Dynamic Mechanical Allodynia—One Clinical Sign, Several Mechanisms: Five Illustrative Cases

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Abstract: Pain evoked by tangential movement across the skin is usually defined as dynamic mechanical allodynia (DMA). Some patients complain of DMA as troublesome as spontaneous pain and refer a marked interfering with activities of daily living and sleep. Pathophysiology of DMA is complex and can be related to several mechanisms, both nociceptive and neuropathic. Five exemplificative clinical cases of DMA are presented, each associated to a possible specific mechanism: injured skin DMA, peri-injured skin DMA, far injury DMA, nerve-confined DMA and fear DMA (pseudo allodynia). The identification of these subcategories of DMA can stimulate further studies aimed at evaluating the usefulness of a mechanism-based therapy for the different clinical forms of DMA.

Key Words: pain, tactile allodynia, dynamic mechanical allodynia, pain mechanisms, disability

INTRODUCTION

The International Association for the Study of Pain (IASP) defines allodynia as “pain due to a stimulus which does not normally provoke pain.”¹ Allodynia is frequently an unstable clinical sign whose biological role can change over time. When it is the consequence of an acute injury, it tends to disappear in a few hours and has a protective role by promoting healing of the injured body part.² However, when it persists for months or years after the injury, allodynia becomes disabling and may have a marked negative impact on the patient’s quality of life and sleep.

Dynamic mechanical allodynia (DMA) is a peculiar type of allodynia where the pain is evoked by tangential movement across the skin. It is also called tactile allodynia, brush allodynia, or brush-evoked pain.³,⁴ There are diseases, such as postherpetic neuralgia, in which DMA is the most important type of stimulus-evoked pain.⁵,⁶

Dynamic mechanical allodynia is probably the most enigmatic of painful symptoms, and its mechanism is largely unknown. Today, it is considered one of the prevalent characteristics of neuropathic pain⁷,⁸ and is attributed to either activation of sensitized peripheral nociceptive receptors or activation of A-beta fibers, the most important low-threshold mechanoreceptors.⁹ The aim of the present case series was to try to identify the
main clinical types of DMA and give an overview of current knowledge about the main mechanisms underlying it.

**CLINICAL CASES**

**Case 1-Injured Skin DMA**

The first case refers to a 62-year-old female who suffered a hot water burn injury while cooking at home. She accidentally spilled boiling water on her leg and complained of severe burning pain for several hours. Immediately afterward she noted several blisters on the skin and put a cold, wet towel on her painful leg, but the unpleasant burning sensation persisted for several hours. The patient presented at the Pain Unit 3 weeks after the burn with the continued complaint of an unpleasant burning sensation in her left leg, particularly while stroking the skin. The physical examination revealed red, blotchy skin without blisters and an area of DMA in the painful part of the leg (Figure 1). After specific therapies, the DMA disappeared and the burn healed with little scarring.

**Case 2-Peri-injured Skin DMA**

The patient was a 41-year-old female who complained of wound pain following a traumatic injury to the ankle. She was hit by a sharp stone during a mountain walk and went to the nearest hospital where the wound was sutured. Five weeks after the injury, she presented at the Pain Unit due to persistent pain at the ankle. The patient complained of deep joint pain during walking with worsening in the evening when the pain sometimes became spontaneous. The physical examination of the painful ankle showed a circular area of DMA (Figure 2) associated with alldynia to deep pressure and passive movement of the ankle joint. An X-ray revealed no fracture or other bone lesions. We suspected an infection and both types of pain (deep and superficial) completely disappeared after antibiotics were administered for 4 weeks.

**Case 3-Far-Field DMA**

The third case involves a male patient with congenital aganglionosis of the distal bowel (Hirschsprung disease). In 2009, at the age of 33 years, he underwent a right hemicolecction and the joining of the small intestine to the rectum to alleviate persistent and severe constipation. The operation was complicated by a visceral infection and the development of chronic pain in the right abdomen and ipsilateral dorso-lumbar region. When he was referred to the Pain Unit, the physical examination revealed severe deep and superficial alldynia with a clear DMA in the cutaneous fields of the right T9-T10-T11 dermatomes (Figure 3). Thus far this painful syndrome has been resistant to several treatments and its management remains challenging.

![Figure 1](image1.jpg)

**Figure 1.** Injured skin dynamic mechanical allodynia (DMA)—Area of DMA on the skin of a patient who suffered a localized burn to her left leg. The DMA area was virtually confined to the inflamed skin and very reproducible. The patient complained of mild spontaneous pain in the same area (case number 1).

![Figure 2](image2.jpg)

**Figure 2.** Peri-injured dynamic mechanical allodynia (DMA)—Area of DMA on the skin of a patient who suffered a penetrating injury of the skin 5 weeks earlier. The DMA area was unstable in size but showed the same circular pattern of distribution during repeated testing. The patient complained of pain during walking and inconstant spontaneous pain (case number 2).
The term far-field DMA refers to the DMA located in intact skin with an approximately dermatomal distribution but not confined to the skin territory of a peripheral nerve nor that surrounding a skin lesion. Figure 3 illustrates an intact skin area with DMA presenting the above-mentioned characteristics.

Case 4—Nerve-confined DMA
The fourth case refers to a 53-year-old woman who suffered pain after surgery for neurolysis of the superficial radial nerve. She was referred to the Pain Unit because of persistent pain in her right hand, in particular a deep pain at the wrist and a more superficial dysesthetic pain in the radial part of the dorsal surface of the hand. Her history revealed surgery for the repair of the triangular fibrocartilage complex, followed by immobilization in a cast for 7 weeks. During that period, the patient continuously complained of dysesthesia in her hand. After the cast was removed, a clinical diagnosis of radial nerve entrapment was made and surgical neurolysis of the distal superficial radial nerve was performed. Nevertheless, she continued to experience dysesthesia and thus was referred to the Pain Unit. The physical examination showed the presence of a DMA confined within the boundaries of the skin territory of the right superficial radial nerve (Figure 4). Electroneurography (ENG) confirmed persistent axonal damage of the right superficial radial nerve while a new MRI revealed an associated degenerative joint disease on the radial side of the right wrist. In addition, the neurodiagnostic skin biopsy demonstrated involvement of small-diameter fibers, confirming that the nerve lesion could not be considered a simple nerve entrapment.

5- Fear DMA (pseudoallodynia)
This case refers to a 55-year-old woman who suffered from post-traumatic pain after her left hand was crushed during work. After 3 years, the patient arrived at the Pain Unit complaining of persistent pain in her left hand and forearm. She reported pain since the trauma, with a clear lowering of the pain threshold following mechanical stimulation. A recent MRI of the hand was negative for active lesions and the neurophysiological tests were completely normal.

During the visit, the patient (with closed eyes) withdrew her left upper limb when stimulated with a brush. The distribution of this pseudo-DMA was irregular, continued to change after each stimulus and disappeared during distracting maneuvers. She started a treatment consisting in progressive exposure to mechanical stimuli and after a few weeks the pseudoallodynia completely disappeared.

DISCUSSION

Case 1—Injured Skin DMA
The decreased pain threshold in the injured skin was first described in the classic experiments of Lewis who called it “primary hyperalgesia.” When tactile allodynia is
strictly confined to a skin area with clear signs of inflammation (Figure 1), it can be attributed to the inflammation mechanisms, as clearly suggested by IASP Pain Terminology which states that the term “allodynia is taken to apply to conditions which may give rise to sensitization of the skin, for example, sunburn, inflammation, trauma.” Accordingly, DMA could easily be attributed to the sensitization of free nerve endings located in the skin, a pain mechanism usually called peripheral sensitization. There is evidence that an increased firing of nociceptors in the primary painful area induces or maintains DMA. The suggestion of a pathogenetic role of surviving sensitized primary afferent nociceptors in the genesis of DMA was confirmed by the significant worsening of DMA following topical application of capsaicin or increasing the local skin temperature.

Unfortunately, several animal studies failed to confirm this hypothesis in both inflamed tissues and neuropathies. The DMA observed at an injury site could also be explained by the development of sensitivity to mechanical stimuli in previously insensitive afferents as demonstrated in primates and in cats or by the widening of receptive fields of primary mechanical nociceptive neurons surrounding the site. This last mechanism involves the activation of silent collateral branches, leading to an increase in spatial summation and, in turn, a decrease of the mechanical pain threshold. It has been well described in monkeys and rats and seems to involve A-fibers rather than C-fiber mechano-heat nociceptors.

Although DMA occurring at the injury site has been preferentially linked to peripheral mechanisms, the lack of evidence supporting the sensitization of C-mechano-nociceptors suggests a possible role of central sensitization, a mechanism usually attributed to secondary DMA.

**Case 2—Peri-injured Skin DMA**

In humans, an extension of the DMA into the surrounding unaffected skin has been described in healthy volunteers after heat injury to the skin or intradermal injection of capsaicin. Similar extension of the DMA has been observed in patients with postherpetic neuralgia after stimulation of primary afferent nociceptors by topical application of capsaicin to the painful skin. In the case presented here, the peri-injured DMA was observed in the skin covering a deep nociceptive lesion (Figure 2).

The decreased pain threshold in the unaffected skin was called “secondary hyperalgesia” by Lewis who described this phenomenon for the first time in 1942. In recent years, most researchers have agreed on a prevalence of central mechanisms. In particular, in the event of sustained discharge of C afferent fibers following a tissue lesion, the central nervous system is constantly activated and weak stimuli acquire the property of transmitting strong messages inside and outside the lesion. This “central sensitization” is widely considered a possible cause of alldynia. As elegantly demonstrated by microneurographic recording in humans, mechanical allodynia occurring in skin surrounding the injury is sustained by unmyelinated afferents present in the injured skin, but is mediated by large-diameter fibers located in the skin surrounding the lesion. The DMA observed outside the skin lesion has been related to an enlargement of the receptive field of spinal nociceptive neurons, particularly the wide dynamic range neurons, mainly located in the deep layers of the spinal dorsal horn.
It should be underlined that central sensitization is a reversible phenomenon: when it is sustained by a specific peripheral nociceptive firing, the sensitization and related secondary allodynia disappear when the firing stops. This is probably true only for DMA and not for punctate secondary hyperalgesia, that is, the reduced pain threshold of punctate stimuli outside the site of lesion. There is indeed evidence that once the punctate secondary hyperalgesia develops, the anesthetic block of impulses traveling from the injured site is not able to significantly reduce the hyperalgesic area, suggesting that the hyperalgesic phenomena tend to persist independently from the peripheral inputs.

The occurrence of DMA in areas surrounding the lesion can be mediated via large-diameter (A-beta) fibers in different ways. Interestingly, in the case of experimental neuropathy, large-caliber afferent neurons begin to release neurotransmitters usually released by nociceptors, such as substance P and CGRP. This phenotypic switching allows these neurons to acquire some properties of nociceptors and thus to maintain the central sensitization.

Case 3—Far-Field DMA

Referred DMA (or far-field DMA) can be considered an extension of secondary DMA, with which it shares possible pain mechanisms: enhanced synaptic excitation of central (spinal) pain transmission neurons or reduced synaptic inhibition. It can be considered the clinical sign of the pathophysiological phenomenon known as “referred hyperalgesia.” This type of allodynia can be generated by noxious stimulation of tissues located far from the allodynic skin, deep tissues (muscle, viscera) included. The classic studies by Lewis described the presence of pain evoked by light cutaneous stimulation in the region of referred pain. This was confirmed in other studies on referred pain following the injection of hypertonic saline into the interspinous ligaments of volunteers. Referred DMA is believed to be sustained by central mechanisms, as supported by a body of evidence showing that cutaneous mechanical allodynia can be the consequence of sensitization of convergent dorsal horn neurons by noxious stimulation of viscera and deep tissues.

Several clinical conditions are characterized by far-field DMA, and it is well known that diseases involving deep tissues can generate DMA. A common example of this type of DMA is headache, particularly migraine and cluster headache.

Case 4 Nerve-confined DMA

Allodynia and hyperalgesia are commonly considered characteristic signs of neuropathic pain (for a recent review see Jensen and Finnerup). In particular, DMA has been observed in patients with different neuropathic pain conditions that can be caused by several mechanisms (for a recent review see Cohen and Mao). Interestingly, neuropathic pain mechanisms can involve not only neurons but also glial cells, as demonstrated by animal studies showing that experimental neuropathic pain induces an important (micro) glial activation resulting in an hyperexcitability of the dorsal horn.

According to the new definition of neuropathic pain and the proposed grading system, neuropathic pain conditions are characterized by a pain distribution corresponding to the topographic representation of a peripheral innervation territory or of a body part in the CNS. When the DMA is confined inside a neurological skin territory, it cannot be included in the previous definitions and the term neuropathic DMA can be used. Indeed, given that the activation of unmyelinated fibers is mandatory for the development of secondary allodynia, the evidence of allodynia strictly confined to the cutaneous field of a lesioned nerve (neuropathic allodynia) cannot be attributed to the activation of small-caliber fibers. In other words, if the latter were involved in the genesis of this form of DMA, the area of allodynia would exceed the nerve skin territory. Hence, neuropathic DMA is strongly suggestive of a selective dysfunction of large-diameter fibers. There is good evidence that C-nociceptors are not always involved in DMA. For example, (1) the flare response, a typical sign of C-nociceptor activation, is rarely observed in the allodynic skin; (2) DMA rarely occurs in patients with small-fiber neuropathy, a frequently painful neurological disease characterized by the loss of small-diameter nerve fibers; (3) epidermal innervation which is represented only by small-diameter fibers does not correlate with brush-evoked pain intensity in the cutaneous area of DMA in patients with postherpetic neuralgia. Therefore, mechanisms other than C-nociceptor sensitization must be invoked as possible mechanisms of neuropathic DMA. It is important to underline that the involvement of large-diameter fibers is clearly compatible with the redefinition of neuropathic pain as “pain arising as a direct consequence of a lesion or disease affecting the somatosensory system.” The somatosensory system is indeed composed of the
spino-thalamic tract and the lemniscal system, the latter being the large-diameter fiber system.

Despite “cultural resistance” to acceptance that pain can be evoked by the activity of low-threshold afferents, this hypothesis is progressively being accepted by pain researchers and the term “A-beta pain” has been coined.24

Microneurographic recordings have elegantly demonstrated in humans that in the case of myelin damage without axonopathy the gentle stimulation of low-threshold mechanoreceptor terminals located in the receptive field of the lesioned neurons can trigger a multiplication of ectopic impulses generated at the lesion site. This abnormal pattern of nerve firing was observed in patients with documented peripheral neuropathy and positive sensory symptoms.44,45

Finally, the results of several animal and human studies suggest that tactile allodynia can be carried by large myelinated fibers.46–48

Case 5—Fear DMA (pseudoallodynia)

We coined this term to identify the disproportionate withdrawal of the painful part of the body during any maneuver representing a potential stimulus. This avoidance behavior is frequently seen in patients who experience the so-called “fear of pain.” It is actually a sort of “pseudoallodynia” because there is no pain, only fear of it. This condition is known to influence several painful conditions and could have an important role in the development of pain-related disabilities and the transition from acute to chronic pain.49 To differentiate true allodynic conditions from enhanced hyperprotective responses, it is important to realize that some patients in pain develop a strong fear of painful stimuli that can be confused with severe allodynia. In this situation, any attempt to touch the painful part of the body induces an enhanced response aimed at avoiding any kind of stimulus. In our experience, if the patient is sufficiently reassured during the examination, this “pseudoallodynia” can disappear, at least for a period of time.

Although avoidance behavior has a protective role in acute painful conditions, it becomes a maladaptive response if allowed to persist. Avoidance behaviors have been closely associated with catastrophic belief in the so-called “fear-avoidance models”50,51 currently considered an important cause of the disabilities observed in chronic pain patients.49

CONCLUSIONS

Dynamic mechanical alldynia is a sign of several pain syndromes and cannot be considered a pathognomonic sign of neuropathic pain. Although this imprecise concept has slowly been corrected by some researchers and opinion leaders, the idea that any pain evoked by tactile stimulation is neuropathic persists in the thinking of many pain physicians. In this case series, we have tried to underline that, in the clinical setting, DMA shows a wide variability that frequently misleads the physician in the interpretation of the patient’s clinical picture. In addition, we have tried to emphasize that there are several mechanisms, both nociceptive and neuropathic, able to induce and sustain DMA. Finally, no less important is the necessity that physicians be aware that a fear-related “pseudoallodynia” exists and that it is important to recognize and deal with it appropriately. The 5 types of DMA described herein, each associated with a possible specific mechanism, can stimulate further studies aimed at evaluating the usefulness of a mechanism-based therapy for the different clinical forms of DMA.

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