The effect of divided and directed attention on the magnitude of spatial summation of pain

Michał Katra[1], Wacław M. Adamczyk[1]

[1] Laboratory of Pain Research, Institute of Physiotherapy and Health Sciences, The Jerzy Kukuczka Academy of Physical Education, Katowice, Poland

Correspondence to: Michał Katra, email: michal.katra1@gmail.com

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Abstract

Background: Spatial summation of pain (SSp) is observed when the experienced pain intensity increases when the painful area enlarges. Despite many years of research on SSp, the effect itself and its clinical relevance are still not fully understood.

Aims: This narrative review article focuses on the effect of SSp as a physiological mechanism as well as the procedure for assessing pain modulation in humans. In particular, a line of research on the moderating effect of attention on SSp is presented and discussed.

Summary: So far, studies on SSp have shown promising outcomes for pain reduction and pain diagnosis in patients experiencing widespread pain. When attention manipulation procedures are used in the context of the area of pain, a hypoalgesic effect can be observed. This effect, combined with other techniques targeting the somatosensory system, can contribute to developing comprehensive sensory-discriminative training aimed at reducing pain.

Key words

spatial summation, pain, cold pressor, attentional modulation, receptive fields.

Introduction - pain

In the medical community, pain is one of the most commonly reported symptoms that patients report [1–3]. An in-depth diagnosis, based on subjective and physical examination, enables precise therapy selection to improve function and reduce or completely eliminate the pain [4]. Pain is a subjective sensation that is significantly influenced by biological, psychological, and social factors [5,6]. This concept is reinforced by the International Association for the Study of Pain (IASP) established definition of pain: "An unpleasant sensory and emotional experience associated with, or resembling that associated with actual or potential tissue damage." [6]. This definition indicates the important role played by the central nervous system (CNS) and cognitive factors in the experience of pain [7].

Mechanisms of pain formation

Based on the modern taxonomy of pain, three primary mechanisms of pain can be distinguished, characterized by different pathogenesis: neuropathic, nociceptive, and nociplastic [8,9].

The concept of nociplastic pain has been introduced relatively recently, and the underlying biological conditions are not fully understood. It is defined as pain resulting from information processing dysfunction in the nervous system, despite the absence of damage to tissues and structures of the somatosensory system, whose activity in the case of primary damage leads to the sensation of pain. This may indicate the existence of pain as a condition rather than a symptom resulting from actual or potential tissue damage [10]. The idea behind the new classification system was based on findings from studies of "nonspecific" pain syndromes, such as fibromyalgia, tension-type headache (TTH), or irritable bowel syndrome (IBS) [8,11].

Neuropathic pain is a consequence of direct damage to the structures of the nervous system or infection involving elements of the somatosensory system. Examples of complaints on the neuropathic pain spectrum are those associated with cancer, diabetic neuropathy, phantom pain, or spinal cord injury (SCI) [12]. Nociceptive pain results from actual or potential tissue damage, excluding nervous system tissues. Due to the subject matter of this article, this pain mechanism will be discussed in detail. The mechanism of nociceptive pain is based on four sequentially mentioned stages: transduction, transmission, modulation, and perception [13].

The initial stage (transduction) is the process of converting a nociceptive stimulus into an electrical impulse. As a result of the irritation of nerve endings, such as by stimuli of a thermal or chemical nature, they are activated, and the energy of the stimulus is converted into an electrical impulse. The next stage (transmission) is the process of conducting the resulting electrical impulse to the posterior (dorsal) horns of the spinal cord and the higher levels of the CNS. This is possible via two types of nerve fibers, which are protrusions of the I nociceptive neuron located in the posterior medullary ganglion: the Aδ (A-delta) fiber and the C-fiber [14]. Myelinated Aδ fibers form receptive fields with a relatively small surface area, so the patient is usually able to pinpoint a painful spot on the body, such as from a sting or blow. Due to their myelinated sheath, these fibers conduct nerve impulses at a speed of about 12-30 m/s [13]. Stimuli conducted by these fibers can lead to primary, sudden pain with precise localization, which subsides with the extinction of the nociceptive stimulus. Type C fibers do not have a myelin sheath and, therefore, conduct impulses much more slowly, i.e., about 0.5-2 m/s. They form extensive receptive fields of a "cross-linked" nature, and as a consequence, the patient has difficulty localizing the site of pain with accuracy. As a result of irritation of receptors located on sensory nerve endings, the stimulus is conducted toward the posterior horns of the spinal cord, where information about damage or potential damage is transmitted to the higher levels of the CNS via ascending tracts: the spinal-thalamic anterior and lateral tracts [13].

Both tracts intermingle in the brainstem and switch in the ventral posterolateral thalamic nucleus (VPL), from where projections are further transmitted to the primary and secondary somatosensory cortex. These centers are primarily responsible for processing sensory aspects of nociception, such as its peripheral location and stimulus intensity. Pain is modulated in the midbrain and the medulla oblongata. Descending pathways responsible for inhibiting or pacing pain in the spinal cord begin in these structures. Located in the midbrain, the periaqueductal gray matter (PAG) and the rostral ventromedial medulla (RVM) play the most significant role in inhibiting pain through descending pathways. Modulation involves the stimulation, inhibition, and summation of irritant stimuli. The final component of nociceptive pain formation is perception itself, occurring in the quaternary sensory neurons of the cerebral cortex. At this stage, there is a conscious sensation of pain, an evaluation of its intensity of emotional expression, and a possible change in behavior [13,14]. Further information processing involves the structures of the amygdala and hypothalamus, the insula, and the cingulate gyrus, the anterior part of which is involved in the formation of the affective aspect of pain [15,16].

From the above description, it is clear that pain is a complex experience. Despite numerous studies on its mechanisms, factors such as pain "radiation," spatial summation, and the influence of attention on pain sensations remain poorly understood [17–23].

Spatial summation of pain

From a neurophysiological point of view, spatial summation of pain (SSp) is a well-studied process of stimulus integration at the cellular level of nociceptive neurons [24] and in relation to sensory systems such as the somatosensory system (perception of touch, pressure, temperature) [25–27], auditory [28] or visual [29]. Summation occurs when subliminal stimuli stimulate the same neuron, leading to its generation of an action potential [30–32]. Interestingly, spatial summation also applies to pain perception itself, not limited to summation in the Sherringtonian meaning. Research on pain indicates an increase in its severity, with an increase in the irritated area of the body. This effect has been observed and successfully replicated in numerous laboratories but is still poorly understood, especially regarding the factors affecting the magnitude and efficiency of the summation itself [17,20,21,23,33,34]. An important fact is that the SSp effect is equally strong within the nociceptive stimulation of a single dermatome, as well as when stimulating the surfaces of adjacent dermatomes, indicating the integration of nociceptive information in supraspinal centers [27]. Studies on SSp have shown that this phenomenon may depend on a number of factors, such as the efficiency of local stimulus integration, the type of stimulus, and the afferent fibers mediating the effect (Aδ or C fibers) [22].

Previously published studies indicate that SSp can be induced by two independent mechanisms: an increase in the area of nociceptive stimulation or as a result of an increase in the distance of the nociceptive stimuli located, however, close enough for the phenomenon to occur at all. Concerning the paradigm, depending on the size of the area subjected to nociceptive focus stimulation, the SSp phenomenon can be observed when, as the area increases, the intensity of pain experienced increases [20,34-36]. This is due to the integration of stimuli by stimulated nociceptive neurons in the area of their receptive fields (RF) [37]. A second, separate mechanism can occur when the number of nociceptive stimuli and the distance between them are increased [17,33,37]. Price et al. [37] showed that this is related to the mechanism of recruitment of nociceptive neurons located within stimulated sites, leading to sensory integration from a larger neuronal pool, resulting in the intensification of pain. It is worth noting that increasing the spatial separation of the stimuli (at 0cm, 5cm, and 10cm) did not significantly affect SSp and pain intensity, while the qualitative and quantitative stimulus evaluation abilities of the participants in this study were altered.

For SSp dependent on the distance of nociceptive foci, an important factor is the use of adequate separation between foci. Optimal separation is necessary to induce summation. An excessive separation can induce pain inhibition due to the "pain through pain" inhibition mechanism, which is underpinned by Diffuse Noxious Inhibitory Control (DNIC) of irritant stimuli [19].

Effect of attention on the spatial summation of pain

In many sensory modalities, the processing of afferent stimuli is modulated by attention and its manipulation procedures, causing a change in sensory experience. For example, in a study conducted by Quevedo and Coghill [23], pain induced by nociceptive stimuli 10 cm apart (skin temperature stimulation 49°C) was evaluated. Participants were asked to rate pain based on three techniques that engaged the subjects' attention differently. Namely, an overall assessment of pain from both nociceptive foci (SSp condition) and divided and focused attention techniques. In the divided attention technique, subjects were tasked to evaluate separately the pain induced by two stimuli, one after the other. In contrast, during the directed attention procedure, subjects were tasked with assessing pain intensity from one nociceptive focus only, ignoring the other. As a result of the attention manipulation, a significant effect of the divided attention effect was observed in abolishing the SSp phenomenon and reducing pain intensity. The focused attention procedure did not result in a statistically significant reduction in pain despite the lower pain scores obtained when compared to the overall technique, i.e., overall pain assessment from the two areas stimulated simultaneously.

A similar effect of reducing pain intensity due to the introduced attentional targeting procedure was observed in a study by Defrin et al. [19]. The subjects evaluated pain intensity as a result of thermal nociceptive stimulation using two stimulators, with one located 5 or 30 cm apart. The authors observed spatial summation due to simultaneous stimulation with stimuli 5cm distant from each other ($p < 0.05$). However, the summation was not as strong when the stimulators were 30cm apart. In another part of the same study, participants were asked to rate pain only from one stimulated body area, ignoring the other. While the attentional focus condition had no effect on SSp inhibition when the pain being assessed was 5cm distant from the other painful area, the pain was reduced when the distance was 30 cm.

The attention of a subject to a nociceptive stimulus can be a factor modulating pain through changes in the size of the receptive field (RF) of nociceptive neurons subjected to stimulation [23]. Studies suggest that pain intensity can be modified by the manipulation tasks of the subject's attention. For example, electrophysiological recordings conducted on animals [38] indicate that attention can influence the expansion or shifting of the receptive fields of spinal cord neurons such that they begin to respond to nociceptive stimuli located on the contralateral side. Pain intensity can be enhanced by using tasks that require the integration of nociceptive information from large areas of the body. The opposite factor would be the use of tasks requiring spatial discrimination of stimuli, which could reduce pain intensity.

Previously published studies on the effects of attentional manipulation on the SSp phenomenon have relied exclusively on nociceptive stimulation with spatial separation of stimuli. In the study conducted by Adamczyk et al. [39], subjects were subjected to nociceptive stimulation within a single, extensive area of the body (the hand). The procedure was conducted using the Cold Pressor Task (CPT) paradigm, which involves the use of low-temperature water (5°C) to induce SSp. Forty participants (N=40, 20 women) took part in the experiment. The core of the study consisted of three cold water hand immersion techniques. Prior to the test, a line separating the two segments was drawn on the palmar part of the subjects' hand. During the procedure, subjects immersed only the radial segment, the ulnar segment, or both segments simultaneously (SSp), and rated the intensity of pain (0-100 scale). During the divided attention condition, subjects immersed the entire arm and rated pain intensity from both segments sequentially, one after the other. In contrast, subjects rated pain intensity from only one segment in the directed attention condition. The results of the study confirmed both a pronounced effect of inducing SSp ($p<0.001$) and complete abolition of SSp in the condition with divided attention ($p<0.001$) and targeted attention ($p<0.001$). This indicates that both targeted or divided attention to a nociceptive stimulus can be used to transform a person's pronociceptive profile into an antinociceptive, pain-inhibiting profile [19,23]. Namely, when subjects divide their attention between nociceptive stimuli, they reduce the integration of receptive fields to assess each stimulus more accurately. The result can be an abolition of SSp and a reduction in perceived pain [19,23,39].

The results described here are conceptually relevant to understanding the mechanisms that modulate pain. Previous studies on the effects of attention manipulation in the context of SSp have mainly used a thermal stimulus based on high [19,23] and low temperatures [39]. From a scientific point of view, it is necessary to conduct further studies on this phenomenon using other modalities, more subjects, or attention manipulation procedures within the stimulated area (both for the SSp paradigm dependent on the area of action of the nociceptive stimulus and the number of nociceptive stimuli). Indeed, the paradigm of obtaining SSp through high-temperature thermal stimulation [19,23,27,34,37] is as successful as other studies that have used compressive stimuli [21], electrical stimuli [17,40] and low-temperature stimulation [21,35,36,41]. In addition, conducting studies on groups of patients with different forms of pain may also contribute to a better understanding of the mechanisms of the SSp effect and the influence of attention on this effect.

Attempts to replicate the study design using the aforementioned elements could provide key reports on the impact of using targeted and divided attention on SSp. This would expand the research findings and bring the implications of the results closer to clinical practice. Therefore, further research in the area of attention manipulation relative to the pain focus offers promising possibilities for a "targeted" hypoalgesic effect.

Clinical implications

The effect of SSp is clinically significant, especially for patients suffering from chronic and widespread pain. Nociceptive stimuli from extensive areas of the body can lead to uncontrolled, increasing pain and its spread over time [42], significantly affecting the patient's psychophysical state [43]. Interestingly, the summation effect, being strongly influenced by the attention of the subject/patient, can have important implications for diagnosis and therapy. A patient who focuses only on the strongest pain focus may "underestimate" the proper (usually higher) pain intensity level. The consequence of which it is possible to make a misdiagnosis of both the location and severity of the pain, which can ultimately imply the implementation of an inappropriate form of therapeutic management. Inadequate treatment can, in turn, prolong the recovery process [44]. A key element in such a case may be the introduction of a procedure of focused attention (on the foci/focal point/s of pain), with the aim of precise diagnosis within the extensive pain site [39].

The results discussed in this paper, indicating a reduction in pain intensity under the influence of attention manipulation, offer the prospect of developing new therapeutic methods based on so-called sensory-discrimination training [45]. In this training, patients are presented with stimuli (mainly tactile) that are subjected to discrimination, e.g., the patient/caregiver makes a decision on the location of the stimulus. Such tasks enriched with targeted or directed attention to pain can contribute significantly to developing effective therapeutic protocols [46].

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