

## METHODOLOGY, MECHANISMS & TRANSLATIONAL RESEARCH SECTION

### Original Research Article

# Clinical Criteria of Central Sensitization in Chronic Pelvic and Perineal Pain (Convergences PP Criteria): Elaboration of a Clinical Evaluation Tool Based on Formal Expert Consensus

Amélie Levesque, MD,\* Thibault Riant, MD,\*† Stéphane Ploteau, MD,\*‡ Jérôme Rigaud, PhD,\* and Jean-Jacques Labat, MD;\* for Convergences PP Network

\*Federative Pelvic Pain Center, Department of Urology, and †Department of Gynecology-Obstetrics and Reproductive Medicine, Nantes University Hospital, Nantes, France; ‡Department of Pain Management, Maurice Bensaïgnor Multidisciplinary Pain Center, Centre Catherine de Sienne, Nantes, France

Correspondence to: Amélie Levesque, MD, service d'urologie, 1, place Alexis Ricordeau, CHU de Nantes, Hôtel Dieu, 44093, Nantes, France. Tel: +033 240 08 39 12; Fax: +033 240 08 39 25; E-mail: amelie.levesque@chu-nantes.fr.

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### Abstract

**Background.** The evaluation of chronic pelvic and perineal pain (CPP) is often complex. The patient's description of the pain often appears to be disproportionate to the limited findings on physical examination and/or complementary investigations. The concept of central sensitization may allow better understanding and management of patients with CPP.

**Objective.** The aim of this study was to elaborate a clinical evaluation tool designed to simply identify sensitization in pelvic pain.

**Methods.** A list of 63 items was submitted to 22 international CPP experts according to the Delphi method.

**Results.** Ten clinical criteria were adopted for the creation of a clinical evaluation tool: 1) pain influenced by bladder filling and/or urination, 2) pain influenced by rectal distension and/or defecation, 3) pain during sexual activity, 4) perineal and/or vulvar pain in response to normally nonpainful stimulation, 5) pelvic trigger points (e.g., in the piriformis, obturator internus, and/or levator ani muscles), 6) pain after urination, 7) pain after defecation, 8) pain after sexual activity, 9) variable (fluctuating) pain intensity and/or variable pain distribution, 10) migraine or tension headaches and/or fibromyalgia and/or chronic fatigue syndrome and/or post-traumatic stress disorder and/or restless legs syndrome and/or temporomandibular joint dysfunction and/or multiple chemical sensitivity.

**Conclusions.** This process resulted in the elaboration of a clinical evaluation tool designed to identify and appropriately manage patients with CPP comprising a sensitization component.

**Key Words.** Pelvic Pain; Sensitization; Chronic Pain; Assessment

### Introduction

Some patients with chronic pelvic and perineal pain (CPP) present complex manifestations, comprising pain and dysfunction that are not confined to a single organ system (lower urinary tract, lower gastrointestinal tract, genital tract).

These syndromes can be associated with varying degrees of symptoms suggestive of bladder pain syndrome, dyspareunia, and/or irritable bowel syndrome. These patients sometimes also experience pain comprising a neuropathic component (burning, tingling, prickles, and perineal allodynia) [1], and physical examination may reveal muscle trigger points (piriformis, obturator internus, levator ani, and iliopsoas) suggestive of myofascial pain.

The gap between clinical symptoms and pathological signs is a constant feature of these pain syndromes. The patient's description of the pain often appears to be disproportionate to the limited findings on physical examination and/or complementary investigations (imaging, endoscopy, infectious work-up), and any observed anatomical lesions or variants, on their own, cannot explain the patient's pain.

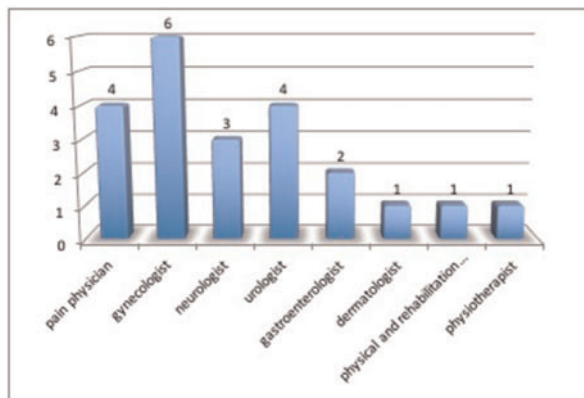
This type of pain is disconcerting and can sometimes be a source of discouragement both for the patient and for the various organ specialists involved: gynecologists, urologists, gastroenterologists, pain physicians, etc. The absence of a visible lesion able to explain the patient's pain can lead to misunderstanding for both the patient and the doctor. This can contribute to treatment failures, alteration of the patient-doctor relationship, or even excessive psychiatric diagnoses.

Another possible explanation for these pain syndromes would be sensitization, as described by Woolf in 1983 [2]. Central sensitization would result from increases in membrane excitability and synaptic efficacy. It is a manifestation of the plasticity of the somatosensory nervous system in response to activity, inflammation, and neural injury.

Central sensitization encompasses altered sensory processing in the brain, malfunctioning of descending pain inhibitory mechanisms, increased activity of pain facilitatory pathways, and long-term potentiation of neuronal synapses in the anterior cingulate cortex.

Because central sensitization results from changes in the properties of neurons in the central nervous system, the pain is no longer coupled, as acute nociceptive pain is, to the presence, intensity, or duration of noxious peripheral stimuli. Finally, Woolf synthesizes sensitization by decreased nociceptive thresholds (primary hyperalgesia), a more intense and a more prolonged response to a nociceptive stimulus, and spatial extension of the painful zone (secondary hyperalgesia) [2–5].

The concomitant presence of several clinical hypersensitivity syndromes, such as irritable bowel syndrome, functional dyspepsia, fibromyalgia, temporomandibular joint dysfunction, chronic pelvic pain syndrome, and chronic fatigue syndrome, also suggests a central dysfunctional mechanism [6–8]. Teams specialized in pelvic diseases have developed the concept of pelvic organ cross-talk, corresponding to the secondary symptomatic



**Figure 1** Distribution of the various specialties of the experts.

impact on adjacent organs via a “cross-sensitization” phenomenon [9].

Organ specialists classically analyze pain as being proportional to an organic lesion, which can be treated by treating this organic lesion. However, in the context of CPP, treatment of the organic lesion (when present) remains necessary, but is not always sufficient to relieve the pain.

The concept of sensitization, applied to the pelvis, provides a pathophysiological model in order to explain some of these unexplained situations (interstitial cystitis/bladder pain syndrome, urethral syndrome, provoked vulvodynia, irritable bowel syndrome, etc.). This concept could also be used to identify patients with a risk of chronic postoperative pain [10], allowing the proposal of new treatment strategies.

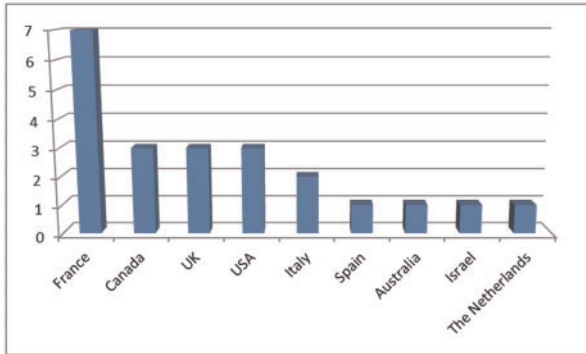
The objective of this study was to select the most significant clinical criteria of sensitization in the context of CPP and propose a clinical evaluation tool that can be easily used in routine clinical practice.

## Methods

We used the Delphi method described by Dalkey and Helmer in the 1960s [11,12] to reach a formal expert consensus on clinical criteria of sensitization in chronic pelvic and perineal pain.

We selected a panel of experts on the basis of their scientific and/or clinical experience in the field. This work was initiated on the occasion of the second World Congress on Abdominal and Pelvic Pain in Nice in 2015. The experts were selected from among the experts present. A total of 22 international experts, from seven different specialties and nine different countries, participated in the study (Figures 1 and 2).

The experts were asked to vote on a list of 63 items in English elaborated by a steering committee



**Figure 2** Distribution of the various nationalities of the experts (N = 22).

(Supplementary Data). This list comprised 56 items already discussed in a preliminary unpublished study conducted by the French-speaking Convergences PP group in 2012 (<http://www.sifud-pp.org/data/videos/flash-conferences/2012-nimes/015/SWF/index.htm>) in addition to three proposed items designed to characterize the target population and another four proposals defining the domains to be explored.

After recalling the definition of sensitization (Supplementary Data), we invited the experts to answer the following question for each item on the list: Do you consider this clinical element to be suggestive of sensitization in pelvic pain?

Responses were scored between 1 and 9 (1 = totally irrelevant item, 9 = totally relevant item). All scores and any associated comments remained anonymous.

The survey was performed via the Internet between March and July 2016 on the SurveyMonkey website (<https://fr.surveymonkey.com>).

The criteria were submitted to four rounds according to the following modalities of the Delphi method:

- first round: each expert was asked to score each item between 1 to 9;
- second round: the experts were informed about the median scores of the first round and were asked to attribute a new score in light of the group's opinion in the first round and provide a written argument when they did not agree with the group's opinion;
- third round: the experts were informed about the median scores of the second round, the arguments in support of opposing opinions, and were asked to attribute a new score in light of the group's opinion in the second round and the arguments in support of opposing opinions, and the experts sharing the group's opinion were asked to justify their position;
- fourth round: the experts were informed about the median scores of the third round and were asked to

attribute a final score by taking opposing opinions and arguments into account.

Items that achieved a strong consensus (all scores > 7/9) by the second round were not included in the following two rounds in order to simplify the procedure. Items with a median score at the fourth round  $\geq 7$  and with no more than two scores < 7 were considered to reflect a strong consensus. Conversely, items with a median score  $\leq 3$  were eliminated. Finally, items with a median score  $\geq 7$  but with more than two scores < 7 were considered to reflect a moderate consensus [13].

A plenary meeting attended by some of the experts of the study during the Convergence PP congress in Aix-en-Provence, France (September 2016), discussed the modalities of presentation of the final criteria of sensitization in chronic pelvic and perineal pain. Following this meeting, the final version of the clinical evaluation tool was submitted by e-mail to all experts who participated in the Delphi process for final validation.

## Results

Twelve items achieved a strong consensus: median score  $\geq 7$  with no more than two scores < 7:

- vulvodinia;
- perineodynia;
- intolerance of tight underwear;
- multiple muscle trigger points;
- pain or dysfunction affecting at least two of the following systems: genital tract, urinary tract, gastrointestinal tract;
- irritable bowel syndrome: discomfort, diarrhea, constipation;
- history of fibromyalgia;
- history of chronic fatigue syndrome;
- pain on bladder filling;
- pain on sexual activity;
- diffuse pain syndrome;
- history of dysfunctional pain: temporomandibular joint dysfunction, migraine, fibromyalgia syndrome.

Six items achieved a moderate consensus: median score  $\geq 7$  and more than two scores < 7:

- history of post-traumatic stress disorder, anxiety/depression;
- unable to use tampons during menstrual periods;
- pain in at least two of the following territories: pelvis, buttock, perineum, lower limbs;
- variable symptoms over time;
- variable pain distribution;
- variable expression of clinical symptoms.

The other items on the list did not achieve a consensus and were therefore not included in the clinical evaluation tool.

Some of the 18 items that achieved a strong or moderate consensus were combined, as they were considered to

**Table 1** Convergences PP Criteria

	Lower urinary tract	Lower digestive tract	Genito-sexual tract	Mucocutaneous areas	Muscular system
Lower pain perception thresholds	<input type="checkbox"/> Pain influenced by bladder filling and / or urination	<input type="checkbox"/> Pain influenced by the distension and / or rectal emptying (materials, gas)	<input type="checkbox"/> Pain during sexual activity	<input type="checkbox"/> Perineal and/or vulvar pain in response to normally non-painfull pressure (allodynia) (e.g. pain preventing Tampons used during menstruations, or discomfort with tight clothing)	<input type="checkbox"/> Pelvic trigger points (e.g., localized to piriformis, internal obturator and/or levator ani musculature)
Temporal distribution	<input type="checkbox"/> Pain after urination	<input type="checkbox"/> Pain after defecation	<input type="checkbox"/> Pain after sexual activity		
Symptoms variability	<input type="checkbox"/> Variability in pain intensity (evolving with high and low) and / or variability in painful topography				
Associated syndroms	<input type="checkbox"/> Migraine or tension headaches and/or fibromyalgia and/or chronic fatigue syndrome and/or post-traumatic stress disorder and/or restless leg syndrome and/or temporo-mandibular joint disorder and/or multiple chemical sensitivities				

This clinical tool is applicable to patients with chronic pelvic and perineal pain lasting more than three months, reporting symptoms that appear to be disproportionate to the findings of physical examination and complementary investigations (including an infectious work-up, imaging, and endoscopy). This questionnaire does not assess pain intensity or the psychosocial impact of pain. The presence of five or more items is suggestive of sensitization of pelvic pain.

be redundant or to have a similar significance (e.g., vulvodinia and perineodynia or fibromyalgia and diffuse pain syndrome). These criteria were presented in a table complying with the pathophysiological concept of central sensitization (elements reflecting lowering of nociceptive thresholds, elements reflecting spatial diffusion, elements reflecting temporal diffusion, the concept of symptom variability, and concept of clinical predisposition).

A table (Table 1) comprising the following 10 items was finally proposed to the 21 experts:

1. pain influenced by bladder filling and/or urination;
2. pain influenced by rectal distension and/or rectal emptying;
3. pain during sexual activity;
4. perineal and/or vulvar pain in response to normally nonpainful stimulation;
5. pelvic trigger points (e.g., in the piriformis, obturator internus, and/or levator ani muscles);
6. pain after urination;

7. pain after defecation;
8. pain after sexual activity;
9. variable (fluctuating) pain intensity and/or variable pain distribution;
10. migraine or tension headaches and/or fibromyalgia and/or chronic fatigue syndrome and/or post-traumatic stress disorder and/or restless legs syndrome and/or temporomandibular joint dysfunction and/or multiple chemical sensitivity.

Nineteen experts (90.5%) validated this final list of criteria as a clinical evaluation tool. This clinical evaluation tool has been called the "Convergences PP Criteria."

**Discussion**

This original study, in the absence of evidence-based medicine, achieved an expert consensus, allowing the proposal of a simple clinical evaluation tool to identify sensitization in chronic pelvic pain. This clinical tool should guide the physician's clinical interview and physical examination to identify a state of pain sensitization

The Delphi method is used in many fields, to predict events, to predict technological progress, to define education and public transport policies, etc. It is based on an essential principle—"two heads are better than one"—resulting in the creation of committees, advisory boards, juries, consumer panels, referendums. In 1963, Dalkey showed that the group response (median of individual responses) was always more reliable than the response of a single person, even an expert [12]. This method also allows discussion between experts without the constraints of face-to-face discussion, thereby overcoming the influence of dominant speakers (poor correlation between knowledge and confident speech) and the biases induced by personal interests (the desire to be right).

Despite the desire to adopt a global approach to the patient, the criteria of this clinical tool focus on the pelvic and perineal region. One of the experts did not validate the questionnaire due to the absence of a psychosocial criterion. The purpose of this tool was to identify a mechanism of chronic pain, as previously performed for the neuropathic pain questionnaire (DN4), and this psychosocial dimension was therefore not included. Given its importance in the development and treatment of central sensitization, psychosocial aspects must be a part of the global pain evaluation [14,15].

Patients with CPP obtain insufficient relief of their symptoms, they often consult many doctors without obtaining a precise diagnosis or appropriate management, and they sometimes have the impression of being abandoned by the medical profession. This clinical tool can help both the doctor and the patient determine the etiology of the pain and propose better, more rational management. A clinical model of this concept is illustrated by the heterogeneity of interstitial cystitis/bladder pain syndrome (IC/BPS). Many experts from various learned societies have proposed diagnostic criteria based on analysis of the symptoms: ESSIC [16], American Urological Association [17], European Association of Urology [18], International Consultation on Incontinence [19]. All of these diagnostic criteria include the concept of bladder pain and at least one urinary symptom (frequency and/or pain on bladder filling) present for at least six months, in the absence of urinary tract infection or any other identifiable cause. Two types of bladder pain syndrome can be distinguished: those associated with urothelial lesions (Hunner lesions) observed during cystoscopy with hydrodistension performed under general anesthesia and those without Hunner lesions that are considered to be essentially due to bladder hypersensitivity phenomena. IC/BPS by bladder hypersensitivity is often associated with sexual disorders (vulvodynia), gastrointestinal disorders (irritable bowel syndrome), myofascial pain, and generalized sensitization phenomena (fibromyalgia) [20]. Differentiation of these two subtypes of bladder pain syndrome could be facilitated by the use of the Convergences PP Criteria. Unexplained pelvic pain accompanied by minimal endometriosis lesions or that persists after surgery for endometriosis constitutes

another example [21]. Recently, Constantini displayed that visceral pain enhances fibromyalgia symptoms, probably augmenting the level of central sensitization. He also showed the benefits on hyperalgesia after treatment of visceral pain [22]. The existence of pelvic sensitization does not exclude underlying organ pathology. Treatment of the affected organ will always have to be undertaken where possible, and the means of treatment will have to be adapted to the state of sensitization.

The Convergences PP Criteria are applicable to patients with chronic pelvic and perineal pain lasting more than three months, reporting symptoms that appear to be disproportionate to the findings of physical examination and complementary investigations (including an infectious work-up, imaging, and endoscopy).

We did not claim with this study to explain underlying phenomena or to determine whether central or peripheral sensitization was the cause of patients' pain. Nevertheless, spinally mediated central sensitization as described by Clifford Woolf (temporal wind-up, dynamic mechanical allodynia, after sensation) seems to better explain the clinical dissociation between pain and the triggering stimulus.

The repetition of complementary investigations and especially invasive procedures (endoscopy or laparoscopy) is suspected to participate in the chronicity of pain. Early recognition of these sensitization phenomena could also lead to moderate diagnostic strategies. Central sensitization appears to be a predominant risk factor for postoperative pain as well [23]. Recognition by the practitioner of sensitization as a risk factor for postoperative pain [24] could enable the arrangement of a prevention strategy. The usual pain treatments—maintenance treatments (tricyclic antidepressants, antihyperalgesic agents, etc.), more specific treatments of sensitization (ketamine, etc.), transcutaneous electrical nerve stimulation techniques, targeted physiotherapy, and mind-body therapy—could then be proposed to these patients seen by organ specialists (urologists, gastroenterologists, gynecologists), highlighting the importance of multidisciplinary management in this setting [25].

Finally, this tool could be used to constitute a homogeneous subgroup of patients in order to conduct specific studies and develop adapted curative and preventive treatments.

This clinical evaluation tool cannot be used to establish a diagnosis at the present time, but can only guide the physician's understanding of the patient's clinical situation.

Psychometric validation of this tool is currently underway. A cutoff score indicating a diagnosis of sensitization also needs to be defined. This work has been initiated and is also underway. Nevertheless, a score >5/10 appears to be suggestive of sensitization.



Basic research also needs to determine the links between these clinical criteria and measurable sensitivity threshold data (nociception) in the various pelvic and perineal organs in “sensitized” patients compared with control subjects.

### **Conclusion**

The creation of this clinical evaluation tool by means of the Delphi method was based on an expert consensus on clinical criteria suggestive of pelvic and perineal pain related to a sensitization mechanism. This easy-to-use tool should facilitate the clinical detection of sensitization in CPP, including by physicians who are not pain specialists. This tool provides physicians with a pathophysiological model to explain these chronic pain syndromes, beyond the strict framework of organ specialties.

Finally, this tool defines an homogenous subgroup of patients presenting a particular susceptibility to nociceptive stimuli. It should help to develop a better pain management for these patients and the proposal of treatment adaptation strategies designed to limit the development of postoperative pain.

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### **Supplementary Data**

Supplementary Data may be found online at <http://pain-medicine.oxfordjournals.org>.

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