoints; green: gall bladder (GB) meridian; Blue: bladder (BL) meridian; black: governing vessel (GV)[7]

There are twelve regular meridians and eight extra meridians, and different types of meridians are named after different systems of the body. For example, the gall bladder (GB) meridian, among other effects, helps to regulate the health of gall bladder and the flow of bile. Stimulation of these points is thought to release the blockage of energy, producing beneficial effects in other regions and organs down the meridian.[7] This concept was explored by a recent study using Magnetic Resonance Imaging (MRI) and Positron Emission Tomography (PET) which demonstrated that stimulation of acupoints produced an electric activity in the areas of brain which are corresponding to the regions of the body controlled by the acupoints.[8]

There are different modalities for acupuncture. A practitioner may use regular dry needles, heated needles, or heat the acupoints (moxibustion), connect the needles to electricity for enhanced stimulation (electroacupuncture), use pressure instead of needles to stimulate acupoints (acupressure), or use laser instead. Additionally, injections into acupoints with substances, for example with vitamin B12, can be done to enhance stimulation.

Purpose of this literature review is to study the effects which acupuncture can elicit for pain management for canine patients, and how effective these effects are. This research paper aims to answer these questions by discussing the results from various literature from Asian, European and American databases, discuss the possible limitations of them and finally discuss the possibilities of clinical applications. As mentioned earlier, there are multiple facets to be considered when studying pain and management of it, and the subjective nature of pain combined with the lack of methods to accurately measure the degree of pain makes it a challenging job. In the following chapters of this paper, the effectiveness of acupuncture as a pain management modality will be evaluated by discussing studies utilizing multiple indicators of pain and analgesia, such as the release of specific pain-related biochemical molecules in body, observation of changes in behavior of the dog or in the vital parameters that are known as signs of pain, as well as indicators of general well-being.

3 GOAL

This literature review aims to study the effects of acupuncture for pain management for canine patients. First, the physiological pain pathway will be explained in a brief summary. The analgesic effects of acupuncture will be evaluated by focusing on two main indicators of pain relief. The first indicators are the biochemical molecules with pain relieving effects, which are released in the animals' body upon acupuncture therapy. The second indicators are the decreased signs of pain displayed by the animal, which may be physiological signs of pain such as increased heart rate; or signs of general well-being of the animal. The conclusion of the literature review will be discussed in the later parts of this research paper, which will include imitations of the studies reviewed and their methods, as well as areas which need improvement. Finally, clinical applications of acupuncture for pain management including treatments of specific medical conditions that may particularly benefit from acupuncture will be discussed.

4 LITERATURE REVIEW

4.1 METHOD

This research paper will study the effects of pain management by acupuncture in canine patients by literature review. There are various methods used to measure the degree of pain in dogs, and different sources use different methods. In this review, the analgesic effects of acupuncture therapy will be assessed by mainly focusing on two indicators of pain relief.

The first group of indicators are the biochemical molecules with analgesic properties that are released during acupuncture therapy of a canine patient. Measuring the amount of these molecules can be used to assess the analgesic effects of acupuncture; increased release of the analgesic molecules in the body means that there will be less pain signals firing, therefore there will be decreased pain. They can help to explain the physiological basis of the analgesic effects of acupuncture. This part of the research will start with a brief summary of the physiological pain pathway (**chapter 4.2.1**). The actions of the analgesic biochemical molecules released during acupuncture therapy will be explained in detail in the following chapters (**chapter 4.2.2, 4.2.3, 4.2.4**), which will be divided into three parts: local, segmental and suprasegmental; each representing a region of the body or the nervous system.

The second group of indicators are decreased signs of pain displayed by the animal. These signs can be observed by the owner or the veterinarian. It is important to consider these indicators in this research, as the degree of pain relief the animal experiences in practice may not necessarily correlate to the theoretical analgesic effects the analgesic biochemical molecules are supposed to produce. There may be a variety of reasons for this. For example, pain is not a mere sensation but the perception of a combination and modification of various sensory information, therefore simply measuring the analgesic biochemicals that are released in the body of an animal in pain may not accurately explain the entirety of the pain processing. Furthermore, there may be placebo effects, or unknown analgesic mechanisms that cannot be fully explained by the biochemical molecules which can be detected in the body. Studying

the second group of indicators, the decreased signs of pain displayed by the animal, can reflect the effects of acupuncture in practice, its placebo effects, as well as suggest unknown mechanisms of pain relief by acupuncture that are not well explained by the detected biochemical molecules.

There are many scales and systems available for the second group of indicators, the signs of pain displayed by the animal. Examples include pain assessment scales based on signs of physiological pain, as well as scoring systems that focus on assessing quality of life. The former allows assessment of direct and immediate pain. The latter may help to reflect the degree of emotional pain and the general well-being of the patient, which may be used to study the effects of acupuncture as a more holistic approach to pain management.

To prevent biased data collection and improve reliability, data will be collected from a variety of different sources from Asian, European and American databases. Main search engines used for this research paper are Google Scholar, PubMed, VIN websites, and the keywords used for searching are acupuncture, pain, analgesia, and canine.

4.2 ANALGESIC EFFECTS OF ACUPUNCTURE DEMONSTRATED BY RELEASE OF BIOCHEMICAL MOLECULES

4.2.1 Physiological pain pathway

According to literature, physiological pain can be originated by largely three components, which are acute high intensity stimuli, tissue injury or inflammation, and peripheral nerve injury. When there is a pain signal generated by one of these origins, the body experiences "acute pain" [3]. The identification of pain is known as nociception. When a pain stimulus induces an electrochemical signal that surpasses the threshold in the receptors, the signal is transferred along the nerves of the peripheral nervous system to the central nervous system. In the central nervous system, the receptors relay the pain signal, and the information can be modified, which is explained by the gate control theory. This theory will be explained in connection to the analgesic effects of acupuncture in **chapter 4.2.3.**

Figure 2. shows the system of pain transmission, which can be divided into three sectors: local, segmental and supraspinal.

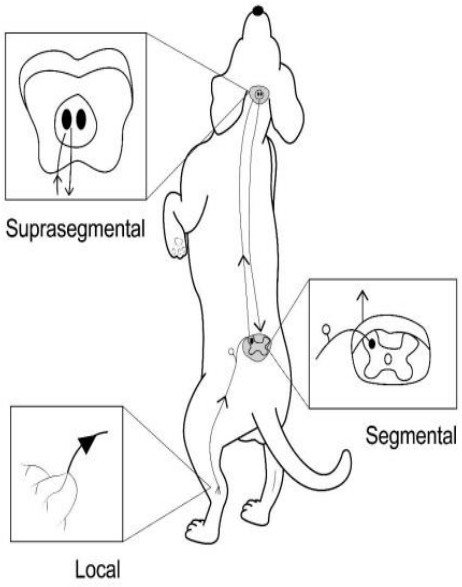

Figure 2. Schematic drawing of the pain pathway[5]

The local system is comprised of the first order neurons. These neurons are called Aδ and C afferent fibers, also known as the nociceptors. They directly generate the signals upon sensation of pain. The Aδ fibers respond to both low and high intensity mechanical and thermal stimuli, whereas C fibers respond mainly to high intensity mechanical, thermal and chemical stimuli. There are also Aβ afferent fibers which are responsible for the low intensity stimuli, therefore these do not normally generate pain stimuli. Any analgesic effects of acupuncture acting on this part of the nervous system will cause local analgesic effects, discussed in **chapter 4.2.2.**

Propagation of the pain signal to the next part of the pain pathway takes place at the axon terminal of the afferent nerve fibers. At the level of interneuronal synapsis, there are many receptors and channels which carry neurotransmitters to the adjacent neurons. These receptors and channels vary in their type or modality of the input as well as the threshold level of the input at which they are activated. For example, the low threshold transducers are activated upon lighter stimuli such as light physical touch, while the high threshold transducers such as transient receptor potential cation channel subfamily V members (TRPV) are activated upon extremely intense, possibly painful stimuli.[3] These receptors and channels play a significant role in the workings of acupuncture, as there are a variety of types of acupuncture such as using heated needles, pressure (acupressure), laser, electricity (electroacupuncture), allowing the targeting of certain types of receptors and channels in this region that transmit certain types of pain. The signal is then transferred to the dorsal root ganglia, then to the spinal cord. The dorsal root ganglia are the main point of the synthesis of primary afferent neurotransmitters.[3]

The spinal cord functionally can be divided into a number of sections, known as laminae, each containing pathways propagating specific types of electrical impulses to specific parts of the brain. The laminae and their functions are illustrated in **Figure 3**.

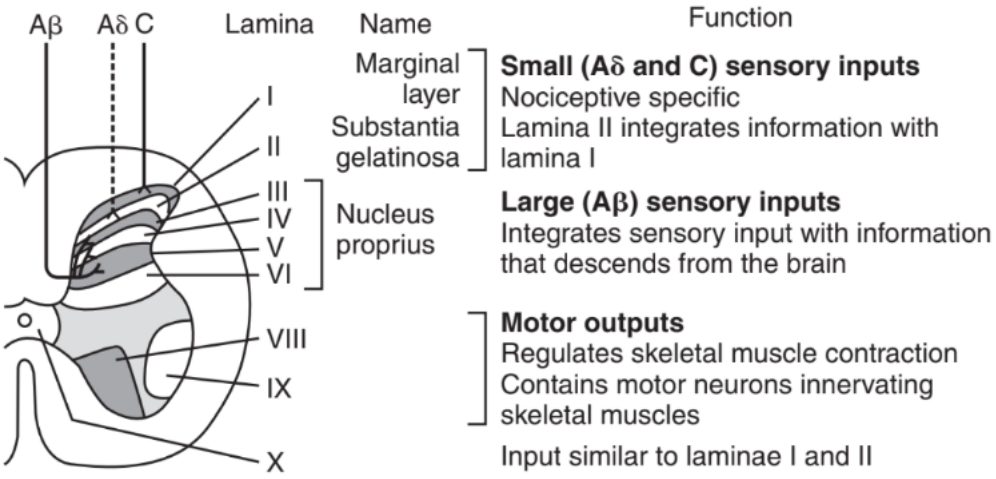

Figure 3. Illustration of the spinal cord and its laminae[3]

The neurons of the marginal layer, also known as Lamina I receive nociceptive and thermal input from the δ and C afferent fibers, and propagate the information to the medullary reticular formation (RF), nucleus of the solitary tract and lateral parabrachial area, periaqueductal gray matter (PAG), and to the thalamus. Similarly, substantia gelatinosa, or Lamina II, mostly receives nociceptive and thermal input from the afferent fibers.[3] The dorsal horn of the spinal cord, which consists of Lamina I-VI (and Lamina X which is physically not part of the dorsal horn) is the region where processing and encoding of pain stimuli occur. Acupuncture acting on this part of the nervous system can be referred to as the spinal or segmental effects, and the physiological basis of these effects will be explained in **chapter 4.2.3.** with examples from literary sources.

The brain is the end point of the pain signal pathway, where recognition and modification of pain stimuli take place. Pain stimuli in the dorsal horn of the spinal cord travel to the brain through mainly two pathways; illustrated by **Figure 4**: the somatosensory pathway (Figure **4A**) and the affective-motivational pathway (Figure **4B**).

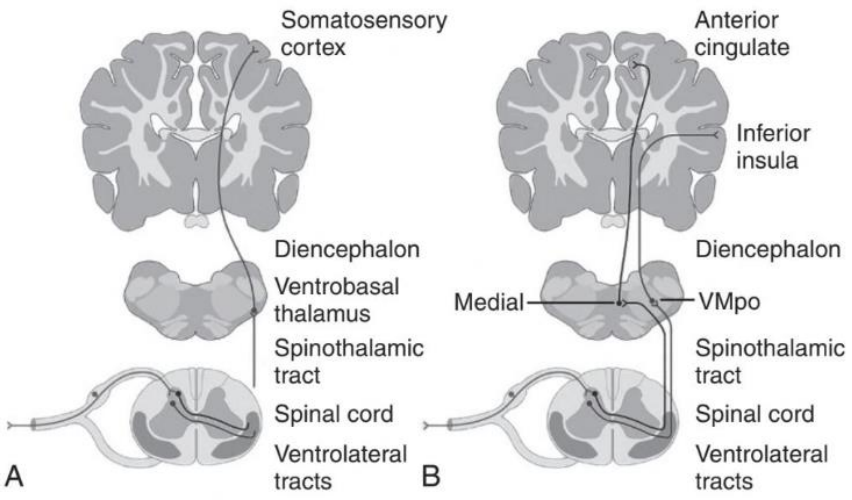

Figure 4. Schematic drawing of somatosensory pathway (4A) and affective motivation pathway (4B)[3]

Both pathways travel through the spinothalamic tracts in the dorsal horn of the spinal cord. The somatosensory pathway, which projects into the ventrobasal thalamus is primarily responsible for recognition of the origin and the intensity of the pain stimuli. The affective motivation pathway, projecting into the medial thalamus, and further into the limbic system, is responsible for processing the emotionality regarding pain. These connections demonstrate the higher-order processing of the pain at the level of the brain and the averse emotional reaction to it.[3]

The final perception of pain is the result of various inputs from neural pathways. Apart from the somatosensory and affective motivation pathways discussed above, billions of interneurons in the brain receive and modify motor, autonomic and endocrine information from several other parts of the nervous system. These sensory inputs are then coordinated in the reticular activating system (RAS) in the brainstem, then relayed through the PAG to the hypothalamus and the thalamus, and the somatosensory cortex. The PAG is also responsible for transferring information from the higher parts of the brain to the spinal cord, and modifying of the pain stimuli through endogenous opioids, and is therefore deemed a crucial part of the suprasegmental part of the pain pathway.[3] Further details of the analgesic effects of the acupuncture on the brain will be discussed in **chapter 4.2.4.**

4.2.2 Local analgesic effects of acupuncture

The local analgesic effects of acupuncture are initiated upon the insertion of the needle into the fascia and tissue matrix of an acupoint. Stimulation of the local tissue elicits response from mainly three components in the regions, which are the fibroblasts, the vasculature and the local nerve endings. Physical stimulation by the needle leads to release of various biochemicals by the fibroblasts. This process is known as mechanotransduction, which allows cells to convert mechanical stimuli into biochemical signals, forming the basis of the workings of acupuncture.[9]

One immediate effect of the insertion of the needle is the increased blood flow to the area and activation of the local immune system through the following mechanism: the insertion of the needle results in a microtear of the local tissue, activating Hagemann's tissue factor XII and the local coagulation cascade in turn. Then plasminogen, protein kinins, and prostaglandins are produced. The microinjury also induces the degranulation of the mast cells, releasing histamine, heparin, proteases, and bradykinin. Increased blood flow and activation of the local immune system due to release of these biochemicals produce anti-inflammatory and analgesic effects.[10]

The insertion of the needle deforms the fascia and the tissue matrix, stimulating the local afferent nerve endings. As a result, local axon reflex is triggered, causing the De Qi response, which is described as an instant sensation in the location of needle insertion traveling through the nerves.[7] Not only the cells of the nervous system are affected by acupuncture, but also involved are the lymphocytes, macrophages and granulocytes which release endogenous opioids into the tissue, suppressing the transmission of the pain signal along the nervous system by acting at the nerve endings of the peripheral nerves of the pain pathway.[11]

Release of the endogenous opioids, which are strong analgesic molecules naturally produced in the body, plays a crucial role in the analgesic effect of acupuncture. Acupuncture directly activates peripheral sympathetic nerve fibers, during which process the adrenergic receptors are activated by norepinephrine release. Activation of the adrenergic receptors enhances the release of endogenous opioids such as beta endorphins by inflammatory cells.[11] Sympathetic nerve fiber activation also produces the analgesic effect through the increase of the

expression of specific intercellular adhesion molecules in the blood vessels around inflamed tissue, leading to further release of beta endorphins met-enkephalin in the region.[11] The amount of cannabinoid CB2 receptors in the tissue increase upon stimulation by acupuncture leads to upregulation of endogenous local opioids as well, as well as directly suppressing sensory nerve activity.[11]

The analgesic effect is further enhanced by decreasing levels of prostaglandin E2 and COX-2 activity as well as the local inflammatory cytokines such as tumor necrosis factor α, interleukin 1β and interleukin 6.[11] Decreased levels of these inflammatory molecules help to decrease the level of pain, as well as other characteristics of inflammation such as redness, swelling, heat and loss of function. Studies have also demonstrated the direct and indirect analgesic effects by the release of purine neurotransmitters such as ATP and adenosine by the local tissue on acupucnture.[12]

4.2.3 Segmental analgesic effects of acupuncture

The gate control theory of pain, first proposed by Melzack and Wall in 1965, provides that pain modulation is carried out by the interactions between the neurons at the spinal level, during which non-painful input closes the "gates" to painful input.[13] This knowledge can be applied to understand the mechanism of analgesia by acupuncture, as needling or applying pressure causes the Aβ afferent fibers to generate non-painful sensory signals, effectively "gating" the nociceptors, which are Aδ and C afferent fibers, blocking the propagation of pain signals through the spinal cord.

An area of skin, known as a dermatome, is innervated by numerous afferent neuron fibers arising from a single dorsal root of a specific spinal nerve. However, the innervation of the dermatomes appears to be not as straightforward as scientists originally thought, as new evidence showed that there is significant overlap in the innervation of adjacent dermatomes.[10] For example, nerves innervating three different points on L3 dermatomes may not all arise from the dorsal root of the L3 spinal nerve, but rather, they may be arise from the dorsal roots arising from the adjacent spinal nerves L2 and L4. This concept is explained in an illustration of human dermatomes in **Figure 5.**

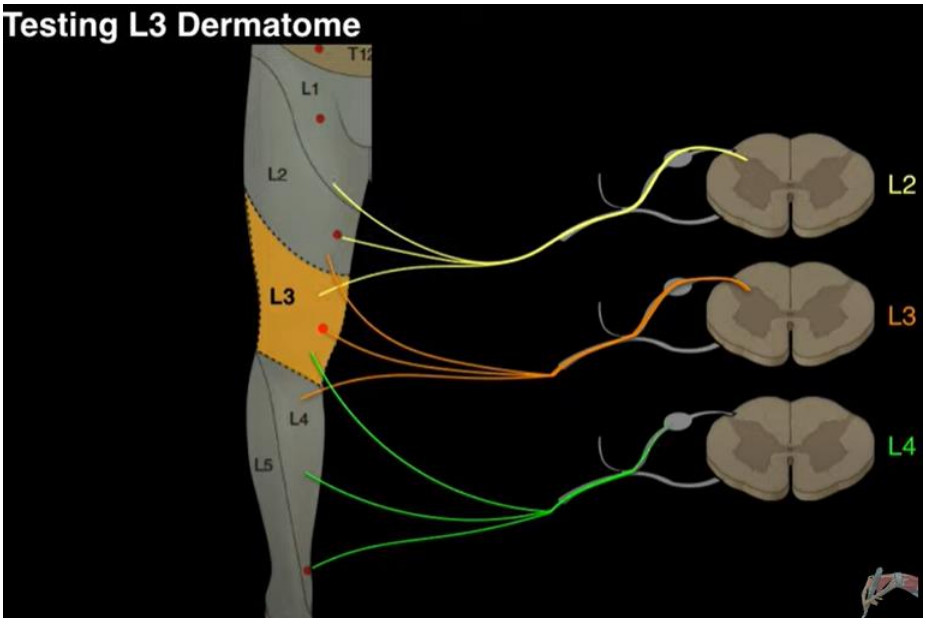

Figure 5. L1, L2 L3 Dermatomes and innervation of them by dorsal roots arising from L2, L3 and L4 spinal nerves[14]

This has important implications in acupuncture therapy, as treatment focused on one skin area, or dermatome may treat other spinal segments which supply the dermatome.[10]

Various studies also indicate that the propagation of pain signals at the spinal level are inhibited by several biochemical molecules released upon acupuncture, such as spinal opioids, serotonin, norepinephrine, glutamate, cytokines and signal molecules.[11] Increasing levels of these molecules supresses the activity of the N-methyl-D-aspartate (NMDA) receptors in the dorsal horn of the spinal cord. The NMDA receptors are activated by glutamate, which is an excitatory neurotransmitter, and the activation of these receptors is associated with hyperalgesia and neuropathic pain.[7] Suppression of the NMDA receptors leads to decreased uptake of the excitatory neurotransmitter glutamate released upon nociception, therefore decreased pain signal transmission. This is achieved by increased levels of serotonin, noradrenaline and endogenous opioids in the spinal cord during acupuncture.[7] The increased serotonin levels in the spinal cord also further enhances the pain relieving effect of acupuncture by facilitating the inhibiting ability of γ-aminobutyric acid, commonly known as GABA, by activating the serotonin receptors (5-hydroxytryptamine 1A receptors, or 5-HT1AR) expressed on GABAergic neurons.[11] Enhancement of GABA, which is a inhibitory neurotransmitter, inhibits pain signal transmission in turn.

Stimulation by acupuncture induces pain relief by reducing spinal glial cell and astrocyte activation, which decreases levels of cytokines released by them, namely IL1β, IL-6, TNFα, COX-2, and PGE2.[15] Substance P, which is released by the spinal gray matter and promotes the propagation of nociceptive signals, is also inhibited by acupuncture. As in the peripheral nervous system, COX-2 activity is inhibited as well, also leading to anti-inflammatory effects.[5] A study by Zhao demonstrates that the levels of N/OFQ, a powerful opioid peptide widely distributed in the spinal cord gray matter with a strong analgesic potential, are increased by acupuncture, inhibiting the pain responses induced by C fibers. They also claim that acupuncture helps to increase the levels of acetylcholine and dopamine in the spinal cord, both molecules inhibiting pain signalling.[16]

4.2.4 Suprasegmental analgesic effects of acupuncture

Like many other neuronal activities of the brain, the analgesic effects of acupuncture in the brain are poorly understood and is a difficult field to study, partly due to the complex nature of the interneuronal connections of the brain. According to an extensive literature review on the pain relieving ability of acupuncture by Dewey and Xie, the parts of the brain that are involved in processing pain are the medulla oblongata, the pons, and the reticular activating system (RAS) in the brainstem; and the PAG, the hypothalamus and the pituitary gland, the thalamus, and the cerebral somatosensory cortex.[5] Regarding studies that have focused on the analgesic effects of acupuncture at the molecular level have shown that the analgesic molecules released include beta endorphins, enkephalin, noradrenaline, dopamine and serotonin, oxytocin and adrenocorticotrophic hormone, which all help to suppress incoming nociceptive input from the lower parts of the nervous system.[5]

Evidence from MRI results in experimental animal models the “anti-nociceptive” parts of the brainstem that are stimulated upon acupuncture correspond to the acupuncture points on the limb. Interestingly, activation of these points will activate the intended brainstem regions without producing a measurable segmental effect. In contrast, an acupuncture point on the back for instance, may produce a brainstem or a segmental response depending on the intensity of the stimulation. This suggests the possibility that certain combinations of different acupuncture points in different regions of the body may produce local, segmental and suprasegmental analgesic effects at the same time, maximizing the pain-relieving effect of acupuncture.[5]

Neuroplasticity, which is the ability of the nervous system to change its structure, functions or connections by reorganization usually occurs in a clinically harmful way in the CNS, in which, pain signalling pathways are enhanced. Studies show acupuncture leads to beneficial neuroplasticity preventing or reversing the detrimental changes in the brain due to chronic neuropathic conditions via suppressing microglial cell activation and the release of inflammatory mediators, and promoting the release of analgesic neurotransmitters.[7] This knowledge maybe be clinically significant as scientists try to develop new treatment plans for chronic neurological diseases, which often accompany neuroplastic changes which are challenging to reverse.

4.3 ANALGESIC EFFECTS OF ACUPUNCTURE DEMONSTRATED BY OBSERVATION OF DECREASED SIGNS OF PAIN

Release of the biochemical molecules with analgesic properties in the body during acupuncture may not explain the entire mechanism of pain relief by acupuncture, and the degree of pain relief the animal actually experiences after the therapy may not necessarily correlate to the theoretical analgesic effects which have been demonstrated by the studies of biochemical molecules. Therefore, it is crucial to study the analgesic effects of acupuncture therapy in practice.

There are several ways to measure pain in a dog. Physiological pain generated by high intensity stimuli trigger a particular set of behavior in a dog, such as grumpy or depressed mood, decreased acts of play, vocalization, decreased ability to walk, trot, gallop or jump, or to lie down or get up.[17] which can be recognized by the owner and the veterinarian. Pain also induces a multitude of physiological responses, such as increased heart rate, breathing rate, arterial blood pressure, salivation and mydriasis. This allowed the development of a number of different pain indices created by several researchers to measure pain as accurately as possible, which are readily used by many studies on the effects of acupuncture for pain management. **Figure 6.** Shows an example of a pain assessment scale based on the physiological and behavioral cues.

Score	Description
0	• No pain, patient is running, playing eating, jumping, bouncy • Sitting or walking normally • Sleeping comfortably with dreaming • Normally affectionate response to caregiver • Heart rate should be normal; if elevated, it is due to excitement • Cats rub their face on the caregiver's hand or cage, may roll over and purr • Cats and dogs groom themselves when free of pain • Appetite is normal • Behavior different from this not associated with pain may be associated with apprehension or anxiety • Apprehension or anxiety can be a feature of hospitalized patients
1	• Probably no pain • Patient seems to be normal, but condition is not as clear-cut as previous category • Heart rate should be normal or slightly increased because of excitement

2	• Mild discomfort • Patient still eats or sleep but may not dream • May limp slightly or resist palpation of the surgical wound, but otherwise shows no signs of discomfort • Not depressed • There may be a slight increase in respiratory rate; heart rate may or may not be increased • Dogs may continue to wag their tail and cats may still purr during interaction with the caregiver • Reassess within the hour, and then give an analgesic if condition seems worse
2	• Mild pain or discomfort • Patient limps or guards incision or the abdomen may be slightly tucked up if abdominal surgery was performed • Looks a little depressed • Cannot get comfortable • May tremble or shake • Seems to be interested in food and may still eat a little but somewhat picky • This could be a transition from category two so you notice a change from being comfortable to becoming restless as though the analgesia is wearing off • Respiratory rate may be increased an A little shallow • Heart rate may be increased or normal depending on whether an opioid was given previously • Cats may continue to purr and dogs may wag their tail even when they are in pain, therefore disregard these behaviour patterns as indicators of comfort • Needs analgesia • The analgesic selected depends on whether it is a repeat administration or dose in as patient with moderate to severe pain or the patient has a problem resulting in mild to moderate pain
4	• Mild to moderate pain with the patient resisting touching of the operative site injured area painful abdomen or neck for example • Guarding or splinting of the abdomen or stretching all four legs • May look, lick, or chew at the painful area • the patient may set or lie in an abdominal position and is not curled up or relaxed • May tremble or shake • May or may not seem interested in food • May start to eat and then stop after one or two bites • Respiratory rate may be increased or shallow • Heart rate may be increased or a normal • Pupils may be dilated • May whimper (dog) or give up plaintive meow (cat) occasionally, be slow to rise, and hang the tail down • There may be no weight bearing or only a toe touch on the injured limb • Is somewhat depressed in response to the caregiver • Cats may lie quietly and not move for prolonged periods
5	• Moderate pain, similar to previous category but condition progressing • Patient may be reluctant to move depressed or inappetent and may bite or attempt to bite when the caregiver approaches the painful area • Trembling or shaking with head down maybe a feature, depressed • The patient may vocalise when caregiver attempts to move it or when it is approached • There is definite splinting of the abdomen if affected, or the patient is unable to bear weight on an injured or operative limb • The ears may be pulled back • The heart and respiratory rates may be increased • Pupils may be dilated • The patient lies down but does not really sleep or may stand in the praying position if there is abdominal pain

6	• Increased moderate pain • Similar to previous category, but patient may vocalise or whine frequently without provocation and when attempting to move • Heart rate may be increased or within normal limits if an opioid was administered previously • Respiratory rate may be increased with an abdominal lift • Pupils may be dilated
7	• Moderate to severe pain • The patient is quite depressed and is not concerned with its surroundings but usually responds to a direct voice • The patient urinates and defecates without attempting to move, cries out when moved, or spontaneously or continually whimpers • Occasionally, an animal does not vocalize • Heart and respiratory rates may be increased • Hypertension may also be present • Pupils may be dilated
8	• Severe pain • Signs same as previous category • Vocalising may be more of a feature, or animal is so consumed with pain that it does not notice your presence and just lies there • With severe trauma, the patient may not be able to move or cry because of the increased pain with this activity and therefore remains motionless an extremely depressed • The patient may thrash around in the cage intermittently • With some traumatic or neurologic pain the patient may scream especially cats when being approached • Tachycardia with or without tachypnea with increased abdominal effort and hypertension, is usually present even if an opioid was given previously although these can be unreliable parameters if not present
9	• Severe to excruciating pain • Signs same as previous category, but patient is hyperesthetic • The patient trembles involuntarily when any part of the body in close proximity to wound or injury is touched because of neuropathic or severe inflammatory pain • This degree of pain can cause death
10	• Signs same as previous category, but patient admitting piercing screams or almost comatose • The patient is hyperesthetic or hyperalgesia • The whole body is trembling, and pain is elicited wherever you touch the patient • This degree of pain can cause death

Figure 6. Pain assessment scale guide by Mathews *et al*[2]

Another popular method is to assess to which extent the quality of life of a canine patient has improved after acupuncture treatment, which includes questions regarding vitality, pain, distress or anxiety of the dog.[18] This method focuses on the long-term results and also includes emotional pain and general well-being of the patient as opposed to a temporary relief of physiologic pain. A good example of a study using both of these methods to assess the effectiveness of pain management is the extensive study on the effects of acupuncture on pain and quality of life of 181 dogs published by the Canadian Veterinary Medical Association demonstrates that both the pain and the quality of life of dogs with neurological or musculoskeletal conditions have significantly improved after acupuncture therapy over a

period of 24 weeks.[19] This study used three validated questionnaires to evaluate the improvement of pain and quality of life after acupuncture therapy, the Helsinki Chronic Pain Index (HCPI), VAS (Visual Analogue Scale) and the quality of life assessment (QLA). According to the results of this study, acupuncture therapy used alone, or in combination with adjuvant analgesics, was effective in treating pain and improving quality of life of dogs with neurological or musculoskeletal diseases, with the average increase of approximately 60%, from around 20% in the first few weeks to 80% by the end of 24 weeks in the success rate of the treatment, across all pain indices.

For specific pains characteristic for specific types of diseases, physiological changes in the affected organ may be observed in order to accurately assess the analgesic effects of acupuncture. For instance, in case of visceral pain, changes in the motility of the intestines may be observed using ultrasound. Decreased signs of inflammation in histopathology may also help to indicate the analgesic and anti-inflammatory effects of acupuncture.

The following part of this literature review will study the analgesic effects of acupuncture mainly evaluated by changes in behavioral and physiological signs of pain. This part will be sectioned into different disease groups which are: Acupuncture for pain management in musculoskeletal diseases (**chapter 4.3.1**), Acupuncture for visceral pain (**chapter 4.3.2**), Acupuncture for pain management in respiratory diseases (**chapter 4.3.3**), Acupuncture for management of gingival and dental pain (**chapter 4.3.4**), Acupuncture for management of cancer pain (**chapter 4.3.5**) and Acupuncture for management of postoperative pain (**chapter 4.3.6**). Separating different disease groups allows to study the analgesic effects of acupuncture in different organ systems which may help to identify clinical applications for treatment of particular diseases.

4.3.1 Acupuncture for pain management in musculoskeletal diseases

In addition to the alleviation of physiologic pain and the improvement of the general quality of life, acupuncture therapy has been demonstrated to be useful in treating pain in patients with more specific groups of diseases; acupuncture can be especially effective in patients suffering from degenerative joint disease which often triggers musculoskeletal and neuropathic pain due to the decreased joint mobility, inflammatory alterations within the joint, and compression of the surrounding nerves, respectively. Acupuncture has been shown to decrease pain and improve quality of life in canine patients with the intervertebral disk disease (IVDD) by several studies.[19] Another study also showed that neck pain and tetraparesis in IVDD and spondylosis deformans were improved after dry needling or electroacupuncture.[20] A Korean study on the effects of acupuncture in patients with IVDD showed that the back pain significantly decreased, and the clinical signs disappeared after acupuncture combined with steroid therapy.[21]

A controlled study investigated effects of acupuncture to decrease the recovery time of experimental spinal cord injury and pain in dogs using foreign body insertion which compressed 25% of the diameter of the spinal cord. The results showed that the recovery time was significantly shortened in case of electroacupuncture combined with corticosteroid therapy, and there was no significant difference in the change in recovery time between electroacupuncture alone and corticosteroid treatment alone.[22] The effects of dry needle acupuncture focusing on the acupoints around L4-L6 may improve pain from stifle diseases, as this spinal segment is responsible for sensory stimuli in the stifle region, and a study has demonstrated that senior dogs with cranial cruciate ligament (CCL) ruptures have seen recovery of their stifle function with no surgical intervention after acupuncture therapy accompanied by Chinese herbal medicine for 6 to 10 months.[23]

In contrast, there is contradicting evidence from different studies to support the analgesic effects of acupuncture in canine patients with hip dysplasia. A study by G. T. Jaeger and colleagues demonstrated in a controlled double blind clinical trial in 78 dogs that the gold implantation of 24 carat gold inserted at five different acupuncture points resulted in great improvements in mobility and reductions in signs of pain compared to the placebo group, which was consistent with the veterinarian and the owners' gait assessment.[24] On the other

hand, another study involving gold implantation at the acupoints GB29, GB30 and BL54 concluded that there is no significant difference in the improvement of pain and gait in dogs with hip dysplasia treated with gold implantation compared to the control group which had the same number of non-acupuncture points of their skin punctured.[25] However, it is difficult to directly compare the results of these two gold implantation studies, as the study by G. T. Jaeger did not specify which acupuncture points were used. Another controlled study on hip dysplasia compared the effects of acupuncture, carprofen and placebo in 54 dogs with hip dysplasia showed that the owner's assessments of pain did not significantly differ between the three groups, though there were definite improvements in pain in all three.[26]

4.3.2 Acupuncture for visceral pain

Acupuncture alters blood flow in the local tissue and promotes general circulation by release of certain biochemical molecules in the body, it can be used to regulate autonomic activity, which helps promote normal functioning of the viscera, such as peristalsis and digestion, and help to decrease visceral pain.[10]

A study demonstrated in dogs that both electroacupuncture and regular acupuncture induced significant increases in bicarbonate and sodium production by the stimulation of the secretion of non-parietal cells, and also caused a marked decrease in gastric acid production, of which effects may be used to treat gastric ulcers. The study suggests the involvement of somatic afferent-visceral reflex to explain the mechanism, as this effect was completely blocked by pretreatment of a local anaesthetic or anticholinergic agent.[27] This study does not focus specifically on the pain aspect of the stomach dysfunction, but it may be assumed that improvement of excessive stomach acid production will reduce the ulcer formation and the visceral pain accompanied. Another study which evaluated the stimulation of two acupoints by observing the change in peristalsis of the duodenum in 15 beagles using Doppler ultrasonography found that the frequency of intestinal motility increased after acupuncture stimulation.[28] Again, this study does not specifically address the visceral pain aspect, but the results suggest that acupuncture may be used to treat intestinal motility abnormalities such as constipation, and by treating the disease, it may decrease the visceral pain arising from the contractions of the smooth muscle layers. Similarly, a carefully controlled study on the myoelectric activity of intestines of rats using permanent electrode implants showed a significant increase of it after acupuncture treatment, indicating increased muscular activity and peristalsis.[29]

Conversely, the intestinal motility showed a decrease after acupuncture treatment in a study, but still in favor of treating disease. The study was conducted to observe the effect of acupuncture in rats with colitis. It showed that the colonic motility and inflammation significantly decreased after acupuncture treatment at acupoint GV01 compared to the control group which included the same number of rats with colitis given acupuncture treatment at random locations that were not acupoints.[30] This study evaluated the improvement of the disease by looking at the histopathology and myeloperoxidase activity,

which can be both used as indicators of inflammation, and the results showed decreased scores of adhesion and macroscopic damage as well as significantly decreased myeloperoxidase activity in colitic rats after acupuncture treatment. The results also show that naloxone pretreatment of the colitic rats prevented these effects of acupuncture, suggesting the possible involvement of endogenous opioids in the mechanism of the acupuncture treatment.

Results of the study on colitic rats is further supported by another similar study on the colonic motility of dogs. Acupuncture on various acupoints in conscious dogs with electrode implants in the proximal colon showed that the acupoint GV01 decreased the total duration and the frequency of contractility, effectively reducing the colonic motility. However, acupuncture of 7 main Large Intestine (LI) Meridian acupoints (LI1, LI2, LI3, LI4, LI5, LI6 and LI 11) had no significant influence on the colonic motility.[31] Therefore, certain acupoints may be used to decrease the symptoms of colitis like smooth muscle spasms causing diarrhoea, dehydration and following worsening of the condition of the patient. Another study of rats with artificially induced inflammatory bowel syndrome (IBS), which is a disease causing persistent and recurrent abdominal pain, showed that electroacupuncture can be used to alleviate symptoms of IBS such as increased sensitivity to visceral pain, chronic visceral hyperalgesia, often seen in patients with IBS. In this study, IBS was induced in 8 to 21 day old rats by inserting a silica gel balloon in the descending colon, and distending the balloon twice a day for two weeks. The rats were then allowed to reach adulthood, and were tested for presence of visceral hyperalgesia by observing and scoring the abdominal withdrawal reflex after inserting a distendable latex balloon. The study suggests downregulation of NDMA receptors as the mechanism of electroacupuncture in treating visceral pain, as the immunohistochemical staining results showed increased expression of NMDA receptors in the control group, but showed no changes in the expression of the receptor in the group treated with electroacupuncture, as well as decreased scores of the abdominal withdrawal reflex in rats. However, the research team adds that in-depth understanding requires further clarification of neurobiological mechanisms.[32]

4.3.3 Acupuncture for pain management in respiratory diseases

Human studies demonstrated that acupuncture is effective for reducing both systolic and diastolic blood pressure, possibly via the mechanism of the release of the local biochemical molecules such as nitric oxide.[33] There are also several studies which have shown increased quality of life of patients with respiratory diseases after acupuncture therapy. A study, carried out by Thai researchers, demonstrated that acupuncture therapy was useful for improving heart rate variability, oxidative stress level, exercise tolerance and the quality of life in tracheal collapse patients.[34] A case study of a 5 year old female Belgian Malinois with pneumonia, published in 2022, reported that the patient was not completely cured but its quality of life was significantly improved after a treatment scheme involving various traditional Chinese therapies including acupuncture, electroacupuncture and pneumoacupuncture.[35] Another study on the effectiveness of electroacupuncture for treating reperfusion-mediated ventricular tachyarrhythmia in rats demonstrated a significantly lower incidence of ventricular tachyarrhythmia from 100% in the control group to 25% in the group with acupuncture treatment in the rats with experimental occlusion and reperfusion of the left coronary artery.[36] The acupoints used in this experiment, PC-5 and PC-6 are known to regulate heart activity and decrease cardiac pain.

4.3.4 Acupuncture for management of gingival and dental pain

Choi et al investigated the analgesic effects of electroacupuncture for treatment of dental pain in dogs compared to xylazine treatment as the control group. The treatment involved electroacupuncture in a healthy dog. Obnoxious stimuli are generated using pinching by mosquito forceps, blade and polyglycolic acid at the location between the canine and 4th maxillary premolar teeth, and the gingival area, and the analgesic effect was evaluated using the assessment of the vital signs, blood chemistry and pain scoring. The result showed that the analgesic effect by electroacupuncture was better than that of xylazine, suggesting the possibility to use acupuncture for an anaesthesia in minor dental surgeries.[37]

Kweon et al evaluated the effects of non-acupoint electrical stimulation on the dental and gingival pain of dogs. In their study, experiments were performed in anesthetized dogs, and the dental and gingival pain was measured by an electrode inserted in the digastric muscle, and noxious stimuli were generated by bipolar electrodes inserted into areas of the oral cavity. Non-acupoint electrical stimulation was delivered to the femoral triangle area, and interestingly, the results showed that low frequency electrical stimulation of non-acupoint led to decreased pain signals.[38] This study raises a very important question regarding the relevance of acupoints in electroacupuncture, as simple electrical stimulation at a random area of the body has been shown to produce analgesic effects. Further research appears to be necessary to determine whether the acupoints can enhance the effects electroacupuncture. While controlled human trials have successfully demonstrated the efficacy of electroacupuncture, such as Lei et al, which compared the treatment group to the control group with electrical stimulation at randomized non-acupoints,[39] there is a lack of strong veterinary evidence. It should be also noted that this study was carried out in human patients with Parkinson's disease, which is not an oral condition.

4.3.5 Acupuncture for management of cancer pain

There have been active research efforts to study the efficacy of acupuncture for treating cancer-related pain for different types of cancer in the last decade, and many sources agree that acupuncture have been successfully demonstrated to have analgesic effects in cancer patients. A review of evidence-based research of acupuncture for treating cancer claims that acupuncture improved the patients' condition regarding pain, discomfort, quality of life and drug associated side effects.[40] Another article on cancer treatment states that "acupuncture can be effective for relieving pain caused by cancer and may help balance the energy flow throughout the body".[41] With regard to treating pain in bone cancer, an article published in a North American veterinary medicine journal states that "acupuncture analgesia is extremely useful for pelvic, radius or ulna, and femoral bone pain in addition to cutaneous discomfort secondary to radiation therapy".[42]

Many studies use the Karnofsky Performance Status Scale (KPS), illustrated by **figure 7**, which allows the assessment of the effects of cancer treatment on their basic functional capacities. This scale does not include direct physiological pain as part of the criteria, but it may be used to make educated guesses about the degree of the life quality improvement in cancer patients, which may be used to assess emotional pain and general well-being of the patient. A study using Sa-Ahm, a traditional Korean acupuncture method in combination with herbal therapy, to treat a senile golden retriever with oral fibrosarcoma showed that the tumor necrosis began 8 months into the treatment, with the KPS at 50%, at which level the patient requires considerable assistance, and as tumor necrosis led to regression of the tumor with decreased facial selling, with the KPS increasing to 80% to 100%, at which levels the patient is able to perform normal activity with minor or no symptoms of the disease.[43]

Score (%)	State of health
100	Can perform normal activity with no symptoms of the disease
90	Can perform normal activity with minor symptoms of the disease
80	Can perform normal activity with effort, with some symptoms of the disease
70	Can carry out normal activity but cares for self
60	Requires occasional assistance but is able to care for most of personal needs
50	Requires considerable assistance and frequent medical care
40	Disabled and requires special assistance and medical care
30	Severely disabled and hospital admission is indicated
20	Very sick, hospital admission is necessary and active supportive treatment is required
10	Moribund with fatal processes progress rapidly
0	Dead

Figure 7. Karnofsky Performance Status Scale (KPS)

A study in an eight year old male Irish setter with gastric adenocarcinoma used acupuncture treatment in combination with Korean herbal therapy and conventional therapy including ampicillin, enrofloxacin, amoxicillin-clavulanic acid, famotidine, metoclopramide, and sucralfate demonstrated that the therapy reduced the size of the tumor significantly and treated the stomach ulcers completely, only leaving minor ulcerated lesions in the duodenum. The Karnofsky performance maintained at 90-95% after 120 days of therapy, indicating good quality of life.[44]

4.3.6 Acupuncture for management of postoperative pain

Many studies demonstrate the effectiveness of acupuncture for relieving post operative pain, which can be extremely severe and often requires large doses of analgesic medication such as opioids. Therefore, the use of acupuncture for this purpose may help reduce the dose of the post operative medication thus reducing the risk of the side effects as well. One study compares the effectiveness of acupuncture and morphine as a post operative pain control method in 30 dogs that all have undergone mastectomy. The post operative pain was measured using a numerical rating scale derived from a combination of several indicators of pain which were the heart rate, respiratory rate, arterial blood pressure, salivation, mydriasis, vocalization and agitation, body position and response to palpation of the incision site. **Figure 8.** Shows the criteria which was used for scoring postoperative pain in dogs.

TABLE 1 - Criteria used for scoring postoperative pain in dogs.

Observation	Criteria	Score
Heart rate	</= 10% above preoperative value	0
	11% - 30% above preoperative value	1
	31% - 50% above preoperative value	2
	> 50% above preoperative value	3
Respiratory rate	</= 10% above preoperative value	0
	11% - 30% above preoperative value	1
	31% - 50% above preoperative value	2
	> 50% above preoperative value	3
Arterial blood pressure	</= 10% above preoperative value	0
	11% - 30% above preoperative value	1
	31% - 50% above preoperative value	2
	> 50% above preoperative value	3
Salivation	Normal	0
	Above normal	1
Mydriasis	No	0
	Yes	1
Vocalization	Quiet	0
	Crying, responds to calming attempts	1
	Crying no response	2
Agitation	Asleep or calm	0
	Mild agitation	1
	Moderate agitation	2
	Severe agitation	3
Body position	Sternal and relaxed	0
	Protecting the incision site, including lateral and fetal position	1
		2
Response to palpation of the incision site	No response	0
	Mild response, looks at incision site	1
	Turns head for the incision site, mild vocalization	2
	Turns head with intention to bite, severe vocalization	3

Figure 8. Criteria used for scoring postoperative pain in dogs[45]

The results showed that the pain score did not differ between groups, and rescue analgesia was lower for the group treated with electroacupuncture.[45]

A similar study of 35 bitches undergoing ovariohysterectomy using acupuncture and micro-dose pharmacopuncture with carprofen and morphine attempted to compare the effects of carprofen or morphine as post operative analgesics. The pain score was measured after the surgery using a blind observer at1, 2, 4, 8, 12 and 24 hours post-operatively using dynamic visual analogue scale, Glasgow, Melbourne and Colorado university pain scale. Animals reaching over 33% according to the Melbourne scale receiving rescue analgesia with an intramuscular morphine injection. The study found no differences between the treatment groups with acupuncture, micro-dose pharmacopuncture with analgesics, and the control group with the conventional analgesic therapy with carprofen or morphine, concluding that acupuncture or pharmacopuncture were equally effective as morphine or carprofen for post operative pain management.[46]

Another study evaluating the analgesic effects of electroacupuncture in dogs in post operative care after ovariohysterectomy demonstrated that electroacupuncture alone or in combination with electrical stimulation at peri-incisional dermatomes led to decreased amount of postoperative opioid requirement.[47] A controlled clinical trial with 15 dogs undergoing hemilaminectomy due to acute thoracolumbar disk disease showed that during the first 12 hours, there was a significantly lower need for postoperative opioid administration in the treatment group that received electroacupuncture with conventional analgesics, compared to the control group which received only conventional analgesics, and the pain score was also considerably lower in the treatment group. However, after 12 hours the dosages did not differ significantly between groups, and the pain score did not significantly differ between groups after 36 hours of surgery, illustrating the limitations of the use of acupuncture as post operative care. [48]

5 CONCLUSION

Pain is subjective. This makes measurement of the degree of pain experienced by a dog a challenging task. There can be a number of individual factors, such as the genetic factors and stress, that may influence the degree of pain experienced by dogs even with the same age, breed, and medical condition. In case of emotional pain, we cannot judge the intensity of the feeling because of its subjectivity. To further complicate the problem, even if a group of dogs experience a pain of the same intensity, they may not display the same signs, or the signs of the same intensity. This means that individuals grouped into categories such as a particular medical condition may still have great disparity in the results, leading to inaccurate conclusions. Another challenge when it comes to the measurement of pain is that there is no technology available which allows accurate measurement the pain signalling in an animal. A few studies which are cited in this research paper measure the differences in myoelectrical activity (EMG) in order to study the effect of a modality of pain management, assuming that this activity increases with increased intensity of the pain signalling,[29] nonetheless, there is no universal set of values to accurately measure the quantity of pain. This predisposes many pain studies to errors and biases.

Nevertheless, there seems to be an abundance of evidence supporting the effectiveness of acupuncture in pain management, both in studies focusing on the measurement of analgesic biochemical molecules released in the body; and on the measurement of pain by using different pain indices. For the former, endogenous opioids have been demonstrated to play a major role in analgesia of all three parts of the nervous system (local, spinal and brain),[11] as well as regulation of various receptors and channels responsible for afferent sensory function and nociception.[11] Other biochemical molecules with analgesic effects released during acupuncture include histamine, heparin, proteases, bradykinin, tumor necrosis factor α, beta endorphins, enkephalin, noradrenaline, dopamine and serotonin, oxytocin and adrenocorticotrophic hormone.[11] In the latter studies, canine patients with musculoskeletal diseases seem to particularly benefit from acupuncture therapy, which may be explained by the acupuncture directly acting on the nerve and fascia at the location of the disease, relieving the patient of musculoskeletal and neuropathic pains which often accompany these diseases.

However, acupuncture does not seem to work as well for analgesia in all types of musculoskeletal diseases. While all four studies we have discussed for treatment of pain in IVDD patients by acupuncture or electroacupuncture have demonstrated significant improvement of pain and recovery time of the disease,[19,20,21,22,23] the results for hip dysplasia were contradicting.[24,25,26] The two studies of the three we looked at found no clear evidence that acupuncture was useful to improve pain and gait of the patients.[25,26] Another limitation rises in the studies which evaluated the effect of acupuncture for treatment of visceral pain. Firstly, there was a substantial lack of experimental data on canine patients, which made using evidence from other species such as rats was necessary for this paper.[29,30,32] Therefore, conclusions derived from such data may have limited value for canine treatment. Furthermore, few studies focused on treating the visceral pain itself via acupuncture, and most focused on the effect on the motility of the visceral wall.[28, 29, 30, 31] While one may infer that regulating the intestinal motility and therefore treating the disease will most likely improve visceral pain originating from the spasms of the smooth muscle layer, there is limited evidence for the effects of acupuncture for directly treating the visceral pain in canine patients. Lastly, A study showed that only some acupoints induced clinically significant results, and other acupoints such as the large intestine points (LI1, LI2, LI3, LI4, LI5, LI6 and LI11) in the study of colitic rats showed no effect on the gut motility, although these acupoints are supposed to primarily act at the large intestine.[31] This may be attributed to the lack of skills of the acupuncturist to stimulate an acupoint accurately, the individual anatomical or physiological differences, or the irrelevancy of the acupoints.

As for respiratory diseases, two studies claimed that the quality of life improved in canine respiratory patients after acupuncture treatment,[34, 35] and another controlled experimental study on rats demonstrated improvement of ventricular tachyarrhythmia.[36] Again, there is little data on canine patients, as well as little focus on treating cardiac and respiratory pain among the studies. Nevertheless, the quality of life was reported to be improved in the two studies which may imply decreased emotional pain and enhancement of general well-being. Unfortunately, neither of the canine studies used physiological or cardiac pain as a criterion for the quality of life assessment, and no conclusions regarding direct analgesic effects could be derived.

A study on the gingival and dental pain demonstrated significant analgesic effects by electroacupuncture, however, it did not use acupoints for electroacupuncture, raising an important question; whether electrical stimulation at a random point of the body is enough to generate the same analgesic effects or the acupoints are relevant.[38]

There is evidence that acupuncture may be used to treat cancer and cancer related pain, and all of the studies used in this literature review agreed that acupuncture was effective for tumor regression and enhancement of the quality of life of the patient.[40,41,42,43] However, no studies directly focused on treating pain caused by cancer. Instead, most studies focused on assessing quality of life using scales such as the Karnofsky Performance Status Scale.[43,44] This means while the degree of improvement of cancer patient's condition and quality of life by acupuncture therapy could be judged, accurate data on its direct analgesic effects may be insufficient. Two studies included a case review of only one patient, making it difficult to judge the exact effects of acupuncture due to the limited sample size.[43,44]

Evidence seems more convincing for the analgesic effect of acupuncture for treating post operative pain. Four controlled studies published in the Journal of Brazilian Society for the Development of Research in Surgery all agreed that acupuncture was as effective as conventional analgesics such as morphine, carprofen and meloxicam for treating post operative pain as well as for decreasing the dosages of rescue analgesia with opioids.[45,46,47,48] This knowledge may be used to use electroacupuncture in post operative care of risk patients which are usually considerably more prone to opioid side effects. However, acupuncture does not seem to be an appropriate candidate for completely replacing the conventional analgesics yet, as all of the studies had to use rescue analgesia at some point after surgery, when the effects of acupuncture alone was not enough to maintain a low pain scoring, though the dose and frequency of the rescue analgesia were significantly decreased.

Lastly, it is important to note that none of these studies were conducted at a large scale. The highest number of samples collected was only 181 dogs,[19] which assessed the analgesic effects of acupuncture for musculoskeletal and neurological patients, and there are some case studies on the same topic based on a sample size as small as 1 dog.[35,43,44] Although great effort was made to retrieve all relevant data across different databases, and carefully select the well-structured and controlled studies, there is insufficient relevant data compared to the

human studies in this field. Furthermore, many of these studies used a variety of different methods to measure pain and quality of life, subjecting them to inaccuracy and biases. Future studies in this area may improve the validity of their results by increasing the sample size, using more homogenized sample groups, for example using individuals from the same line with the same medical conditions, using accurate and standardized pain scales, using appropriate control groups, using accurate techniques for acupuncture, and finally utilizing adequate statistical models.

In conclusion, there is clear evidence to support the efficacy of acupuncture as an alternative method for pain management in various groups of diseases, and some diseases responded to acupuncture better than others. However, evidence is inconsistent across similar studies, as some studies showed that there is no analgesic effect from acupuncture compared to the control group.[25,26] Additionally, the studies have multiple limitations such as insufficient sample sizes and use of non-standardized pain scales. Accordingly, acupuncture may be recommended for pain relief and improving quality of life of canine patients with specific conditions such as IVDD, cancer and post-operative pain, but it may not be a first-choice treatment. For the best results, it is recommended to combine conventional therapy with acupuncture, and utilize various modalities such as heated needles, electroacupuncture or laser acupuncture, as different dogs or diseases may respond to one better than others. Further large-scale investigations with standardized experiment methods should be conducted to produce compelling evidence supporting the efficacy of acupuncture to treat pain in a wider variety of canine diseases.

6 SUMMARY

This literature review aims to evaluate the effects of acupuncture on pain management for canine patients. The analgesic effect of acupuncture was evaluated by reviewing relevant literature using two main indicators of analgesia; the release of analgesic biochemical molecules, and the decreased physiological or behavioural signs of pain displayed by the animal. The studies revealed that there are encouraging results suggesting analgesic effects of acupuncture in canine patients with different groups of diseases. However, there was inconsistency in the results of a few studies regarding the efficacy of acupuncture compared to the placebo and the control groups.[25,26] Limitations of the studies include the insufficient sample sizes and the use of non-standardized experiment methods. Conclusively, acupuncture may be recommended to canine patients with specific conditions such as IVDD, cancer or post-operative pain for analgesia and improving quality of life, but it may not be a first-choice treatment. For the best results it is recommendable to combine conventional therapy with acupuncture, and utilize various modalities such as heated needles, electroacupuncture or laser, as some modalities may suit some individuals or medical conditions better. Further large-scale investigations with standardized experiment methods should be conducted to produce compelling evidence supporting the efficacy of acupuncture to treat pain in a wider variety of canine diseases.

7 REFERENCES

1. Hurley JV., 1972. Acute inflammation. Edinburgh, London: Churchill Livingstone
2. Mathews, K. A., 2000. Pain Assessment and General Approach to Management. Veterinary Clinics of North America-Small Animal Practice, 30(4), pp. 729–755.
3. Gaynor, J. and Muir, W., 2015. Handbook of veterinary pain management. St. Louis, Missouri: Elsevier.
4. World Small Animal Veterinary Association, 2022, 2022 WSAVA guidelines for the recognition, assessment and treatment of pain. https://wsava.org/global-guidelines/global-pain-council-guidelines, accessed on 19 September 2022
5. Dewey, C.W., Xie, H., 2021. The scientific basis of acupuncture for veterinary pain management: A review based on relevant literature from the last two decades. Open Vet. J. pp. 203–209.
6. Wright, B.D., Acupuncture for the treatment of animal pain. Vet. Clin. Small Anim. Pract. 2019. 49, pp. 1029–1039.
7. Huntingford, J.L. and Petty, M.C., 2022. Evidence-Based Application of Acupuncture for Pain Management in Companion Animal Medicine. Veterinary Sciences, 9(6), pp. 252.
8. Kim, J., Bae, K.H., Hong, K.S., Han, S.C. and Soh, K.S., 2009. Magnetic resonance imaging and acupuncture: a feasibility study on the migration of tracers after injection at acupoints of small animals. Journal of acupuncture and meridian studies, 2(2), pp.152-158.
9. Langevin, H.M., Acupuncture, connective tissue, and peripheral sensory modulation. 2014. Crit. Rev. Eukaryot. Gene Expr. 24, pp. 249–253.
10. Fry, L.M., Neary, S.M., Sharrock, J. and Rychel, J.K., 2014. Acupuncture for analgesia in veterinary medicine. Topics in Companion Animal Medicine, 29(2), pp.35-42.
11. Zhang, R., Lao, L., Ren, K. and Berman, B.M., 2014. Mechanisms of acupuncture-electroacupuncture on persistent pain. Anesthesiology 120.
12. McDonald, J.L., Cripps, A.W. and Smith, P.K., 2015. Mediators, receptors, and signalling pathways in the anti-inflammatory and antihyperalgesic effects of acupuncture. Evidence-Based Complementary and Alternative Medicine.
13. Melzack, R. and Wall, P.D., 1965. Pain Mechanisms: A New Theory: A gate control system modulates sensory input from the skin before it evokes pain perception and response. Science, 150(3699), pp. 971-979.
14. Morton D., Albertine K., Foreman B., 2011. The Big Picture: Gross Anatomy. The McGraw-Hill Companies Inc.: New York.
15. Liang, Y., Qiu, Y., Du, J., Liu, J., Fang, J., Zhu, J. and Fang, J. 2016. Inhibition of spinal microglia and astrocytes contributes to the anti-allodynic effect of electroacupuncture in neuropathic pain induced by spinal nerve ligation. Acupunct. Med. 34, pp. 40–47.
16. Zhi-Qi Zhao, 2008. Neural mechanism underlying acupuncture analgesia. Progress in Neurobiology, Volume 85, Issue 4,
17. Hielm-Björkman, A.K., Rita, H. and Tulamo, R.M., 2009. Psychometric testing of the Helsinki chronic pain index by completion of a questionnaire in Finnish by

owners of dogs with chronic signs of pain caused by osteoarthritis. American journal of veterinary research, 70(6), pp. 727-734.
18. Reid, J., Wiseman-Orr, M.L., Scott, E.M. and Nolan, A.M., 2013. Development, validation and reliability of a web-based questionnaire to measure health-related quality of life in dogs. Journal of Small Animal Practice, 54(5), pp. 227-233.
19. Silva, N.E., Luna, S.P., Joaquim, J.G., Coutinho, H.D. and Possebon, F.S., 2017. Effect of acupuncture on pain and quality of life in canine neurological and musculoskeletal diseases. The Canadian Veterinary Journal, 58(9), pp. 941.
20. Liu, C.M., Chang, F.C. and Lin, C.T., 2016. Retrospective study of the clinical effects of acupuncture on cervical neurological diseases in dogs. Journal of Veterinary Science, 17(3), pp. 337-345.
21. Jeong, S.M. and Park, S.W., 2004. Application of traditional acupuncture on canine intervertebral disc disease. Journal of Veterinary Clinics, 21(1), pp. 49-51.
22. Yang, J.W., Jeong, S.M., Seo, K.M. and Nam, T.C., 2003. Effects of corticosteroid and electroacupuncture on experimental spinal cord injury in dogs. Journal of veterinary science, 4(1), pp. 97-101.
23. Lee, L.V., 2019. Non-Surgical Treatment for Cranial Cruciate Ligament Rupture in Senior Dogs: A Retrospective Case Series. American Journal of Traditional Chinese Veterinary Medicine, 14(1).
24. Jaeger, G.T., Larsen, S., Søli, N. and Moe, L., 2006. Double-blind, placebo-controlled trial of the pain-relieving effects of the implantation of gold beads into dogs with hip dysplasia. Veterinary Record, 158(21), pp. 722-726.
25. Hielm-Bjorkman, A., Raekallio, M., Kuusela, E., Saarto, E., Markkola, A. and Tulamo, R.M., 2001. Double-blind evaluation of implants of gold wire at acupuncture points in the dog as a treatment for osteoarthritis induced by hip dysplasia. Veterinary Record, 149(15), pp. 452-456.
26. Teixeira, L.R., Luna, S.P., Matsubara, L.M., Cápua, M.L., Santos, B.P., Mesquita, L.R., Faria, L.G., Agostinho, F.S. and Hielm-Björkman, A., 2016. Owner assessment of chronic pain intensity and results of gait analysis of dogs with hip dysplasia treated with acupuncture. Journal of the American Veterinary Medical Association, 249(9), pp. 1031-1039.
27. Zhou, L. and Chey, W.Y., 1984. Electric acupuncture stimulates non-parietal cell secretion of the stomach in dog. Life sciences, 34(23), pp. 2233-2238.
28. Chae, M., Jung, J., Seo, M., Lee, K., Nam, T., Yang, I., Yoon, Y. and Yoon, J., 2001. Ultrasonographic observation of intestinal mobility of dogs after acupunctural stimulation on acupoints ST-36 and BL-27. Journal of Veterinary Science, 2(3), pp. 221-226.
29. Tabosa, A., Yamamura, Y., Forno, E.R. and Mello, L.E.A.D.M., 2002. Effect of the acupoints ST-36 (Zusanli) and SP-6 (Sanyinjiao) on intestinal myoelectric activity of Wistar rats. Brazilian Journal of Medical and Biological Research, 35, pp. 731-739.
30. Kim, H.Y., Hahm, D.H., Pyun, K.H., Lee, S.K., Lee, H.J., Nam, T.C. and Shim, I., 2005. Effects of acupuncture at GV01 on experimentally induced colitis in rats: possible involvement of the opioid system. The Japanese journal of physiology, 55(3), pp. 205-210.
31. Kim, H.Y., Hahm, D.H., Pyun, K.H., Lee, H.J., Nam, T.C. and Shim, I., 2006. Effect of traditional acupuncture on proximal colonic motility in conscious dogs. Journal of veterinary medical science, 68(6), pp. 603-607.

32. Liu, H., Zhang, Y., Qi, D., & Li, W. 2016. Downregulation of the spinal NMDA receptor NR2B subunit during electro-acupuncture relief of chronic visceral hyperalgesia - the journal of Physiological Sciences.
33. Flachskampf, F.A., Gallasch, J., Gefeller, O., Gan, J., Mao, J., Pfahlberg, A.B., Wortmann, A., Klinghammer, L., Pflederer, W. and Daniel, W.G., 2007. Randomized trial of acupuncture to lower blood pressure. Circulation, 115(24), pp. 3121-3129.
34. Chueainta, P., Punyapornwithaya, V., Tangjitjaroen, W., Pongkan, W. and Boonyapakorn, C., 2022. Acupuncture Improves Heart Rate Variability, Oxidative Stress Level, Exercise Tolerance, and Quality of Life in Tracheal Collapse Dogs. Veterinary Sciences, 9(2), pp. 88.
35. Dragomir, M., Ardelean, A., Nadal, L.L. and Ober, C., 2022. The use of Complementary medicine and Pneumo-Acupuncture to treat muscle atrophy and chronic respiratory disorders in a dog: A case report. Cluj Veterinary Journal, 27(1), pp. 3-9.
36. Lujan, H.L., Kramer, V.J. and DiCarlo, S.E., 2007. Electroacupuncture decreases the susceptibility to ventricular tachycardia in conscious rats by reducing cardiac metabolic demand. American Journal of Physiology-Heart and Circulatory Physiology, 292(5), pp. H2550-H2555.
37. Choi, K.H., Lee, J.Y., Park, C.S., Jeong, S.M., Kim, D.H. and Kim, M.C., 2009. Analgesic Effects on the Oral Cavity by Electroacupuncture in Dogs. Journal of Veterinary Clinics, 26(6), pp. 568-573.
38. Kweon, H., Song, H.G. and Lee, S.H., 1996. The Inhibitory Effect of Low Frequency Electrical Stimulation on the Dental and Gingival Pain of Dog. Journal of the Korean Academy of Pediatric Dentistry, 23(2), pp. 525-536.
39. Lei, H., Toosizadeh, N., Schwenk, M., Sherman, S., Karp, S., Sternberg, E. and Najafi, B., 2016. A pilot clinical trial to objectively assess the efficacy of electroacupuncture on gait in patients with Parkinson's disease using body worn sensors. PloS one, 11(5), p.e0155613.
40. Ge L, Wang Q, He Y, Wu D, Zhou Q, Xu N, Yang K, Chen Y, Zhang AL, Hua H, Huang J, Hui KK, Liang F, Wang L, Xu B, Yang Y, Zhang W, Zhao B, Zhu B, Guo X, Xue CC, Zhang H; International Trustworthy traditional Chinese Medicine Recommendations (TCM Recs) Working Group, 2022. Acupuncture for cancer pain: an evidence-based clinical practice guideline. Chin Med, 17(1):8.
41. Clemmons, R.M., 1997. Integrative treatment of cancer in dogs. University of Florida.
42. Gaynor, J.S., 2008. Control of cancer pain in veterinary patients. Veterinary Clinics of North America: small animal practice, 38(6), pp. 1429-1448.
43. Choi, K.H. and Flynn, K., 2017. Korean Sa-Ahm Acupuncture for Treating Canine Oral Fibrosarcoma. Journal of Acupuncture and Meridian Studies, 10(3), pp. 211-215.
44. Choi, K.H., 2009. Treatment of a dog with gastric adenocarcinoma using acupuncture and the Korean herbal formula modified Chi Am Tang. American Journal of Traditional Chinese Veterinary Medicine, 4(2), pp. 54-61.
45. Gakiya, H.H., Silva, D.A., Gomes, J., Stevanin, H. and Cassu, R.N., 2011. Electroacupuncture versus morphine for the postoperative control pain in dogs. Acta Cirurgica Brasileira, 26, pp. 346-351.
46. Luna, S.P.L., Martino, I.D., Lorena, S.E.R.D.S., Capua, M.L.B.D., Lima, A.F.D.M., Santos, B.P.C.R.D., Brondani, J.T. and Vesce, G., 2015. Acupuncture and pharmacopuncture are as effective as morphine or carprofen for postoperative

analgesia in bitches undergoing ovariohysterectomy. Acta Cirúrgica Brasileira, 30, pp. 831-837.
47. Cassu, R.N., Silva, D.A.D., Genari Filho, T. and Stevanin, H., 2012. Eletroanalgesia para o controle da dor pós-operatória em cães. Acta Cirúrgica Brasileira, 27, pp. 43-48.
48. Laim, A., Jaggy, A., Forterre, F., Doherr, M.G., Aeschbacher, G. and Glardon, O., 2009. Effects of adjunct electroacupuncture on severity of postoperative pain in dogs undergoing hemilaminectomy because of acute thoracolumbar intervertebral disk disease. Journal of the American Veterinary Medical Association, 234(9), pp. 1141-1146.

RSITY OF VETERINARY MEDICINE, BUDAPEST
ed in 1787, EU-accredited since 1995

INTERNATIONAL STUDY PROGRAMS
secretary, student@univet.hu

Thesis progress report for veterinary students

Name of student: ..SUEYEON...KANG.....

Neptun code of the student: ....ETKZZO.....

Name and title of the supervisor: ...DR....EVA..BALOGH.....

Department:..Internal..medicine.....

Thesis title: ...The..effects..of...acupuncture..on..pain..management.....
..for...canine..patients:..A...relevant..review..based..on...relevant.....
..literature.....

Consultation – 1st semester

	Timing			Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2023	6	14	Discussion of the thesis title and topics	
2.	2023	6	18	Student thesis agreement	
3.	2023	7	15	Discussion of relevant literature	
4.	2023	8	03	Discussion of introduction	
5.	2023	8	20	Discussion of conclusion	

Grade achieved at the end of the first semester: .....5.....

Consultation – 2nd semester

	Timing			Topic / Remarks of the supervisor	Signature of the supervisor
	year	month	day		
1.	2023	9	22	First draft of thesis	
2.	2023	10	05	Discussion of relvant literature	
3.	2023	10	20	Discussion of citation and second draft of thesis	
4.	2023	10	30	Third draft of thesis	

5.	2023	11	05	Final draft of thesis	

Grade achieved at the end of the second semester: ……5……..

The thesis meets the requirements of the Study and Examination Rules of the University and the Guide to Thesis Writing.

I accept the thesis and found suitable to defence,

……
signature of the supervisor

Signature of the student: ……

Signature of the secretary of the department: ……

Date of handing the thesis in…14. 11. 2023.

I hereby confirm that I am familiar with the content of the thesis entitled

…The effects of acupuncture on pain management……
……

…for canine patients: A Review based on relevant literature

…… written by …SUEYEON KANG……

(student name) which I deem suitable for submission and defence.

Date: Budapest, ….9….day….11……month ..2023..year

Balogh Éva

Balogh Éva

……

……. Supervisor name and signature

……

Internal Medicine

……. Department