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Neck related arm pain: clinical scenarios to differentiate the underlying IASP-defined pain mechanisms

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Abstract

Neck related arm (i.e.understand upper limb) pain is a common clinical scenario in which the underlying pain mechanisms are not well understood. Neck pain radiating to the arm is not always related to nervous system injury or disease of the (neuropathic pain) but may also be nociceptive (referred) or even nociplastic pain. Unfortunately, patients with such a spatial distribution of pain are often given different diagnoses (e.g., "cervicobrachialgia", "cervicobrachial neuralgia", "cervicobrachial pain syndrome", "cervical radiculopathy"). The confusion associated with these diagnostic terms leads to difficulties in clinical reasoning. So, it seems essential for clinicians to understand and recognize the predominant mechanisms of pain. Three different clinical scenarios present patients with the same spatial distribution of pain but with different predominant pain mechanisms. In the scenarios, subjective and objective examinations are performed to describe and highlight the predominant pain mechanisms that can be related to neck and arm pain: nociceptive, neuropathic and nociplastic. Clinicians should also be aware that the predominant pain can change over time.

Introduction

Neck pain ranks third in Belgium in terms of years lived with disability and sixth worldwide [1]. Neck pain has a high lifetime prevalence (22-70%) and increases in women in the fifth decade of life [2-4]. More importantly, the overall epidemiology of neck pain does not appear to have changed substantially over the past 30 years [5]. Neck pain which is an unpleasant sensory and emotional experience that is or appears to be associated with actual or potential tissue damage in the neck region [6, 7], can be transmitted to the arm via somatic structures [8-11] or neuropathic mechanisms [12, 13]. In these cases, the pain is defined as "cervicobrachial pain" or "cervicobrachialgia", "cervicobrachial neuralgia",

"cervicobrachial pain syndrome", "cervical radiculopathy"). These terms do not describe the underlying pain mechanism, which can be confusing for clinicians and patients. Indeed, a similar clinical picture may underlie different and overlapping pain mechanisms (see Figure 1) [14, 15]. Clinical reasoning is required to recognize the scope of biological and psychosocial factors that need to be assessed and to analyze their involvement in the patient's clinical presentation to individualize the patient's management. Although there is no definitive list of essential clinical judgments including personal and environmental contributing factors [16], [17] have proposed general categories of judgment important to incorporate in all reasoning process. For example, to better understand what we propose to call neck related arm pain (NRAP), it is important to understand the underlying pain mechanisms. Here, arm must be understood as upper limb anatomical region that consists of the upper arm, forearm, and hand.

In this article, we will attempt to clarify and describe the underlying predominant pain mechanisms of NRAP as defined by the International Association for the Study of Pain [18]. Differentiating predominant neuropathic pain from referred nociceptive pain or even nociplastic pain is a clinical challenge but we hope that by using three different clinical scenarios, we can help clinicians to gain more insight into the distinction between the three predominant IASP-defined pain mechanisms.

What are nociceptive, neuropathic and nociplastic pain mechanisms?

Nociceptive pain

The IASP defines nociceptive pain as "pain that arises from actual or threatened damage to nonneural tissue and is due to the activation of nociceptors." [18]. Nociceptive pain can occur when a potential noxious stimulus activates the nociceptors of innervated structures. For example, noxious stimulation of the zygapophyseal joints, spinal ligaments, muscles, or the outer portion of the cervical intervertebral disc is converted into a nociceptive (electrical) signal in the nervous system by transduction. This warning or danger signal is processed in the central nervous system with potential significant brain excitations [19], which may lead to a sensation of pain [14]. In nociceptive pain, the somatosensory nervous system functions normally [14]. However, often described as more localized pain, some patients with neck pain also experience symptoms in the arm, in a region that is topographically distinct from the nociceptive source [6, 9, 10]. This phenomenon is called nociceptive *referred pain* and could be explained by the convergence of nociceptive afferents on second-order neurons [20]. Most often, pain is perceived in regions that share the same segmental innervation. In addition, nociceptive referred pain may extend to the hand in some cases [10].

Neuropathic pain

The IASP defines neuropathic pain as "pain caused by lesion or disease of the somatosensory nervous system" [18]. The most common cause of neuropathic pain in patients with neck pain is related to injury or disease of the peripheral nervous system (e.g., root compression) [14]. The nervous system is affected by the generation of ectopic discharges that bypass transduction [14] and can impair nerve function and lead to sensory and motor deficits .

When describing neuropathic pain, symptoms are often characterized by specific neurological symptoms, such as positive sensory signs (hyperalgesia and/or allodynia) and negative sensory signs (loss of function) [21], and patients often report that pain is lancinating, burning and accompanied by unusual tingling, crawling, electrical discharge, stabbing, or shooting in the arm [14, 22, 23] and radiates downward with a specific radicular distribution [24], however extra dermatomal pain is common [13, 25]. Neuropathic pain is also characterized by spontaneous (occurring without physical stimulation) [26], evoked (abnormal responses to stimuli) [27] or paroxysmal (suddenly recurring and intensified) pain [22]. Symptoms can be intense at specific sites and these are not necessarily proximal [13]. Therefore, some authors use the criterion "arm pain worse than neck pain" which seems to have a high specificity (81%) [28]. While there is currently no standardized approach, neuropathic pain is usually identified using clinical criteria [29, 30]. The diagnosis of neuropathic pain is difficult to make in the firstline care, but certain elements of the subjective
examination can lead the clinician to hypothesize the presence or absence of neuropathic pain. No single element is pathognomonic but pooling the elements from the subjective and then objective examination is the best way to increase the chance of a correct diagnosis [13, 31].

Nociplastic pain

The IASP defines a third category, nociplastic pain, which is described as "pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain" [18]. Indeed, in a person with nociplastic pain, symptoms do not "fit" the known neuroanatomical patterns, and symptom behavior do not follow the usual patterns of increasing and decreasing symptoms with periods of movement and rest (i.e., stimulusdependent pain). Pain is often experienced as diffuse and rarely confined to an anatomical reference pattern [21, 32]. In contrast, pain can occur completely independent of the stimulus (i.e., good days and bad days, regardless of what the person is doing that day), or even after a stimulus that is normally "non-noxious" (i.e., allodynia). Kosek et al. (IASP Terminology Task Force) have described an algorithm to help clinicians identify nociplastic pain [33]. Although this algorithm (grading system) is still a work in progress, the following criteria must be met to classify nociplastic pain: pain duration is at least 3 months, pain is more regionally than locally distributed, pain cannot be entirely explained by nociceptive or neuropathic mechanisms (sensory deficits are not uncommon in non-dermatomal and non-nervous areas of distribution, with generalized hypersensitivity) and there is clinical signs of pain hypersensitivity in the pain region [34]. Mental health problems affect most individuals. Cognitive symptoms, insomnia, and fatigue are common. Nociplastic conditions have a high co-prevalence rate with other chronic pain conditions such as spinal pain, arthritis and headaches [32].

To get a better insight into the distinction between nociceptive, neuropathic and nociplastic pain, we will use three clinical cases (see Figure 1) covering the theoretical aspect of a subjective (SE) and objective examination (OE).

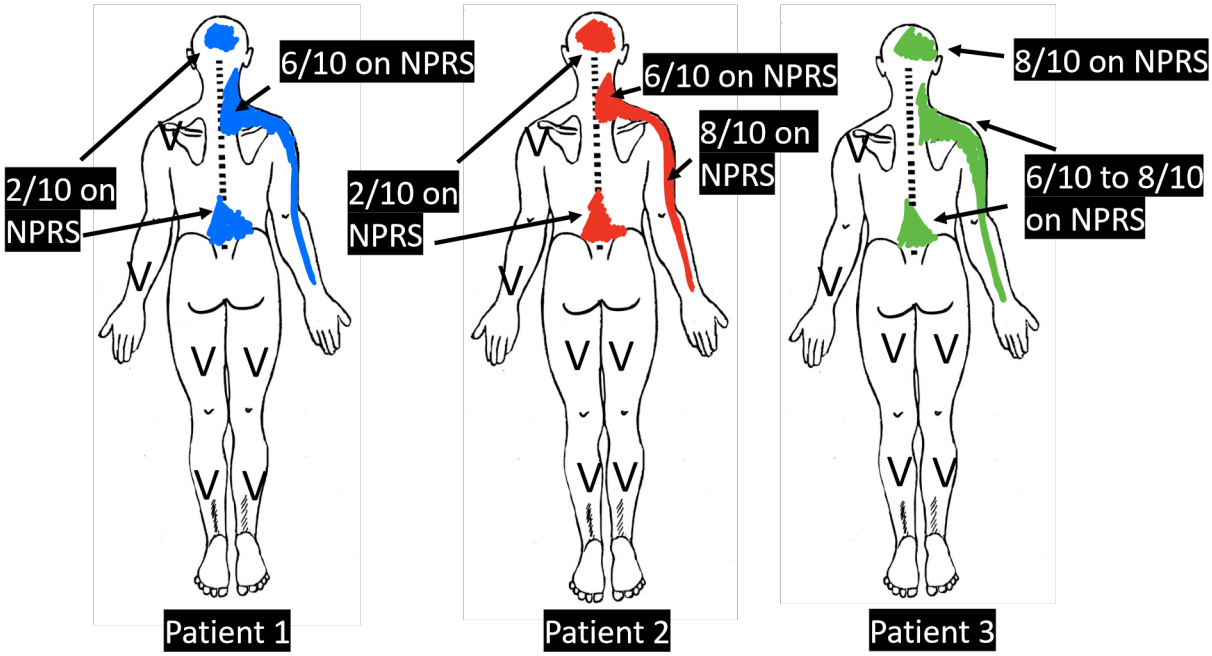

Figure 1. Description of the three body-charts with a spatial distribution of pain that appear similar. NPRS= numerical pain rating scale. V= no pain.

Subjective Examination (SE)

Clinical reasoning for diagnosis or problem classification is based on categories of hypotheses [17] and on the predominant mechanism of pain. The main problem, circumstances and symptoms described by a patient are the first step in hypothesizing the predominant pain mechanism. It is important to listen carefully to patients because the words used to describe neuropathic, nociceptive [29] and nociplastic pain can differ [15, 33-35]. As the management of pain differs depending on the underlying pain mechanism [29, 31], it is essential for clinicians to differentiate neuropathic pain from nociceptive and nociplastic pain [27, 28, 36]. Clinicians should be aware that pain in the arm, is not always due to nerve root or peripheral nervous system injury or disease [10]: somatic sources for CBP symptoms were reported in 80.1% of the cases [37]. In the following section, we detail how the predominant mechanisms of neuropathic pain can be distinguished from the other two mechanisms and hypothesize how this can be done, as it depends on considering a combination of characteristics [21].

Interpretation of subjective examination

When asked to describe the pain, Patient 1 states that the pain is acute, localized mainly in the neck and radiating into the arm and forearm to the hand (6/10 on numerical pain rating scale (NPRS)). The pain is described as dull and sharp. The pain intensifies in all seated positions (working at a computer or watching television), especially in positions where the cervical spine is extended [38, 39]. Pain increases when the patient turns the head to look to the right and/or upward. Patient 1 noted that the

intensity of the pain decreases rapidly, especially when he avoids moving his head too much (e.g., by standing more upright while working at the computer). Patient 1 also mentions low-back pain and headaches (2/10 on NPRS) on some days, but these pains are not currently present and are only related to long car trips. The presence of proportionate and distinct symptoms, associated with clear local, mitigating and aggravating factors and the fact that Patient 1 does not describe any negative or positive neurological symptoms may suggest the hypothesis of a predominant ***nociceptive pain mechanism*** [38, 39].

When Patient 2 is asked to describe the pain, he mentions acute pain (6/10 on NPRS) in the neck that radiates into the arm (8/10 on NPRS) with sensations of burning, tingling and vague pins and needles in the arm. The patient also states that these sensations tend to increase with increasing pain in the neck and shoulder [40]. Patient 2 also mentions low-back pain (2/10 on NPRS), but its intensity is highly dependent on physical activity. Patient 2 also describes recurrent headaches (2/10 on NPRS), which have increased since the onset of this episode of neck pain [21]. Regarding aggravating or relieving factors, the patient states that the pain worsens quite quickly when he is working at the computer (sometimes shooting pain). However, the pain is easily provoked in many situations without a clear trigger, which leads him to describe the pain as "unpredictable" and "it can recur spontaneously". Another key characteristic is that it takes longer for the pain to decrease. The description of symptoms and the presence of positive neurological signs may support the hypothesis of a predominant ***neuropathic pain mechanism*** [41, 42].

When asked about pain, Patient 3 states that he has been suffering from pain in his neck for more than a year, radiating to the arm and now accompanied by severe low back pain (6/10 to 8/10 on NPRS). The patient also suffers from regular headaches (3 to 4 times per week) (8/10 on NPRS). According to the patient, pain intensity is unrelated to aggravating factors, such as activities, and is variable or inconsistent. Sometimes it is associated with movement or activities, but not always, and other times it is associated with stress activities. Turning the head to one side may be more painful, but the patient cannot tell if it is always on the same side. Patient 3 feels that the arm is sometimes heavy and he feels a vague sensation. He also mentions difficulty concentrating, sleep disturbances, chronic fatigue, and that pain varies greatly in intensity and location without knowing why [21, 32]. The presence of chronic, disproportionate,inconsistent and imprecise answers to questions related to the symptom's behavior and without clear neurological symptoms may give rise to the hypothesis of a predominant ***nociplastic pain mechanism*** [21, 32] .

Although the subjective assessments of Patients 1, 2 and 3 provide useful information to hypothesize about the predominant mechanism underlying the "pain mechanism", this is not sufficient to draw a definitive conclusion about the pain mechanism. As part of clear hypothetico-deductive clinical reasoning [43], elements of the Objective Examination (OE), such as neurodynamic and neurological testing, are essential to further test the hypothesis established at SE and guide the clinician toward a differential diagnosis.

Self-completion questionnaires with, or without limited clinical examination [22, 44-46] (e.g., DN4, LANSS, PDQ) have been developed as part of the ES to determine the presence of neuropathic pain, each with disease-specific discriminatory characteristics [47]. The '*Douleur Neuropathique en 4 questions*' (DN4) questionnaire (sensitivity 83%; specificity 90%) [46] was developed to differentiate neuropathic pain from nociceptive pain and appears to have specific discriminating. The short DN4 questionnaire contains 10 items, which yield a score that, if greater than or equal to 4, indicates that

187 the hypothesis of neuropathic pain could be considered. Seven items are used as self-report
188 questionnaire on sensory descriptors and 3 items are scored based on the OE. The speed and ease of
189 administration of a questionnaire such as the DN4 make it a valuable complementary tool for clinicians.
190 However, questionnaires should not replace a detailed subjective and objective examination. Although
191 many screening tools have good sensitivity and specificity, they are reported to fail to diagnose 10–
192 20% of patients with neuropathic pain [47]. To provide clinicians indication of nociplastic
193 predominance, as previously mentioned, the IASP clinical criteria and grading system [33] and also the
194 Central Sensitization Inventory questionnaire (CSI) (sensitivity of 81% to 82.8% and a specificity of
195 54.8% to 75%), could be used to quantify it [34, 48].

196 The list of the most common clinical descriptions of nociceptive, neuropathic and nociplastic pain
197 expressed by patients is shown in Figure 2.

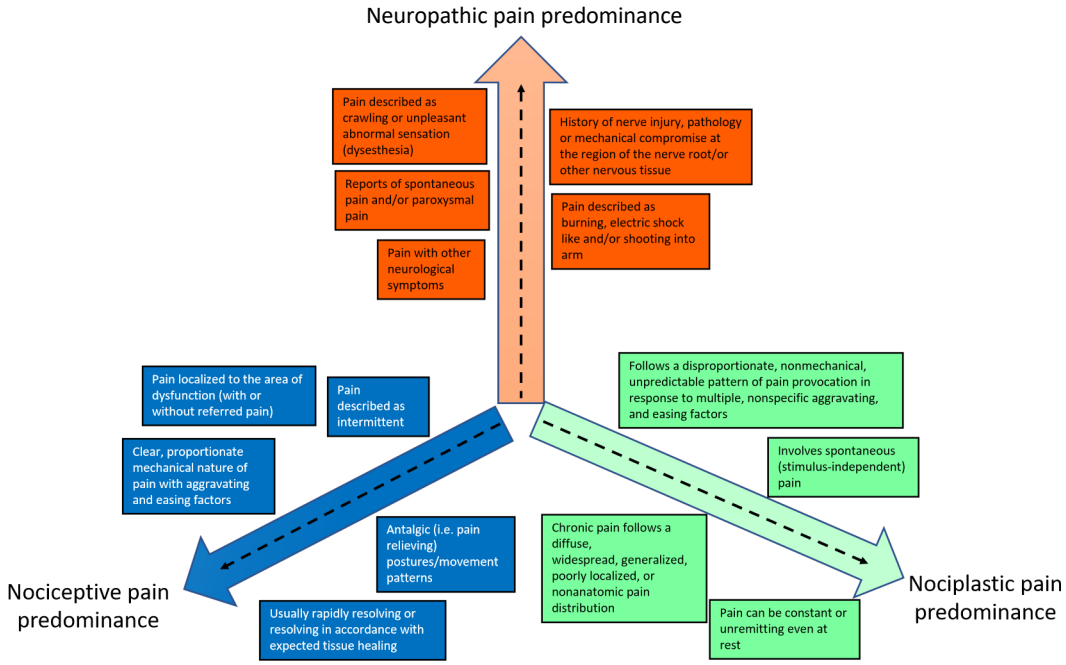

Figure 2. This figure shows different descriptions of pain depending on the underlying mechanism. Selection of relevant clinical descriptors for neuropathic pain (red arrow), nociceptive pain (blue arrow) [49], [39] and nociplastic pain (green arrow) [21, 23]. The 3 different colored arrows show a classification system to help clinicians determine the pain mechanism predominant.

Objective Examination

In patients 1, 2, and 3, a complete OE includes for example: inspection, soft tissue assessment, motor control, examination of active and physiologic/accessory passive movements. If neuropathic pain is suspected, clinicians should carefully perform a neurologic examination of the patient's sensory, motor, and autonomic functions to identify possible neurologic dysfunction (at least the DN4 questionnaire) [42]. As the quantitative sensory tests (QST) is not sufficient alone to diagnosis of neuropathic pain [22, 50], it may be warranted in addition to the neurologic examination [29, 51, 52]. It can be used to assess the somatosensory system function in patients by measuring changes in peripheral and/or central pain sensitivity. It consists of several tests aimed at quantifying the response to sensory stimuli elicited by the application of standardized vibration, pressure, thermal, or electrical stimuli. Neurological examination could reveal neuroanatomical pain distribution, positive and/or negative signs and symptoms (altered reflexes, sensations, and muscle strength) [27]. The presence of hyperalgesia and/or other sensory abnormalities could indicate the presence of neuropathic pain [23].

In addition, a neurodynamic test is essential to assess the mechanosensitivity of the nervous system [53]. A neurodynamic test is positive if it reproduces at least the patient's symptoms and a change in those symptoms with a positive structural differentiation [36, 54, 55]. The Upper Limb Neural Test (ULNT) is considered the most common upper limb test [53] with a specificity of 69% and sensitivity of 97% [56]. It should be noted that, although neurodynamic tests have good sensitivity, they generally have lower specificity and should not be used as stand-alone [57, 58]. To highlight neuropathic pain predominance associated with cervical radiculopathy, clinician could use the following clinical prediction rule [57]: cervical rotation (<60°), neurodynamic testing of the median nerve, cervical spine distraction, and the Spurling test, which has a high specificity of 89% to 100% [53, 59-61]. Clearly, more research is needed to further refine the diagnosis of cervical neuropathic pain.

A patient with nociplastic pain may also have neurologic symptoms, so it is important to be able to differentiate the underlying pain mechanisms between them. These patients may present hypersensitivity to stimuli (e.g., pressure, temperature) and nonspecific neurologic findings on testing or pain that has not a dermatomal distribution [21, 23]. These patients rarely present altered or absent deep tendon reflexes, and motor deficits. Neurodynamic testing could sometimes be positive but with a widespread persistent pain response [21, 23]. As said previously, depending on the evidence found and to better account (or not) for the nociplastic hypothesis, the use of the criteria grading system is a good option and if the clinicians want to score the patient, the self-reported Central Sensitization Inventory (CSI) questionnaire.

Interpretation of the objective examination

The evidence from the SE of Patient 1 suggests that nociceptive pain mechanism is predominant. During OE active movements, Patient 1's neck and arm pain (without neurologic symptoms) increase when he performs extension and right lateral flexion with limited range of motion. When Patient 1 returns to a neutral (starting) position, the pain rapidly decreases. This pattern is similar for passive physiological movements. Pain occurs at a specific location (C56) during unilateral mobilization from right posterior-anterior and decreases rapidly afterwards. Although predominant neuropathic pain is not our primary hypothesis, a neurologic examination is essential when a patient presents with pain that radiates into the upper extremity to confirm normal nervous system function. The negative neurological examination confirms the predominance of ***nociceptive pain mechanism*** in Patient 1.

Because the SE of Patient 2 suggests a predominantly neuropathic pain mechanism, the OE should include a complete neurologic, neurodynamic, and physical examination. On neurologic examination, the Patient 2 described a loss of sensation to light touch in the right forearm and hand (thumb and index finger side) and hyperalgesia to pinpricks compared with the left forearm. Regarding neurodynamic assessment, given the pain in the neck and arm during extension and right cervical lateral flexion, the Spurling test and the median upper limb neural test (ULNT1) are preferable [62]. In Patient 2, the Spurling test and ULNT1 are positive, with reproducible symptoms and with positive structural differentiation for the ULNT. According to the information from the SE and OE of Patient 2, we can confirm the hypothesis of the presence of a predominant ***neuropathic pain mechanism.***

The evidence from the SE of Patient 3 suggests the presence of a predominant nociplastic pain mechanism. Given the evidence at SE, an OE should be performed that includes active movements as well as physiologic and incidental passive movements. With active movements, Patient 3's neck and forearm pain (without clear neurologic symptoms) increase in a disproportionate and unpredictable way (with varying limitations and directions of movement). When Patient 3 returns to a neutral (starting) position, the pain can persist for a few minutes but not systematically. This variable and unpredictable response pattern is similar for passive physiologic movements. The pain is not reproduced at a specific location but starts latently. A neurologic examination is essential if a patient has pain that radiates into the upper extremity, for Patient 3, clinical signs of pain hypersensitivity are present at least in the painful region which is elicited during clinical assessments of mechanical, thermal or cold allodynia [34]. In this case, the ability to discriminate allodynia may be higher in areas distant from the painful region [34].According to the information from the SE and OE of Patient 3, we can confirm the hypothesis of the presence of a predominant ***nociplastic pain mechanism.***

It is important to note that clinicians must be aware of any change in symptomatology and perform further investigations, as neuropathic elements could appear during the patient's follow-up, and could indicate the presence of a serious spinal pathology.

Because the aim of this article is to help clinicians differentiate between the three predominant pain descriptors, only the relevant part of the OE necessary for this purpose is described.

Management should be patient-centered and based on a dynamic biopsychosocial framework [63], that incorporates the various aspects of the International Classification of Functioning (ICF) model [16].

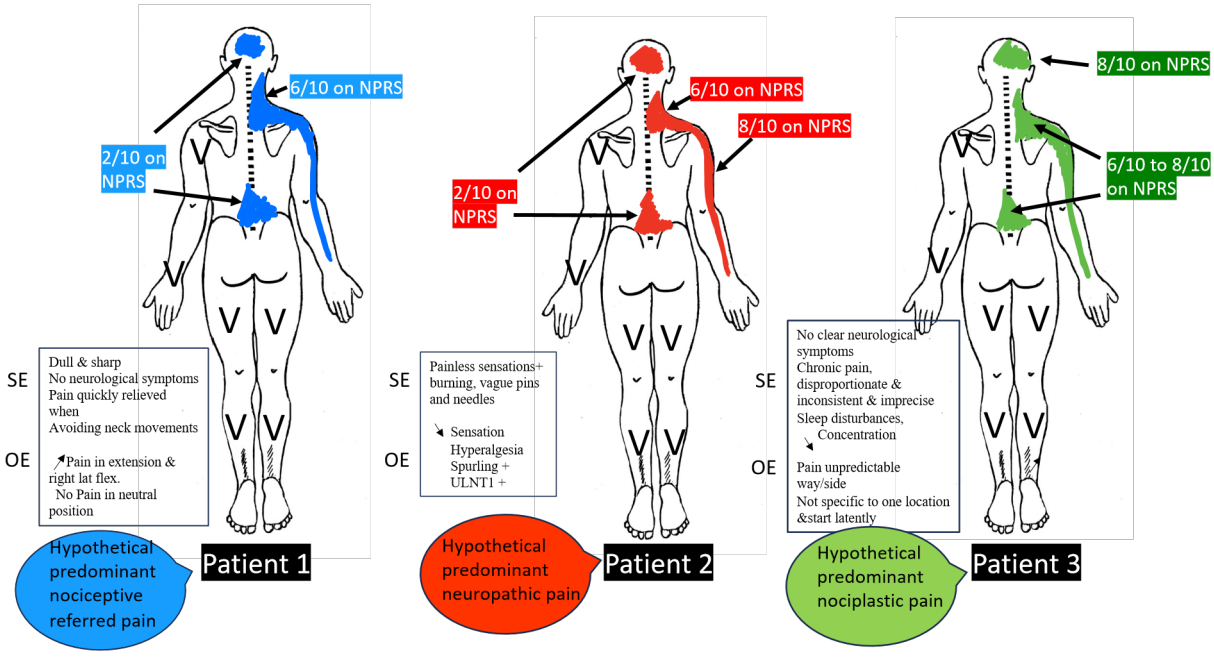

Figure 3. Description of the three body-charts after a complete subjective and physical examination. SE & OE are summarized in the figure. NPRS= numerical pain rating scale. V= no pain. SE= subjective examination. OE= objective examination. ULNT= upper limb neural test1 (median nerve).

Discussion and conclusion

The purpose of this article was to simplify the differentiation of pain mechanisms in people with NRAP to help clinicians and students in their clinical reasoning and practice.

With the elements collected at SE and OE of Patients 1, 2 and 3 we can hypothesize that of a predominant neuropathic, nociceptive or nociplastic pain mechanism is present (see Figure 3). Of course, the clinical examples presented are a caricature that is quite clear and easy to differentiate. However, in clinical practice the distinction between these pain mechanisms is not so straightforward. Clinical reasoning is sometimes complex in patients with NRAP. Although identification of the predominant pain mechanism is essential for effective management, neuropathic, nociceptive or nociplastic pain may share several characteristics which may explain the difficulty in implementing mechanism-based treatment [14, 15, 21, 32]. Indeed, the trichotomous description of pain can be problematic because clinical descriptors, signs, and symptoms can be confusing and overlapping [21, 39]: pure nociceptive or neuropathic or nociplastic pain may actually be very rare in practice [21, 64]. The traditional view that these three mechanisms are separate entities is questioned by some experts and may be due to our propensity to classify items [14, 15, 21, 65]. According toto this view, pain mechanism should probably be considered as continuum (Figure 4) ?

Although the topography of neuropathic, nociceptive, and even nociplastic symptoms could be similar, the description and behavior of pain must be complemented by a thorough objective examination to differentiate the predominant pain mechanisms. We would also caution the clinician (and student) who assesses only the topography of the pain (e.g., radiating into the forearm). Although only 19.9% of CBP cases are factually neuropathic in origin [37], thorough screening is necessary to optimally target therapeutic interventions. Importantly, diagnosing referred somatic nociceptive pain as neuropathic pain should be avoided to prevent a nocebo discourse, as treating a patient with neuropathic pain requires a more cautious approach.

Of course, pain predominance is not the only aspect that the therapist must assess. Analysis of the multidimensional aspect, related to the patient's biopsychosocial sphere is important [16]. It makes explicit what is often implicit, and it includes different categories, such as contributing factors, precautions and contraindications, and the patient's perspectives [66]. These categories also known as "hypothesis families" [66] can be used to encourage the therapist to look behind the potential patho-anatomic structure and to consider the different factors influencing the patient's symptoms [66].
Clinicians should be aware that pain predominance can change over time and so assessing patient's condition requires continuous reassessment at each visit through SE and OE to clarify what the predominant pain mechanism is. Depending on the predominant pain mechanism, adapted passive [31, 55, 62, 67] and active treatments [68, 69], as well as pain education to reassure the patient about the pain experience [36] are carried out. The importance of research in this field will continue to improve our understanding and management of patients.

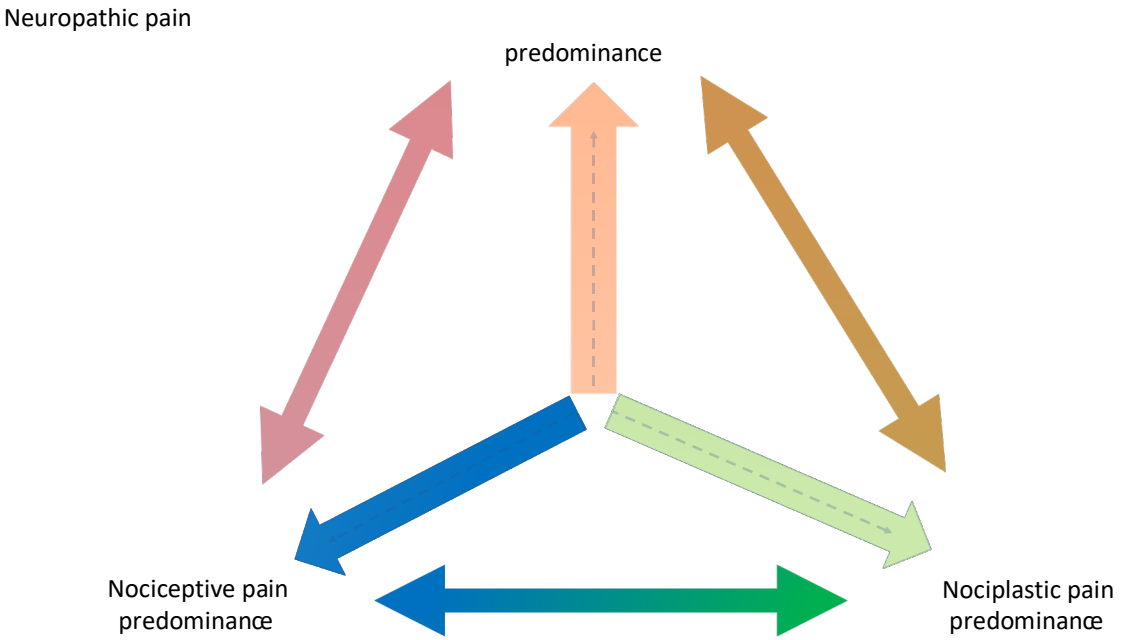

Figure 4. Naïve illustration of the continuum based on the pain predominance mechanisms. Side arrows indicate the continuum.

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