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# Evolution of somatosensory processing signs after nociceptive targeted surgery in patients with musculoskeletal disorders: a systematic review

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## Abstract

Surgery is often advised when conservative treatment fails in musculoskeletal pain conditions, but a substantial proportion still suffers chronic pain after surgery. Somatosensory processing system (SPS) signs were previously studied as potential predictors for chronic postsurgical pain, but results are inconsistent. Therefore, studying the evolution of SPS signs could be of added value. The aim was to summarize all studies that measured how SPS signs evolved after nociceptive targeted surgery in musculoskeletal disorders and to find preoperative, perioperative, and postoperative predictors for the evolution of these SPS signs. Data were summarized, and risk of bias and level of evidence and recommendation were determined. Twenty-one studies were included. Five scored a low, 3 a moderate, and 13 a high risk of bias. In general, no consistent evolution of SPS signs comparing preoperative and postoperative values and predictors for this evolution in musculoskeletal disorders could be found. In most cases, static quantitative sensory testing (QST) did not change or conflicting results were found. On the other hand, dynamic QST mostly improved after surgery. Worthfully mentioning is that worsening of SPS signs was only seen at a follow-up of <3 months after surgery, that conclusions are stronger when evaluating dynamic QST with a follow-up of ≥3 months after surgery, and that pain improvement postsurgery was an important predictor. Future high-quality research should focus on the evolution of SPS signs after nociceptive targeted surgery, accounting for pain improvement groups and focusing on preoperative, perioperative, and postoperative predictors of this evolution.

**Keywords:** Somatosensory processing signs, Musculoskeletal disorders, Musculoskeletal surgery, Central pain mechanisms

## 1. Introduction

Pain is defined as “an unpleasant sensory and emotional experience associated with, or resembling that associated with, actual or potential tissue damage.”<sup>49</sup> Musculoskeletal (MSK) pain is often associated with disorders of the MSK system of the human body, including muscles, joints, tendons, ligaments, and other structures (eg, disks or bursae).<sup>54</sup> When this pain remains present for longer than 3 months and is associated with an underlying MSK condition, the *International Classification of Diseases 11th Revision* (ICD-11) defines it as chronic secondary MSK pain.<sup>25</sup>

In general, conservative treatment, such as medication, injections, or physical therapy, is first-choice therapy to target the nociceptive source of MSK pain. However, when this fails and the patient's pain intensity is still significant with a negative impact on functioning, surgery is often advised.<sup>2,13</sup> Despite that surgery targets the source of nociception, 5 to 85% still experiences chronic postsurgical pain depending on the type of surgery and disorder.<sup>52</sup> According to the *ICD-11*, this postsurgical pain lasts longer than 3 months or beyond the normal healing process after surgery.<sup>25</sup> Different peripheral (eg, specific factors such as malalignment, too much stress on the implant...) and central (eg, disturbed somatosensory processing system [SPS]) originated hypotheses for the persistence of this pain have been described.<sup>10</sup>

Chronic (postsurgical) pain can, apart from peripheral factors, also be associated with a disturbed SPS in which the central nervous system becomes hypersensitive. Not only local but also widespread hyperalgesia and allodynia are indicative for this hypersensitivity, and hyperexcitability of the ascending nerve pathways and a less efficient endogenous pain inhibition system are known as underlying mechanisms.<sup>5,6</sup> Apart from psychosocial, genetic, metabolic, and functional factors, preoperative disturbed SPS signs are proposed as risk factors for chronic postsurgical pain.<sup>7,36,52</sup>

Quantitative sensory testing (QST) can measure and objectify this hypersensitivity, of which pain thresholds, detection thresholds, or dynamic methods—such as the degree of spatial and temporal summation and conditioned pain modulation (CPM)—are an indispensable part.<sup>7</sup> Also questionnaires, such as the Central Sensitization Inventory (CSI) and Pain Sensitivity Questionnaire, could indicate self-reported signs of a disturbed SPS.<sup>14</sup>

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

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Recent reviews are contradictory about the predictive value of a preoperative disturbed SPS for chronic postsurgical pain,<sup>12,51</sup> but none of them considered the evolution of SPS signs from presurgery to postsurgery. The central nervous system is dynamic, and it is postulated that disturbed SPS signs can be caused by the peripheral source of nociception,<sup>39</sup> defined as chronic secondary pain, or are rather independent of identified peripheral biological contributors, defined as chronic primary pain.<sup>25,40,45,55</sup>

When the nociceptive source is targeted by surgery, a normalization of SPS signs could be expected.<sup>20</sup> Nevertheless, a substantial proportion of patients still reports pain.<sup>52</sup> The nociceptive source in combination with disturbed SPS signs (additionally) could be imposed as chronic primary MSK pain; because clear evidence exists that in a long period of obvious dissociation between the medical causes and chronic pain, other factors determine the chronic pain condition. Although both primary and secondary pain can involve overlapping nociplastic (from a sensitized nervous system) and nociceptive (from tissue injury) processes, nociplastic pain mechanisms are particularly relevant in chronic primary pain. The underlying disorder may have been treated successfully, but chronic pain remains and becomes the main complaint in its own right.<sup>45</sup>

As none of the previous reviews focused on the temporal stability or change of signs of SPS in chronic MSK pain, it remains unclear whether SPS signs improve after a nociceptive targeted surgery or not, and whether preoperative, perioperative, and postoperative predictors can be indicated for the evolution of these signs. Therefore, the first aim of this systematic review was to summarize all studies that measure how SPS signs evolve after nociceptive targeted surgery in MSK disorders. The second aim was to find preoperative, perioperative, and postoperative predictors for an improvement or persistence of disturbed SPS signs after surgery.

## 2. Methods

This systematic review is written according to the updated Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.<sup>43</sup>

### 2.1. Eligibility criteria

Studies were eligible if they met all different inclusion and exclusion criteria based on the Population (P), Intervention (I), Comparison (C), Outcome (O) and Study design (S) model. Studies had to measure evolution in SPS signs (O) before and after nociceptive targeted surgery in patients with MSK pain (P) undergoing nociceptive peripheral (MSK disorder) targeted surgery (I). Eligibility criteria can be found in **Table 1**.

### 2.2. Information sources and search strategy

Two electronic databases, PubMed (MEDLINE) and Web of Science (WoS), were searched for potentially eligible literature up to April 21, 2022. A search strategy combined using “AND” and “OR” was set up based on different key words (P, I, O, and S).<sup>16</sup> There were no additional search filters added. The search strategy of the 2 databases can be found in **Tables 2 and 3**. In addition, reference lists of included studies, which were retrieved from the search strategy, were checked for more relevant articles through hand-search methods.

### 2.3. Selection process

Studies were considered relevant based on a 2-phase triple-blind title, abstract, and full-text screening performed by 4 reviewers

(S.V., A.V., N.C., and C.C.). In the first phase, studies were checked independently for eligibility on title and abstract, and in the second phase on full text both with the help of Rayyan.<sup>41</sup> The order of exclusion for the full-text screening was as follows: language > study design > population > intervention > outcome. All conflicts during both phases were solved by consensus.

### 2.4. Data collection and items

Data about the evolution of SPS signs of all studies were retrieved and collected. Data about (1) author, year of publication and study design, (2) participants: study sample and characteristics, and eligibility criteria, (3) outcome measurement method and measures of central SPS, (4) measurement locations, (5) type of surgery, (6) follow-up period, (7) chronic pain measurement, and (8) most important results was extracted. The first reviewer (S.V.) filled in the evidence table, and the second reviewer (L.M.) checked the table independently. Data about the predictors for SPS change over time or SPS sign-related predictors for surgical outcome were also retrieved and collected. Data about (1) author and year, (2) surgical outcome in relation to SPS signs, (3) follow-up period, (4) method, (5) predictor change in SPS signs, and (6) predictor surgical outcome in relation to SPS signs were extracted.

### 2.5. Risk of bias and level of recommendation of studies

The Quality in Prognostic Studies (QUIPS) checklist<sup>23</sup> was used to assess risk of bias (RoB) in the individual studies. Six domains, (1) Study Participation, (2) Study Attrition, (3) Prognostic Factor Measurement, (4) Outcome Measurement, (5) Study Confounding, and (6) Statistical Analysis and Reporting, were scored as having a “low,” “moderate,” or “high” chance for RoB. The first 2 reviewers (S.V. and L.M.) performed the RoB independently and blinded from

**Table 1**

**Eligibility criteria according to Population, Intervention, Comparison, Outcome, Study Design, and Language.**

	Inclusion	Exclusion
P	Human patients with MSK pain disorders	Animal studies Patients with neurological disorders, cardiorespiratory disorders, metabolic disorders, or systemic disorders
I	Peripheral nociceptive targeted (MSK disorder) surgery Separate statistical analyses for the surgery group	
C	/	/
O	QST or questionnaires (CSI, PSQ) focusing on afferent somatosensory processing system signs Measured before and after surgery	Measured only before or only after surgery
S	Full text available	Reviews, meta-analyses, abstracts, letters, congress proceedings, or case reports
L	Articles written in English, Dutch, German, or French	Articles written in any other language

P, population; I, intervention; C, comparison; O, outcome; S, study design; L, language; CSI, Central Sensitization Inventory; MSK, musculoskeletal; PSQ, Pain Sensitivity Questionnaire; QST, quantitative sensory testing.

Table 2

Search strategy related to PubMed.

Population	Intervention	Outcome	Study design
(("Musculoskeletal Diseases" [MeSH] OR "Musculoskeletal Pain" [MeSH] OR "Arthralgia" [MeSH]) OR musculoskeletal disease* OR musculoskeletal disorder* OR musculoskeletal pain OR orthopedic disorder* OR myalgia OR arthralgia) AND ("Humans" [MeSH] OR "Persons" [MeSH] OR human* OR person* OR people)	("Orthopedics" [MeSH] OR "Orthopedic procedures" [MeSH] OR "Surgical Procedures, operative" [MeSH] OR "General surgery" [MeSH] OR "Arthroplasty" [MeSH]) OR surgery OR orthopedic surgery OR orthopedics OR orthopaedics OR operation OR arthroplasty OR replacement OR orthopedic procedures	("Pain Threshold" [MeSH] OR "Sensory Thresholds" [MeSH] OR "Pain Perception" [MeSH] OR "Central Nervous System Sensitization" [MeSH]) OR Quantitative sensory testing OR QST OR pain threshold OR sensory threshold OR detection threshold OR pain perception OR "central nervous system sensitization" OR algomet* OR temporal summation OR spatial summation OR conditioned pain modulation OR CPM OR endogenous pain inhibition OR "diffuse noxious inhibitory control" OR central sensitization OR central pain processing OR pain sensitivity OR pain modification OR pain facilitation OR wind up OR altered nociception	("Pragmatic Clinical Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type] OR "Randomized Controlled Trial" [Publication Type] OR "Clinical Trial" [Publication Type] OR "Cohort Studies" [MeSH] OR "Longitudinal Studies" [MeSH] OR "Follow-Up Studies" [MeSH] OR "Prospective Studies" [MeSH]) OR clinical trial OR randomized controlled trial OR randomised controlled trial OR cohort studies OR prospective studies OR longitudinal studies OR follow-up studies

each other. To create uniform RoB scoring, guidelines for the interpretation of each item were set up based on a previous study.<sup>21</sup> The overall RoB judgement of a study was based on all domains; an overall "low" RoB score meant that all domains were scored as "low" or maximum 1 as "moderate", an overall "high" RoB meant that at least 1 domain was scored as "high" or  $\geq 3$  as "moderate", and all other studies were judged as having an overall "moderate" RoB.

In addition, each study was assigned a level of evidence based on the Oxford Centre for Evidence-Based Medicine (OCEBM) guidelines,<sup>42</sup> of which the scoring was based on study design and RoB assessment.<sup>42</sup> Table 4 summarizes the levels of evidence and grades of recommendation. Thereafter, results from both reviewers (S.V. and L.M.) were compared and discussed until consensus was reached.

To make conclusions, studies were clustered by the first author (S.V.) and grades of recommendation were assigned according to the OCEBM guidelines. Studies were categorized per SPS sign (threshold measurements also split up into local and widespread threshold measurement), MSK disorder, and follow-up period for the first aim. Regarding the second aim, studies were categorized per SPS change and predictor.

3. Results

3.1. Study selection

The PRISMA flowchart reflects the study selection process (Fig. 1). The search strategy yielded 13 eligible studies for inclusion in this

review.<sup>8,11,18,24,27,31,33,35,38,53,56–58</sup> After checking their reference lists, 8 additional studies were eligible.<sup>3,20,30,33,34,36,46,60</sup> This resulted in 21 studies, of which 18 prospective cohort studies<sup>3,11,18,20,30,31,33–37,39,38,46,56–58,60</sup> and 3 randomized controlled trials.<sup>8,24,53</sup> Conflicts in the first (44 studies or 1%) and second (16 studies or 30.7%) screening phase were all solved by consensus. The most prevalent exclusion reasons were "wrong outcome" and "wrong population."

3.2. Risk of bias

The 2 reviewers who scored the RoB (S.V. and L.M.) agreed on 75.0% of the domains and 74.8% of the subdomains. Conflicts were all solved after discussion. The domain "study attrition" suffered by far the highest RoB, mostly because studies did not report the number and reasons for the losses to follow-up or the way that they tried to address these losses.

3.3. Study characteristics, population, and type of surgery

Five different disorders were targeted in the included studies. Seventeen studies included patients with osteoarthritis (OA): hip OA,<sup>3,11,30,33,34</sup> knee OA,<sup>8,20,24,32,33,35,38,46,53,58</sup> shoulder OA,<sup>27</sup> and both hip and knee OA.<sup>31</sup> All these patients received total joint replacement surgery<sup>3,8,20,24,30,31,33–37,39,38,46,53,58</sup> or osteotomy.<sup>29,30</sup> One study included patients with a closed lock temporomandibular joint who received discectomy,<sup>18</sup> and 3 studies included patients with lumbar disk herniation who

Table 3

Search strategy related to Web of Science.

Population	Intervention	Outcome	Study design
Musculoskeletal disease* OR musculoskeletal disorder* OR musculoskeletal pain OR orthopedic disorder* OR myalgia OR arthralgia AND (human* OR person* OR people)	Surgery OR orthopedic surgery OR orthopedics OR orthopaedics OR operation OR arthroplasty OR replacement OR orthopedic procedures	Quantitative sensory testing OR QST OR pain threshold OR sensory threshold OR detection threshold OR pain perception OR "central nervous system sensitization" OR algomet* OR temporal summation OR spatial summation OR conditioned pain modulation OR CPM OR endogenous pain inhibition OR "diffuse noxious inhibitory control" OR central sensitization OR central pain processing OR pain sensitivity OR pain modification OR pain facilitation OR wind up OR altered nociception	/

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**Table 4****Level of evidence and strength of recommendation scoring.**

	Level of evidence		Strength of recommendation
LoE 1a	Systematic review of inception cohort studies or RCTs	A (strong)	Consistent level 1 studies
LoE 1b	Randomized controlled trial or individual inception cohort study with >80% follow-up	B (moderate)	Consistent level 2 or 3 studies or extrapolations from level 1 studies
LoE 1c	All or none case series	C (weak)	Level 4 studies or extrapolations from level 2 or 3 studies
LoE 2a	Systematic review of either retrospective cohort studies or untreated control groups in RCT	D (very weak)	Level 5 evidence or troublingly inconsistent or inconclusive studies of any level
LoE 2b	Individual cohort study (including low-quality RCT, <80% follow-up)		
LoE 2c	"Outcomes" research		
LoE 3a	Systematic review of case-control studies		
LoE 3b	Individual case-control study		
LoE 4	Case series		
LoE 5	Expert opinion		

LoE, level of evidence; RCT, randomized controlled trial.

received sequestrectomy.<sup>56,57,60</sup> In 5 studies, patients received an additional nonsurgical treatment as a prespecified part of the study protocol (postoperative education, exercise, insoles, diet, and pain medication<sup>8,53</sup>; preoperative pain neuroscience education or biomedical education in combination with mobilization<sup>24</sup>; preoperative neuromuscular training<sup>31</sup>; or postoperative placebo or fentanyl pain medication<sup>60</sup>). Patients in the other studies underwent standard usual postoperative care rehabilitation.<sup>3,11,18,20,30,31,33,34,36,37,39,38,46,56–58</sup>

Detailed information about the demographics, eligibility criteria, interventions, and results can be found in **Table 5**.

### 3.4. AIM 1: evolution of somatosensory processing system signs after nociceptive targeted surgery in musculoskeletal disorders

#### 3.4.1. Static quantitative sensory testing—pressure thresholds

**Table 6**, Supplementary Table 1, **Table 7**, and Supplementary Table 2 (available as supplemental digital content at <http://links.lww.com/PAIN/B799>) show the results of pain pressure and pain pressure tolerance threshold (PPT and PPTT). In total, 20 studies measured PPT<sup>3,8,11,18,20,30,31,33–37,39,38,46,53,56–58,60</sup> and 5

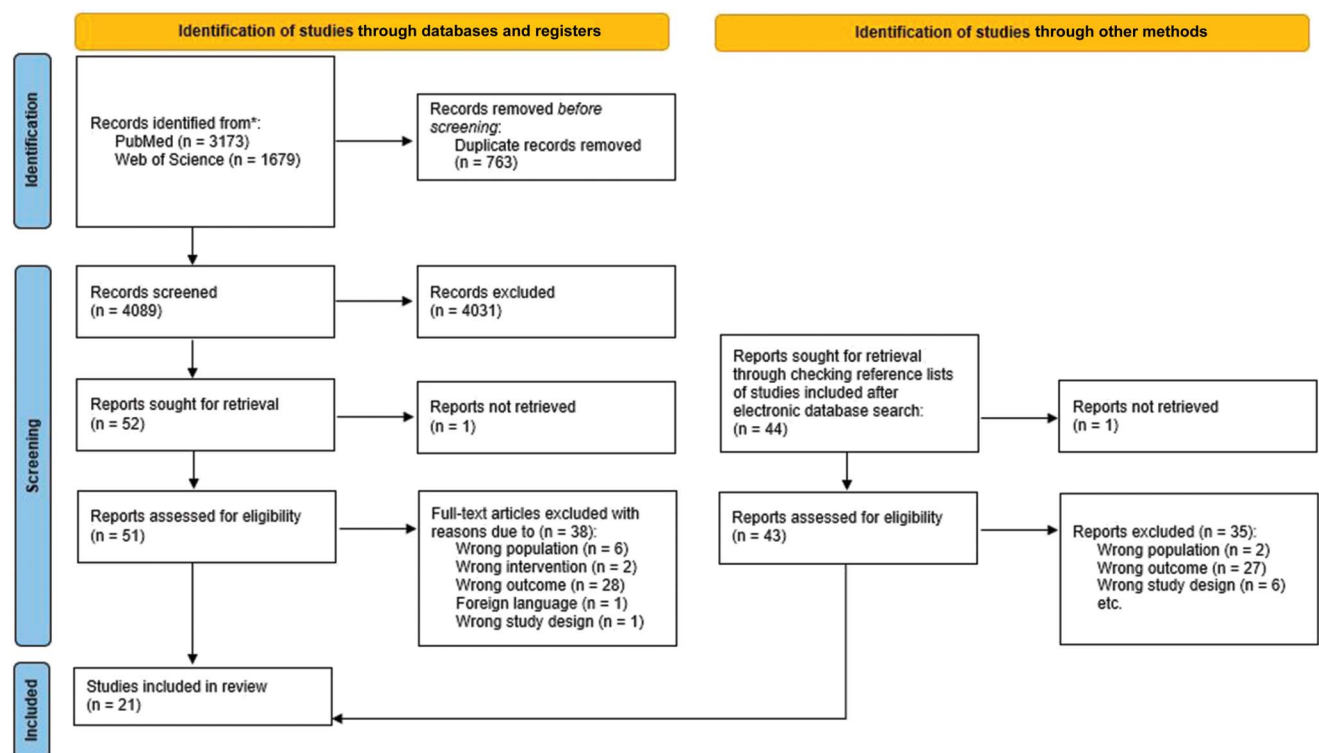
**Figure 1.** PRISMA flowchart. PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses.

Table 5

## Evidence table.

Author, year, and study design	Participants	Study sample and characteristics	Inclusion criteria	Exclusion criteria	Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
Aranda-Villalobos et al. <sup>3</sup> Prospective cohort study	Hip OA	N = 20 Age = 65 y (41–83 y) ♀ = 12 (60%) K&S not reported	-Severe pain (>6/10 on VAS) for >1 y	Previous hip surgery Presence of other pain syndromes Presence of physical/psychological limitation preventing testing Mentally impaired	O: PPT M: Algometer (pain diagnosis and treatment) A: Mean of 3 trials	Bilaterally Second metacarpal bone m. Gluteus medius m. Vastus medialis and lateralis m. Tibialis anterior	THA	3 m after surgery No losses	Change in SPS signs: PPT ↑ 3 m after surgery on All measurement locations ( $P < 0.01$ ), except for vastus lateralis ( $P > 0.05$ ) Changes affected side > unaffected side ( $P$ value not given) Covariates age, sex, and BMI did not influence the PPT ↑ ( $P > 0.05$ )
Arendt-Nielsen et al. <sup>8</sup> RCT	Knee OA	N = 50 Age = 65.8 y (8.7 y) ♀ = 32 (64%) K&S 2: n = 7 K&S 3: n = 21 K&S 4: n = 22	Referred to orthopaedic surgeon Eligible for TKA Diagnosed with knee OA (K&S ≥ 1) ≥ 18 y KOOS ≤ 75	Previous ipsilateral TKA RA Mean pain (>6/10 VAS) in previous week Pregnancy Inability to conform with protocol Inadequacy in Danish	O: PPT M: Algometer (Somedic) A: Mean of 2 trials + mean of all PPTs on all locations	Bilaterally: Peripatellar region m. Tibialis anterior	TKA Nonsurgical treatment: education, exercise, insoles, diet, and pain medication	12 m 4 losses	Change in SPS signs: PPT ↑ 12 m after surgery on both locations
Bjurström et al. <sup>11</sup> Prospective cohort study	Disabling OA pain	N = 15 Age = 68.9 y (56–77 y) ♀ = 9 (60%) K&S not reported	Age ≥ 18 y Persistent OA-related pain ≥ 12 m Average pain NRS score ≥ 4 and/or movement-related pain score ≥ 4 after 5 min walking, spinal anaesthesia during THA	Acute illness Malignancy Immunomodulating treatment Neurological disorder Severe psychiatric disorder Contraindications for lumbar puncture ASA physical status classification >3 Substance abuse < 12 m Poor Swedish-language fluency Inability to provide informed consent	O1–O2: PPT and PTT M: Digital algometer (SBMEDIC) A: Mean of 3 trials O3–O4: Punctate pain and temporal summation M: Monofilament A: O3 pain rating single stimulus, O4 VAS score 10th–1st stimuli O5: CPM M: TS PPT, CS occlusion cuff A: PPT and cuff PPT during CS — without CS and (PPT with CS — PPT without CS)/PPT without CS × 100	Region of maximal pain around the hip Corresponding contralateral side Volar forearm O5: CS: Cubital fossa	THA	18 m Not reported	Change in SPS signs: All PPT and PTT ↑ 18 m after surgery ( $P < 0.05$ ) Punctuate pain ↓ at the forearm 18 m after surgery ( $P = 0.034$ ) TS ↓ in contralateral hip 18 m after surgery ( $P = 0.015$ ) Other results were nonsignificant ( $P > 0.05$ )

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Feldreich et al. <sup>18</sup> Prospective cohort study	Unilateral painful chronic closed lock of the TMJ	N = 18 Age: 18-72 y ♀ = 18 (100%)	Age > 18 y Planned for surgical treatment Diagnosed with unilateral painful chronic closed lock of TMJ	Generalized joint diseases	O1: PPT M: Algometer (Somedic) A: Mean of 3 trials O2: EDT and EPT M: PainMatcher device A: Mean of 3 trials	Bilaterally: O1: m. Masseter Index finger O2: Index finger	Discectomy	6-24 m 7 losses	Change in SPS signs: No changes over time for all SPS signs ( $P > 0.05$ )
Graven-Nielsen et al. <sup>22</sup> Prospective cohort study	Bilateral or unilateral knee OA	N = 20 Age = 68 y (48-86 y) ♀ = 14 (70%) K&S not reported	Severe pain ( $\geq 4/10$ on VAS) >3 m	Other pain problems or sensory dysfunctions Mentally impaired	O1: PPT M: Algometer (Somedic) A: Mean of 2 or 3 trials O2: Cuff PPT M: Double-chamber tourniquet cuff A: Not specified O3: Spatial summation M: Double- and single-chamber tourniquet cuff A: Ratio threshold double-chamber cuff/ thresholds from single-chamber cuff O4: CPM M: TS = PPT (algometer) and cuff PPT (tourniquet cuff) CS = ischemic exercise of left arm with tourniquet cuff A: PPT and cuff PPT during CS — without CS	Bilaterally: O1: Peripatellar region m. Extensor carpi radialis longus m. Tibialis anterior O2-O3: m. Gastrocnemius/m. Soleus O4: TS: infrapatellar location CS: Ipsilateral upper arm	Knee replacement surgery (not specified total or unicompartmental)	5-28 w (60% reassessed 9-18 w) Losses not reported	Change in SPS signs: PPT ↑ after surgery ( $P < 0.04$ ) on all locations Cuff PPT ↑ after surgery in both legs ( $P < 0.006$ ) Spatial summation ratio ↑ only on the affected leg 5-28 w after surgery ( $P < 0.01$ ) CPM improved 5-28 w after surgery: higher ↑ in PPT values ( $P < 0.0001$ ) and cuff PPT values ( $P = 0.055$ ) with CS
Huysmans et al. <sup>24</sup> RCT	Chronic knee OA	N = 54 Age PNE group: 67.7 y (7.8 y) Age control group: 72.8 y (5.6 y) ♀ PNE group = 15 (68%) ♀ control group = 13 (59%) K&S 2: N = 12 K&S 3: N = 21 K&S 4: N = 11	Chronic knee OA diagnosed according to the American College of Rheumatology classification criteria Scheduled for TKA	Other surgery affected knee < 6 m Chronic widespread pain Neurological, metabolic or inflammatory comorbidities Cognitive impairment Illiteracy Inability to speak or write Spanish	O1: CSI M: Questionnaire A: The higher the score, the more central sensitization	NA	TKA + preoperative PNE plus knee joint mobilization OR biomedical education plus knee joint mobilization	Immediate after intervention, 1 m, 3 m 10 losses	Change in SPS signs: The CSI score ↓ after surgery ( $P < 0.001$ , ES: 0.278) (over all 4 time points)

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Izumi et al. <sup>26</sup> Prospective cohort study	Hip OA	N = 40 Age = 65 y (45-81 y) ♀ = 14 (50%)	≥3 m unilateral hip pain while walking with ≥4/10 on VAS Bilateral hip OA if 1 hip was pain free (0/10 on VAS)	Other ongoing pain problems History of chronic pain condition Sensory symptomatic dysfunctions Mental illness	O1: PPT M: Algometer (Somedic) A: Mean of 3 trials O2: Cuff PPT M: Double-chamber tourniquet cuff A: Mean of 3 trials O3: Temporal summation M: Tourniquet cuff A: Mean VAS score 10th stimuli — 1st stimuli O4: Spatial summation M: Single- and double-chamber tourniquet cuff A: Ratio threshold double-chamber cuff/ thresholds from single-chamber cuff O5: Cutaneous pinprick pain sensitivity M: Pinprick device A: 0-10 VAS score O6-09: CDT, WDT, HPT, and CPT M: Contact thermode A: Not specified O10: CPM M: TS = PPT (algometer) and cuff PPT (tourniquet cuff) CS = tourniquet cuff A: PPT and cuff PPT during CS —without CS	Bilaterally: O1: m. Gluteus medius and maximus m. Vastus lateralis M. Tensor fascia latae m. Tibialis anterior m. Extensor carpi radialis longus O2-04: Thigh O5-09: Lateral hip O10: TS: see O1 and O2 CS: Biceps brachii contralateral arm	THA	6 w 4 losses	Change in SPS signs: PPT ↑ on all locations 6 w after surgery ( $P < 0.01$ ) Temporal summation ↓ in patients with pain relief ( $P < 0.002$ ), but not in patients without pain relief ( $P > 0.05$ ) 6 w after surgery Spatial summation ↓ 6 w after surgery ( $P < 0.002$ ) Other results were nonsignificant ( $P > 0.05$ )
Kadum et al. <sup>27</sup> Prospective cohort study	Primary shoulder OA	N = 70 Age = 71 y (53-89 y) ♀ = 31 (50%) Samilson and Prieto classification: OA grade 4	Primary shoulder OA	Secondary OA Contralateral TSA Previous fracture Surgery involving the affected shoulder Non-Swedish speaker	O1: EPT M: PainMatcher unit (medical) A: Mean of 2 trials	Bilaterally: Hand	Stemless anatomical TSA	3 m and 6 m 7 losses	Change in SPS signs: EPT did not change 3 or 6 m after surgery ( $P = 0.09$ )

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Kosek et al. <sup>29</sup> Prospective cohort study	Painful hip OA	N = 14 Age = 53 y (29-66 y) ♀ = 5 (36%)	Radiological OA Severe pain > 1 y Healthy apart from OA No pain contralateral side	Not reported	O1: PPT M: Pressure algometer (Somedic) A: Mean of 2 trials O2: Light-touch DT M: von Frey filaments A: Descending order until sensation disappeared O3-O6: WDT and CDT and HPT and CPT M: Thermode (Thermotest Somedic) A: Mean of last 2 perception levels	Most painful site + corresponding contralateral side: Greater femoral trochanter (n = 11) Buttock (n = 1) Lateral part knee (n = 1) Lateral part calf (n = 1) Lateral (n = 7), frontal (n = 3), medial (n = 2), and dorsal (n = 1) part of the thigh Groin (n = 7) Dorsolateral part calf (n = 5) Knee (n = 7) Ankle (n = 2)	THA (n = 10), osteotomy (n = 2)	6-24 m (mean was 10 m) 2 losses	Change in SPS signs: PPT ↑ on the affected side 6-24 m after surgery ( <i>P</i> < 0.05) Light-touch DT ↓ on the affected side 6-24 m after surgery ( <i>P</i> < 0.01) WDT ↓ on the affected side 6-24 m after surgery ( <i>P</i> < 0.05) Other results were nonsignificant ( <i>P</i> > 0.05)
Kosek et al. <sup>30</sup> Prospective cohort study	Painful hip OA	N = 15 Age: 52 y (29-66 y) ♀ = 6 (40%)	Radiological OA Severe pain > 1 y Considered for surgery Healthy apart from OA	Not reported	O1: PPT M: Pressure algometer (Somedic) A: Mean of 2 trials O2: Light-touch DT M: von Frey filaments A: Descending order until sensation disappeared O3-O6: WDT and CDT and HPT and CPT M: Thermode (Thermotest Somedic) A: Mean of last 2 perception levels + All QST reassessed during and after tourniquet test	Most painful site + corresponding contralateral side: Greater femoral trochanter (n = 11) Buttock (n = 1) Lateral part knee (n = 1) Lateral part calf (n = 1) Lateral (n = 7), frontal (n = 3), medial (n = 2), and dorsal (n = 1) part of the thigh Groin (n = 7) Dorsolateral part calf (n = 5) Knee (n = 7) Ankle (n = 2)	THA (n = 11), osteotomy (n = 2)	6-24 m (mean was 9 m) 2 losses	Change in SPS signs: PPT ↑ 6-24 m after surgery ( <i>P</i> < 0.001), location not specified Light-touch DT ↓ 6-24 m after surgery ( <i>P</i> < 0.001) CDT ↓ 6-24 m after surgery ( <i>P</i> < 0.001) Other results were nonsignificant ( <i>P</i> > 0.05)

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Kosek et al. <sup>31</sup> Prospective cohort clinical trial study	Knee and hip OA	Total N = 134 Hip OA: N = 51 Knee OA: N = 83 Age hip OA = 67.1 y (4.0 y) Age knee OA = 68 (4.3 y) ♀ = 42 (39%)	Primary OA	Posttraumatic OA Rheumatoid arthritis Psoriatic arthritis Severe heart failure Neurological diseases Congenital hip deformities Morbus perthes THA or TKA in last 12 m Dementia Non-Swedish-speaking Use of antidepressant, neuroleptics, anticonvulsive drugs, or steroids	O1-O3: PPT, PP4, PP7 M: Pressure algometer (Somedic) A: Not reported O4: EIA M: PPT measured 5 s after beginning and 30 s during isometric contraction of knee extension (pressure algometer, Somedic) A: Change in PPT during contraction	Bilaterally O1-O3: m. Supraspinatus Lateral epicondyle elbow m. Gluteus Greater trochanter Medial knee O4: m. Quadriceps affected side m. Deltoideus contralateral side	THA, TKA Preoperative individualized, goal-based neuromuscular training	3 m 21 losses	Change in SPS signs: PPTS (EIA) ↑ during contraction 3 m after surgery at m. Quadriceps ( $P < 0.009$ ) Other results were nonsignificant ( $P > 0.05$ )
Kurien et al. <sup>32</sup> Prospective cohort study	Chronic knee OA	N = 50 Age = 66.4 y (8.3 y) ♀ = 30 (60%)	Knee OA	Associated symptomatic hip OA Psychiatric illness Active cancer Sensory dysfunction Contraindication to MRI Other chronic pain condition (fibromyalgia and rheumatoid arthritis)	O1: PPT M: Pressure algometer (Somedic) A: Mean of 3 trials O2-O3: Cuff PPT and PTT M: Single-chamber tourniquet cuff A: Not reported O4: Temporal summation M: Single-chamber tourniquet cuff A: VAS score mean 8th to 10th stimuli—mean 1st to 4th stimuli O5: Temporal summation M: von Frey stimulator A: VAS score 10th — 1st stimulus O6: CPM M: TS = cuff PPT affected side, CS = cuff PPT contralateral leg A: PPT during CS — PPT without CS	O1: Medial, superior, and lateral of patella of affected knee m. Tibialis anterior m. Extensor carpi radialis longus O2-O4: m. Gastrocnemius affected side O5: Affected knee O6: m. Gastrocnemius bilaterally	TKA	6 m 4 losses	Change in SPS signs: PPT ↑ 6 m after surgery at the knee ( $P = 0.02$ ) Temporal summation with cuff and von Frey ↓ 6 m after surgery ( $P = 0.004$ ) Other results were nonsignificant ( $P > 0.05$ )

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Larsen et al. <sup>33</sup> Prospective cohort study	Knee OA	N = 185 Age = 68.8 y (8.92 y) ♀ = 103 (56%)	Knee OA	Use of gabapentinoids, glucocorticoids, opioids, anxiolytics, antiepileptics, and antidepressants Alcohol abuse Other pain treatments outside standard care Malignant conditions Pregnancy BMI > 40 kg/m <sup>2</sup> Affected by other peripheral or central-acting disease Allergy toward chlorzoxazone Preoperative complications Liver disease	O1: Cuff PPT M: Cuff algometer (Cortex Technology) A: One trial O2: CPM M: TS cuff PPT affected side, CS contralateral leg (tourniquet cuff) A: PPT with CS – PPT without CS	Bilaterally: m. Gastrocnemius	Unilateral TKA	12 m 54 losses	Change in SPS signs: No change was seen 12 m after surgery ( $P > 0.05$ )
Lewis et al. <sup>35</sup> Prospective cohort study	End-stage knee OA	N = 29 Age = 68 y (10 y) ♀ = 14 (50%)	VAS 3/10 on $\geq 3$ d per w during past month Scheduled for TKA during next month	Contraindications to MRI Neurological conditions Inability to communicate in English	O1: PPT M: Pressure algometer (Somedic) A: Not reported O2: Temporal summation M: von Frey filament A: VAS score 10th – 1st stimulus + TS presentation = difference $\geq 1$ O3: CPM M: TS PPT affected side, CS cold water immersion A: PPT with CS – PPT without CS + impaired CPM = increase of PPT during CS < 10%	O1-O3: Medial knee O3 CS: Contralateral hand	TKA	3 w, 6 m 0 losses	Change in SPS signs: Temporal summation score ( $P = 0.007$ ) and the presence of temporal summation ( $P < 0.001$ ) $\downarrow$ 3 w and 6 m after surgery CPM change score $\uparrow$ ( $P = 0.033$ ) and presence of impaired CPM ( $P = 0.02$ ) $\downarrow$ 3 w and 6 m after surgery Other results were nonsignificant ( $P > 0.05$ )

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Martinez et al. <sup>38</sup> Prospective cohort study	Knee OA	N = 20 Age = 69 y (2 y) ♀ = 19 (95%)	TKA indicated because of knee OA	Previous surgery/trauma of the knee Preoperative use of opioids Mental disorders preventing an accurate understanding of tests	O1: Mechanical punctuate stimuli pain threshold M: von Frey hairs (Bioseb) A: Not reported O2-O3: HPT and CPT M: Thermotest (Somedic) A: Mean of 3 trials O3: Suprathreshold cold and warmth M: Thermotest (Somedic) A: Not reported O4: Dynamic pain M: Paintbrush A: Painful or not	O1-O3: Patella affected knee Patella contralateral knee Right hand O4: 5 cm above incision affected knee	TKA	1 d, 4 d, 1 m and 4 m Not reported	Change in SPS signs: Mechanical and CPT ↓ at affected knee day 1 and 4 after surgery Other results were nonsignificant ( $P > 0.05$ )
Petersen et al. <sup>46</sup> Prospective cohort study	Severe knee OA	N = 78 Age (group VAS < 3): 68 y (47 y-86 y) Age (group VAS ≥ 3): 72 y (56 y-86 y) ♀ = 46 (59%) K&S: 3 or 4	Severe knee OA Scheduled for TKA surgery OA defined following the American College of Rheumatology classification criteria	Previously diagnosed rheumatoid arthritis or fibromyalgia Fractured knee Presence of other pain problems Sensory dysfunction Mental impairment	O1: PPT M: Pressure algometer A: Not reported	Bilaterally: Peripatellar region m. Tibialis anterior m. Extensor carpi radialis	TKA	2 m, 12 m Not reported	Change in SPS signs: PPT ↑ on all locations except for the m. Extensor carpi radialis longus in the low pain group 2 and 12 m after surgery ( $P < 0.05$ ) PPT ↑ only at the m. extensor carpi radialis in the high pain group 2 and 12 m after surgery ( $P = 0.049$ ) Other results were nonsignificant ( $P > 0.05$ )
Skou et al. <sup>53</sup> RCT	Radiographic and symptomatic knee OA	N = 50 Age = 65.8 y (8.7 y) ♀ = 32 (64%) K&S 2: n = 7 K&S 3: n = 21 K&S 4: n = 22	K&S ≥ 2	Previous TKA on affected side Need for bilateral simultaneous TKA Mean knee pain intensity >60 mm on 100 mm VAS Recurrent disk herniation	O: PPT M: Algometer (Somedic) A: Mean of 2 trials + mean of all PPTs on all locations	Bilaterally: Peripatellar region m. Tibialis anterior	TKA Nonsurgical treatment: education, exercise, insoles, diet, and pain medication	3 m 9 losses	Change in SPS signs: PPT ↑ 3 m after surgery

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Tschugg et al. <sup>56</sup> Prospective cohort study	Single level lumbar disk herniation	N = 52 Age = 44.3 y (10 y) ♀ not given	Single-level lumbar disk herniation (MRI) Sensory dysfunction in the corresponding nerve root distribution of L3 to S1 Indication for sequestrectomy according guidelines DGNC, DGOOC No previous back surgery No metabolic, peripheral nervous system disorders	Recurrent disk herniation	O1: PPT M: Pressure gauge device (Wagner) A: Not reported O2: MDT M: von Frey hairs A: Not reported O3: Pinprick pain threshold M: Pinprick A: Not reported O4-07: CDT, WDT, CPT and HPT M: Sensory Analyser TSA-II (Medoc) A: Not reported O8: VDT M: Rydel-Seiffer tuning fork A: Not reported	A test and control side (not specified)	Sequestrectomy	1 w, 6 m, 12 m 16 losses	Change in SPS signs: PPT ↑ 12 m after surgery ( $P < 0.005$ ) MDT and VDT ↓ 1 w after surgery ( $P < 0.001$ ) MDT ↓ 12 m after surgery ( $P < 0.005$ ) Pinprick pain threshold ↑ 12 m after surgery ( $P$ value not given) CDT ↑ 6 m ( $P < 0.05$ ) and 12 m ( $P < 0.005$ ) after surgery
Tschugg et al. <sup>57</sup> Prospective cohort study	Single level lumbar disk herniation	N = 52 Age not reported ♀ = 21 (40%)	Single level lumbar disk herniation (MRI) Sensory dysfunction in the corresponding nerve root distribution of L3 to S1 Indication for sequestrectomy according guidelines DGNC, DGOOC No previous back surgery No metabolic, peripheral nervous system disorders	Recurrent disk herniation	O1: PPT M: Pressure gauge device (Wagner) A: Not reported O2: MDT M: von Frey hairs A: Not reported O3: Pinprick pain threshold M: Pinprick A: Not reported O4-07: CDT, WDT, CPT, and HPT M: Sensory Analyser TSA-II (Medoc) A: Not reported O8: VDT M: Rydel-Seiffer tuning fork A: Not reported	Not reported	Sequestrectomy	12 m 14 losses	Change in SPS signs: PPT and pinprick pain threshold ↑ 12 m after surgery ( $P < 0.005$ ) CDT ↑ and MDT ↓ 12 m after surgery ( $P < 0.005$ ) PPT, pinprick pain threshold, CDT, MDT, and VDT improved in the group with complete restoration of sensory function after surgery ( $P < 0.05$ ) Pinprick pain threshold, MDT, and CDT improved in the group with disturbed sensory function after surgery ( $P < 0.05$ )

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Table 5 (continued)

Author, year, and study design	Participants				Outcome, measurement method, and analysis of central SPS sign	Measurement location	Type of surgery + additional treatment in study (if performed)	FU + losses to FU	Results (change in SPS signs after surgery)
	MSK disorder	Study sample and characteristics	Inclusion criteria	Exclusion criteria					
Vaegter et al. <sup>58</sup> Prospective cohort study	Knee OA	N = 15 Age = 66.3 y (5.9 y) ♀ = 7 (47%)	Scheduled for unilateral TKA K&S ≥ 2 Able to use a stationary bicycle	Neurological, psychiatric or cardiovascular disease	O1: PPT M: Pressure algometry (Somedic) A: Mean of 2 trials O2-O3: Cuff PPT and PTT M: Tourniquet cuff (NociTech) A: Not reported O4: CPM M: CPT A: PPT with CS – PPT without CS O5: EIH M: aerobic bicycling + isometric muscle + measuring PPTs contraction A: Change in PPT	O1: m. Quadriceps affected side m. Quadriceps nonaffected side m. Biceps brachii dominant side m. Upper trapezius nondominant side O2-O3: Upper leg O4: Foot nonaffected leg	TKA	6 m 1 loss	Change in SPS signs: PPT ↑ 6 m after surgery at m. Quadriceps and m. Biceps brachii of the affected side ( $P = 0.006$ , ES: 0.29) Other results were nonsignificant ( $P > 0.05$ )
Wilder-Smith et al. <sup>60</sup> Prospective cohort study	Disk herniation	N = 30 Age (fentanyl): 44.1 y (27-62 y) Age (placebo): 47.8 (24-64 y) ♀ = 8 (27%)	Not reported	Not reported	O1-O3: Sensation DT, PPT, and PTT M: Constant skin current stimulation	Dermatome most affected by disk prolapse (flanks, ipsilateral and contralateral of incision) + arm	Elective herniated intervertebral disk surgery + placebo or fentanyl	1 h, 2 h, 4 h, 6 h, 24 h, 5 d Not reported	Change in SPS signs: PTT ↓ at the arm in the placebo group 5 d after surgery ( $P < 0.05$ ) PTT ↑ contralateral of the incision in the fentanyl group 4 h after surgery ( $P < 0.05$ ) PTT ↑ in the dermatome region in both groups 4 h after surgery ( $P < 0.05$ ) and also in the placebo group 6 h after surgery ( $P < 0.05$ )

A, analysis; ASA, American Society of Anaesthesiology; CDT, cold detection threshold; CPM, conditioned pain modulation; CPT, cold pain threshold; CS, conditioning stimulus; CSI, Central Sensitization Inventory; DGNC, German Society of Neurosurgery; DGOOC, German Society of Orthopedics and Orthopedic Surgery; DT, detection threshold; EDT, electrical detection threshold; EIA, exercise-induced analgesia; EPT, electrical pain threshold; FU, follow-up period; HPT, heat pain threshold; K&S, Kellgren and Lawrence scale; KOOS, Knee Osteoarthritis Injury and Outcome Score; M, measurement method; m, month; m., musculus; MDT, mechanical detection threshold; min, minutes; MRI, magnetic resonance imaging; MSK, musculoskeletal; N, number; O, outcome; OA, osteoarthritis; PCS, pain catastrophizing scale; PP4, pressure pain threshold corresponding to 4/10; PP7, pressure pain threshold corresponding to 7/10; PPT, pressure pain thresholds; PTT, pain tolerance threshold; RA, rheumatoid arthritis; RCT, randomised controlled trial; s, seconds; SPS, somatosensory processing system; TDT, thermal detection threshold; THA, total hip arthroplasty; TKA, total knee arthroplasty; TMJ, temporomandibular joint; TPT, thermal pain threshold; TS, test stimulus; VAS, visual analogue scale; VDT, vibration detection threshold; VRS, verbal rating score; w, weeks; WDT, warmth detection threshold; y, years old.

**Table 6****Quality assessment.**

Study	1	2	3	4	5	6	Overall RoB	LoE
Aranda-Villalobos et al. <sup>3</sup>	Low	Low	Low	Low	Low	Moderate	Low	1b
Arendt-Nielsen et al. <sup>8</sup>	Low	High	Low	Low	Low	Low	High	2b
Bjurström et al. <sup>11</sup>	Low	Low	Low	Moderate	N/A	Low	Low	2b
Feldreich et al. <sup>18</sup>	High	High	Moderate	Moderate	N/A	Low	High	2b
Graven-Nielsen et al. <sup>22</sup>	High	High	Low	Moderate	N/A	Moderate	High	2b
Huysmans et al. <sup>24</sup>	Low	High	Low	Low	Low	Low	High	2b
Izumi et al. <sup>26</sup>	Moderate	High	Low	Moderate	N/A	Low	High	2b
Kadum et al. <sup>27</sup>	Low	High	Low	Moderate	Low	Low	High	2b
Kosek et al. <sup>29</sup>	Moderate	High	Low	Moderate	N/A	Low	High	2b
Kosek et al. <sup>30</sup>	Moderate	High	Low	Moderate	N/A	Moderate	High	2b
Kosek et al. <sup>31</sup>	Low	Low	Low	Moderate	Low	Moderate	Moderate	1b
Kurien et al. <sup>32</sup>	Low	Moderate	Low	Low	N/A	Low	Low	1b
Larsen et al. <sup>33</sup>	Low	High	Low	Low	High	Low	High	2b
Lewis et al. <sup>35</sup>	Low	Low	Low	Moderate	N/A	Low	Low	1b
Martinez et al. <sup>38</sup>	High	High	Low	Moderate	N/A	Low	High	2b
Petersen et al. <sup>46</sup>	Moderate	Low	Low	Moderate	N/A	Low	Moderate	2b
Skou et al. <sup>53</sup>	Low	Moderate	Low	Low	Low	Low	Low	1b
Tschugg et al. <sup>56</sup>	High	High	Low	Moderate	N/A	Low	High	2b
Tschugg et al. <sup>57</sup>	High	High	Low	Moderate	N/A	Low	High	2b
Vaegter et al. <sup>58</sup>	Moderate	Moderate	Low	Low	N/A	Low	Moderate	1b
Wilder-Smith et al. <sup>60</sup>	High	High	Low	Moderate	N/A	Low	High	2b

Bias due to 1 = study participation, 2 = study attrition, 3 = prognostic factor measurement, 4 = outcome measurement, 5 = study confounding, and 6 = statistical analysis and reporting.  
LoE, level of evidence; N/A, not applicable; RoB, risk of bias.

studies PPTT<sup>11,22,32,58,60</sup> using an algometer or tourniquet cuff. Five studies had a low,<sup>3,11,36,39,53</sup> 3 studies a moderate,<sup>31,46,58</sup> and 12 studies a high RoB.<sup>8,18,20,26,27,29,30,33,38,56,57,60</sup> As a result, taking into account the criteria of **Table 4**, 6 studies received a level of evidence 1b<sup>3,31,36,39,53,58</sup> and the other 14 received a level 2b.<sup>8,11,18,20,26,27,29,30,33,38,46,56,57,60</sup>

### 3.4.1.1. Follow-up <3 months

Widespread PPT improved after total knee arthroplasty (TKA) (moderate conclusion).<sup>22,46</sup> Conflicting evidence for a change in PPT was found after total hip arthroplasty (THA),<sup>26</sup> TKA (only local PPT),<sup>22,35,46</sup> and sequestrectomy.<sup>56,60</sup> Also for PPTT after sequestrectomy<sup>56,57,60</sup> conflicting evidence was obtained. No change of PPTT values after TKA surgery was seen<sup>22</sup> (weak conclusion).

### 3.4.1.2. Follow-up ≥3 months

Pressure pain threshold improved after sequestrectomy<sup>56,57</sup> (moderate conclusion) and PPTT after THA<sup>11</sup> (moderate conclusion). Conflicting evidence was found for the change of PPT after THA surgery<sup>3,11,33–35</sup> and after TKA.<sup>8,22,32,46,53,58</sup> Pressure pain threshold remained unchanged after TKA<sup>22,32,58</sup> (strong conclusion) and after temporomandibular joint discectomy<sup>18</sup> (weak conclusion).

### 3.4.2. Static quantitative sensory testing—thermal thresholds

**Table 6**, Supplementary Table 3, **Table 7**, and Supplementary Table 4 (available as supplemental digital content at <http://links.lww.com/PAIN/B799>) show the results of the cold and warmth detection threshold (CDT and WDT), cold and heat pain threshold

(CPT and HPT), and cold and warmth suprathreshold. Five studies measured CDT and WDT,<sup>26,29,30,56,57</sup> and 6 studies HPT and CPT<sup>26,29,30,38,56,57</sup> by using thermodes of which all studies scored a high RoB and as such a level of evidence 2b.<sup>26,29,30,38,56,57</sup> One study with a high RoB and level of evidence 2b measured warmth and cold suprathreshold by using thermodes.<sup>38</sup>

### 3.4.2.1. Follow-up <3 months

No change of all thermal thresholds was seen after THA<sup>26</sup> and sequestrectomy.<sup>56</sup> Also HPT, widespread CPT, and warmth and cold suprathreshold remained unchanged after TKA, but local CPT worsened after TKA<sup>38</sup> (all weak conclusion).

### 3.4.2.2. Follow-up ≥3 months

A positive change of CDT after sequestrectomy was seen<sup>56,57</sup> (moderate conclusion). Conflicting evidence for CDT and WDT was obtained after THA.<sup>29,30</sup> Following SPS signs remained unchanged after surgery: HPT and CPT after THA<sup>29,30</sup> (moderate conclusion); HPT, CPT, warmth suprathreshold, and cold suprathreshold after TKA (weak conclusion); and WDT, HPT, and CPT after sequestrectomy<sup>56,57</sup> (moderate conclusion).

### 3.4.3. Static quantitative sensory testing—other thresholds

**Table 6**, Supplementary Table 3, **Table 7**, and Supplementary Table 5 (available as supplemental digital content at <http://links.lww.com/PAIN/B799>) show the results of the pinprick threshold, electrical detection and pain threshold (EDT and EPT), vibration detection threshold (VDT), and light-touch detection threshold. Pinprick pain threshold was measured in 5 studies with a pinprick<sup>11,26,38,56,57</sup>; EDT was measured in 1 study<sup>18</sup> and EPT in

**Table 7**  
**Overview of evolution of static quantitative sensory testing after surgery in musculoskeletal disorders.**

Static QST	Overall level of recommendation [references of studies]									
	Hip OA		Knee OA		Shoulder OA		Closed lock TMJ		Disc herniation	
	FU < 3m	FU ≥ 3m	FU < 3m	FU ≥ 3m	FU < 3m	FU ≥ 3m	FU < 3m	FU ≥ 3m	FU < 3m	FU ≥ 3m
PPT (positive change means increased PPT)	Conflicting [31]	Conflicting [3,11,34–36]	Local = conflicting [22,40,52] Widespread = moderate for + change [22,52]	Conflicting [8,22,36–38,40,52,59,64]	/	/	/	Weak for no change [19]	Conflicting [62,66]	Moderate for + change [62,63]
PTT	/	Moderate for + change [11]	Weak for no change [22]	Strong for no change [22,37,64]	/	/	/	/	Conflicting [66]	/
CDT	Weak for no change [31]	Conflicting [34,35]	/	/	/	/	/	/	Weak for no change [62]	Moderate for + change [62,63]
WDT	Weak for no change [31]	Conflicting [34,35]	/	/	/	/	/	/	Weak for no change [62]	Moderate for no change [62,63]
HPT	Weak for no change [31]	Moderate for no change [34,35]	Weak for no change [43]	Weak for no change [43]	/	/	/	/	Weak for no change [62]	Moderate for no change [62,63]
CPT	Weak for no change [31]	Moderate for no change [34,35]	Local = weak for – change [43] Widespread = weak for no change [43]	Weak for no change [43]	/	/	/	/	Weak for no change [62]	Moderate for no change [62,63]
Warmth suprathreshold	/	/	Weak for no change [43]	Weak for no change [43]	/	/	/	/	/	/
Cold suprathreshold	/	/	Weak for no change [43]	Weak for no change [43]	/	/	/	/	/	/
Pinprick pain threshold	Weak for no change [31]	Local = moderate for no change [11] Widespread = moderate for + change [11]	Weak for – change [43]	Weak for no change [43]	/	/	/	/	Weak for no change [62]	Moderate for + change [62,63]
EDT	/	/	/	/	/	/	/	Weak for no change [19]	/	/
EPT	/	/	/	/	Weak for no change [32]	Weak for no change [32]	/	Weak for no change [19]	/	/
VDT	/	/	/	/	/	/	/	/	Weak for + change [62]	Conflicting [62,63]
Light-touch detection threshold	/	Moderate for + change [34,35]	/	/	/	/	/	/	Conflicting [62,66]	Moderate for + change [62,63]

Colors: green = positive change, red = negative change, yellow = conflicting, blue = no change.  
Abbreviations: QST, quantitative sensory testing; MSK, musculoskeletal; PPT, pressure pain threshold; PTT, pressure pain tolerance threshold; CDT, cold detection threshold; WDT, warmth detection threshold; HPT, heat pain threshold; CPT, cold pain threshold; OA, osteoarthritis; m, month; OA, osteoarthritis; +, positive (means improvement of SPS sign); –, negative (means worsening of SPS sign); FU, follow-up. Colors: green = positive change, red = negative change, yellow = conflicting, blue = no change

2 studies with a PainMatcher<sup>18,27</sup>; VDT was measured in 2 studies with a tuning fork<sup>56,57</sup>; and 5 studies measured the light-touch detection threshold with von Frey hairs.<sup>29,30,56,57,60</sup> Only 1 study scored a low RoB,<sup>11</sup> and all the other studies scored a high RoB.<sup>18,26,27,29,30,38,56,57,60</sup> All studies received a level of evidence 2b.<sup>11,18,26,27,29,30,38,56,57,60</sup>

**3.4.3.1. Follow-up <3 months**

Vibration detection threshold improved after sequestrectomy<sup>56,60</sup> (weak evidence). Conflicting evidence was found for a change of light-touch detection threshold after sequestrectomy.<sup>56,60</sup> No change was seen for pinprick pain threshold after THA<sup>26</sup> and sequestrectomy<sup>56,60</sup> and also EPT did not change after total shoulder arthroplasty (TSA)<sup>27</sup> (all weak conclusion). Pinprick pain threshold worsened after TKA<sup>38</sup> (weak conclusion).

**3.4.3.2. Follow-up ≥3 months**

A positive change for widespread pinprick pain threshold and light-detection threshold was reported after THA<sup>11</sup> and sequestrectomy<sup>56,57</sup> (both moderate conclusion). Conflicting evidence was found for VDT after sequestrectomy.<sup>56,57</sup> Finally, following SPS signs remained unchanged: pinprick threshold after TKA,<sup>38</sup> local pinprick threshold after THA,<sup>11</sup> EDT after temporomandibular joint

discectomy,<sup>18</sup> and EPT after temporomandibular joint discectomy<sup>18</sup> and TSA<sup>27</sup> (all weak conclusion).

**3.4.4. Dynamic quantitative sensory testing**

**Table 6**, Supplementary Table 6, **Table 8**, and Supplementary Table 7 (available as supplemental digital content at <http://links.lww.com/PAIN/B799>) show the results regarding dynamic QST. Temporal summation was measured in 4 studies with a tourniquet cuff or monofilament<sup>11,26,32,35</sup>; spatial summation in 2 studies with a tourniquet cuff<sup>22,26</sup>; and CPM in 7 studies, using a test stimulus including (cuff) PPT<sup>11,20,26,32,33,35,58</sup> and a conditioning stimulus including an occlusion or tourniquet cuff,<sup>11,26,32,33,58</sup> ischemic exercise,<sup>20</sup> or cold water immersion.<sup>35</sup> Three studies scored a low,<sup>11,32,35</sup> one study a moderate,<sup>58</sup> and 3 studies a high RoB.<sup>22,26,33</sup> As a result, 3 studies received a level of evidence 1b<sup>32,35,58</sup> and 2 a level of evidence 2b.<sup>11,22,26,33</sup>

**3.4.4.1. Follow-up <3 months**

Temporal and spatial summation improved after THA<sup>26</sup> (weak conclusion) and TKA<sup>22,35</sup> (moderate conclusion for temporal summation and weak for spatial summation). An improvement of CPM was seen after TKA<sup>22,35</sup> (moderate conclusion), but not after THA<sup>26</sup> (weak conclusion).

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**Table 8****Overview of evolution of dynamic quantitative sensory testing and other somatosensory processing signs after surgery in musculoskeletal disorders.**

Dynamic QST and other SPS signs	Overall level of recommendation (references of studies)			
	Hip OA		Knee OA	
	FU < 3m	FU ≥ 3m	FU < 3m	FU ≥ 3m
Temporal summation	Weak for + change [31]	Moderate for + change [11]	Moderate for + change [40]	Strong for + change [37,40]
Spatial summation	Weak for + change [31]	/	Weak for + change [22]	Weak for + change [22]
CPM	Weak for no change [31]	Moderate for no change [11]	Moderate for + change [22,40]	Conflicting [22,37,38,40,64]
CSI	/	/	Weak for + change [28]	Weak for + change [28]
EIA	/	Weak for + change [36]	/	Conflicting [36,64]
Dynamic pain	/	/	Weak for no change [43]	Weak for no change [43]

Colors: green = positive change, red = negative change, yellow = conflicting, blue = no change

QST, quantitative sensory testing; SPS, somatosensory processing system; MSK, musculoskeletal; CPM, conditioned pain modulation; CSI, central sensitization index; EIA, exercise induced analgesia; OA, osteoarthritis; m, month; FU, follow-up.

**3.4.4.2. Follow-up ≥3 months**

Temporal summation improved after THA<sup>11</sup> (moderate conclusion) and TKA<sup>32,35</sup> (strong conclusion), and also spatial summation improved after TKA<sup>20</sup> (weak conclusion). Conflicting evidence for a change of CPM after TKA was found,<sup>22,32,33,35,58</sup> while no change was seen after THA<sup>11</sup> (moderate conclusion).

**3.4.5. Other somatosensory processing system signs**

**Table 6**, Supplementary Table 6, **Table 8**, and Supplementary Table 8 (available as supplemental digital content at <http://links.lww.com/PAIN/B799>) show the results of the remaining SPS signs. Other signs of SPS were measured through exercise-induced analgesia, measured in 2 studies with a moderate RoB and level of evidence 1b<sup>31,58</sup>; tactile allodynia/dynamic pain (whether the stimulus was considered painful or not), measured in 1 study with a paintbrush, scoring a high RoB and level of evidence 2b<sup>38</sup>; and the CSI (self-reported signs), used in only 1 study with a high RoB and level of evidence 2b.<sup>24</sup>

**3.4.5.1. Follow-up <3 months**

The CSI score improved after TKA<sup>24</sup> (weak conclusion), but dynamic pain remained stable<sup>38</sup> (weak conclusion).

**3.4.5.2. Follow-up ≥3 months**

The Central Sensitization Inventory score improved after TKA<sup>24</sup> (weak conclusion). In addition, exercise-induced analgesia improved after THA<sup>31</sup> (weak conclusion), but conflicting evidence was found after TKA.<sup>58</sup> No change was seen in dynamic pain after TKA<sup>38</sup> (weak conclusion).

**3.5. AIM 2: Predictors to change in somatosensory processing system signs over time and somatosensory processing system sign-related predictors for surgical outcome**

Detailed results can be found in **Tables 9–11**. Only 10 studies reported any kind of predictors for the normalization or stability over time of the SPS signs in the form of a prediction model (linear regression),<sup>8,11,26</sup> interaction effect,<sup>33</sup> correlation,<sup>3,8,11,18,58</sup> or difference between groups<sup>24,32,46</sup> (eg, a group with high and low preoperative pain, men vs women, etc). Only 4 studies reported an SPS change-related predictor for the improvement of pain after surgery in the form of a correlation<sup>3,11,18,58</sup> and will be discussed further on. In 7 other studies, SPS-related predictors for postsurgical outcome were reported, but restricted to preoperative or postoperative SPS signs.<sup>26,27,32,33,38,46,57</sup> However, results of these studies will not be reported in the text (are only available in **Table 9**) because studies that only report preoperative SPS signs or only postoperative SPS signs in

relation to chronic pain/poor surgery are not included in the review (out of the scope of this review).

**3.5.1. Static quantitative sensory testing—pressure thresholds**

An improvement of pain-related variables over time<sup>3,8,18</sup> and lower baseline PPT<sup>8</sup> predicted an improvement of PPT over time (moderate and weak conclusion, respectively). Conflicting evidence was found for a change in inflammatory variables over time to predict a change of PPT or PPTT over time,<sup>11</sup> and baseline pain-related variables over time did not predict a change of PPT or PPTT over time<sup>8</sup> (weak conclusion).

**3.5.2. Static quantitative sensory testing—other thresholds**

A change in pain-related variable<sup>18</sup> and in inflammatory factors<sup>11</sup> over time did not predict a change of EPT, EDT,<sup>18</sup> and punctuate pain<sup>11</sup> over time (all weak conclusion).

**3.5.3. Dynamic quantitative sensory testing**

An improvement of pain-related variable over time predicted CPM over time<sup>58</sup> (moderate conclusion). Conflicting evidence was found for a change in inflammatory variables to predict a change of temporal summation and CPM over time,<sup>11</sup> and a baseline pain-related variable did not predict a change of temporal summation and CPM over time<sup>8</sup> (both weak conclusion). In addition, a baseline pain catastrophizing score failed to predict a change of CPM over time (weak conclusion).<sup>33</sup>

**3.5.4. Other somatosensory processing system signs**

An improvement of pain-related variable over time predicted EI<sup>58</sup> over time<sup>58</sup> (moderate conclusion) and also being a woman predicted an improvement of CSI score over time<sup>24</sup> (weak conclusion).

**3.5.5. Somatosensory processing system change-related predictors for improvement of pain**

An improvement in PPT,<sup>3,8,18</sup> CPM, and EI<sup>58</sup> over time predicted and improvement in pain-related variables over time (all moderate conclusion).

**4. Discussion**

The first goal of this systematic review was to summarize all studies that measure how SPS signs evolve after nociceptive targeted surgery in MSK disorders. The second aim was to find

Table 9

**Predictors to change in somatosensory processing system signs over time and somatosensory processing system sign-related predictors for surgical outcome.**

Author, year	MSK disorder	Surgical outcome in relation to SPS sign	FU period	Method	Predictor change in SPS sign	Predictor surgical outcome (PROM) in relation to SPS sign
Aranda-Villalobos et al. <sup>3</sup>	Hip OA	VAS pain in rest in relation to PPT	3 m	Correlation Δ VAS to predict Δ PPT Δ PPT to predict Δ VAS	↓ in VAS = ↑ PPT for: Second metacarpal bone ( $r = -0.353$ , $P = 0.028$ ) m. Gluteus medius ( $r = -0.351$ , $P = 0.002$ ) m. Vastus medialis ( $r = -0.394$ , $P = 0.013$ ) TA not reported	↑ PPT for: Second metacarpal bone ( $r = -0.353$ , $P = 0.028$ ) m. Gluteus medius ( $r = -0.351$ , $P = 0.002$ ) m. Vastus medialis ( $r = -0.394$ , $P = 0.013$ ) = ↓ in VAS TA not reported
Arendt-Nielsen et al. <sup>8</sup>	Knee OA	VAS pain peak, VAS pain 30 min walking, number of body sites with pain in relation to PPT	12 m	Linear regression Baseline PPT to predict Δ PPT and Δ VAS pain rest and walking  Correlation Δ VAS pain in rest and walking to predict Δ PPT Δ PPT to predict Δ VAS pain in rest and walking	Averaged lower baseline PPT values = higher ↑ PPT after adjustment for age, sex, and BMI (affected side: $r^2 = 0.141$ , $P = 0.02$ ; unaffected side: $r^2 = 0.161$ , $P = 0.01$ ) → But still lowest 12 m PPTs both affected ( $r = 0.73$ , $P < 0.001$ ) and nonaffected side ( $r = 0.73$ , $P < 0.001$ ) ↓ in VAS peak pain intensity (affected and nonaffected side: $r = 0.20$ , $P = 0.01$ ) ↓ VAS after 30 min walking (affected side: $r = 0.23$ , $P = 0.01$ ; nonaffected side: $r = 0.17$ , $P = 0.04$ ) ↓ number of body sites with pain (affected side: $r = 0.14$ , $P = 0.09$ ; nonaffected side: $r = 0.16$ , $P = 0.045$ ) = ↑ PPT affected and nonaffected side	Averaged lower baseline PPT = Less ↓ VAS after 30 min (affected side: $r^2 = 0.110$ , $P = 0.02$ ; unaffected side: $r^2 = 0.090$ , $P = 0.04$ ) No predictor for peak pain VAS  ↑ PPT affected and nonaffected side = ↓ in VAS peak pain intensity (affected and nonaffected side: $r = 0.20$ , $P = 0.01$ ) ↓ VAS after 30 min walking (affected side: $r = 0.23$ , $P = 0.01$ ; nonaffected side: $r = 0.17$ , $P = 0.04$ ) ↓ number of body sites with pain (affected side: $r = 0.14$ , $P = 0.09$ ; nonaffected side: $r = 0.16$ , $P = 0.045$ )
Bjurström et al. <sup>11</sup>	Hip OA	Only inflammatory factors in relation to PPT, PTT, punctate pain, temporal summation, CPM	18 m	Linear regression Δ IL-8, Δ IP-10, Δ Flt, Δ MCP-1 to predict Δ PPT, PTT, punctate pain, temporal summation, CPM  Correlation Δ IL-8, Δ IP-10, Δ Flt, Δ MCP-1 to predict Δ PPT, PTT, punctate pain, temporal summation, CPM	↓ IL-8 ( $r^2 = 0.38$ , $P = 0.01$ ) and ↑ IP-10 ( $r^2 = 0.46$ , $P = 0.006$ ) = ↑ all PTT Higher ↑ IP-10 = ↑ arm PPT scores above median ( $P = 0.028$ ) Other results were nonsignificant ( $P > 0.05$ ) ↓ Flt-1 = ↑ temporal summation most painful area ( $r = -0.560$ , $P = 0.030$ ) ↑ IP-10 = improved CPM ( $r = -0.621$ , $P = 0.013$ ) Other results were nonsignificant ( $P > 0.05$ )	/
Feldreich et al. <sup>18</sup>	Closed lock TMJ	NRS pain in relation to PPT, EDT, and EPT	6–24 m	Correlation Δ NRS to predict Δ PPT, EDT, and EPT Δ PPT, EDT, and EPT to predict Δ NRS	↓ NRS = ↑ PPT contralateral index finger ( $r = -0.68$ , $P = 0.02$ ) Other results were nonsignificant ( $P > 0.05$ )	↑ PPT contralateral index finger = ↓ NRS ( $r = -0.68$ , $P = 0.02$ ) Other results were nonsignificant ( $P > 0.05$ )

(continued on next page)



Table 9 (continued)

Author, year	MSK disorder	Surgical outcome in relation to SPS sign	FU period	Method	Predictor change in SPS sign	Predictor surgical outcome (PROM) in relation to SPS sign
Graven-Nielsen et al. <sup>21</sup>	Knee OA	Only evolution in PPT, cuff PPT, spatial summation, and CPM	5-28 w	/	/	/
Huysmans et al. <sup>24</sup>	Knee OA	Only sex in relation to CSI	Immediate, 1 m and 3 m postop	Linear mixed model Difference in sex to predict $\Delta$ CSI	Sex (being a women) = $\downarrow$ CSI / (ES of 0.600 in the PNE group, vs 0.074 in the control group (over all 4 time points), $P = 0.010$ ) compared with men	/
Izumi et al. <sup>26</sup>	Hip OA	VAS pain in rest and after walking in relation to PPT, cuff PPT, temporal summation, spatial summation, cutaneous pinprick pain sensitivity, CDT, WDT, HPT, CPT, and CPM	6 w	Correlation Baseline QST to predict postoperative VAS pain in rest and walking	/	Examined, but results were nonsignificant ( $P > 0.05$ )
Kadum et al. <sup>27</sup>	Shoulder OA	QuickDASH in relation to EPT	12 m	Correlation and linear regression Baseline EPT to predict postoperative QuickDASH	/	Higher baseline EPT = lower postoperative QuickDASH (affected side: $r = -0.80$ , $P < 0.001$ ; $r^2 = -2.20$ , $P = 0.0001$ ; nonaffected side: $r = -0.40$ , $P = 0.02$ ; $r^2 =$ nonsignificant [ $P > 0.05$ ])
Kosek et al. <sup>29</sup>	Hip OA	/ Only evolution of PPT, light-touch DT, WDT, CDT, HPT, and CPT	6-24 m	/	/	/
Kosek et al. <sup>30</sup>	Hip OA	/ Only evolution of PPT, light-touch DT, WDT, CDT, HPT, CPT	6-24 m	/	/	/
Kosek et al. <sup>32</sup>	Knee & hip OA	/ Only evolution of PPT, PP4, PP7, EIA	3 m	/	/	/
Kurien et al. <sup>33</sup>	Knee OA	VAS pain in rest in relation to PPT, cuff PPT and PTT, temporal summation, CPM	6 m	Paired $t$ test Difference in high- and low baseline PainDETECT groups to predict $\Delta$ in PPT, cuff PPT and PTT, temporal summation, CPM Correlation Baseline PPT, cuff PPT and PTT, temporal summation, CPM to predict postoperative VAS	Examined, but results were nonsignificant ( $P > 0.05$ ) / Higher baseline temporal summation = higher postoperative VAS ( $r = 0.343$ , $P = 0.010$ ) Other results were nonsignificant ( $P > 0.05$ )	/
Larsen et al. <sup>34</sup>	Knee OA	VAS pain in rest in relation to CPM	12 m	Correlation Baseline CPM to predict postoperative VAS Linear regression Baseline CPM to predict postoperative VAS Mixed-effects Baseline CPM to predict $\Delta$ VAS Preoperative PCS to predict $\Delta$ CPM	/ / Examined, but results were nonsignificant ( $P > 0.05$ )	Baseline inefficient CPM = higher postoperative VAS ( $r = -0.18$ , $P = 0.04$ ) Examined, but baseline CPM was no independent factor for postoperative VAS ( $P > 0.05$ ) Examined, but results were nonsignificant ( $P > 0.05$ )

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Author, year	MSK disorder	Surgical outcome in relation to SPS sign	FU period	Method	Predictor change in SPS sign	Predictor surgical outcome (PROM) in relation to SPS sign
Lewis et al. <sup>36</sup>	Knee OA	/ Only evolution of PPT, temporal summation, CPM	3 w, 6 m	/	/	/
Martinez et al. <sup>39</sup>	Knee OA	VAS in rest and after walking in relation to mechanical punctuate stimuli pain threshold, HPT, CPT, suprathreshold cold and warmth, dynamic pain	1 d, 4 d, 1 m and 4 m	Correlation Preoperative QST to predict postoperative pain	/	Examined, but results were nonsignificant ( $P > 0.05$ )
Petersen et al. <sup>46</sup>	Knee OA	VAS 24 h in relation to PPT, temporal summation, CPM	2 m, 12 m	Mixed-model ANOVA Difference between baseline low- and high VAS pain group to predict $\Delta$ PPT Correlation Baseline PPT, temporal summation and CPM to predict postoperative VAS  Logistic regression Baseline PPT, temporal summation and CPM to predict postoperative VAS	Examined, but results were nonsignificant ( $P > 0.05$ )  /  /  /	/   Higher baseline temporal summation = higher postoperative VAS ( $r = 0.240$ , $P = 0.037$ ) Other results were nonsignificant ( $P > 0.05$ ) Examined, but results were nonsignificant ( $P > 0.05$ )
Skou et al. <sup>53</sup>	Knee OA	/ Only evolution of PPT	3 m	/	/	/
Tschugg et al. <sup>56</sup>	Lumbar disk herniation	/ Only evolution of PPT, MDT, pinprick pain threshold, CDT, WDT, CPT, HPT, VDT	1 w, 6 m, 12 m	/	/	/
Tschugg et al. <sup>57</sup>	Lumbar disk herniation	NRS pain in relation to PPT, MDT, pinprick pain threshold, CDT, WDT, CPT, HPT, VDT	12 m	Correlation Postoperative QST to predict postoperative NRS	/	Examined, but results were nonsignificant ( $P > 0.05$ )
Vaegter et al. <sup>58</sup>	Knee OA	NRS peak pain in relation to CPM, EIH	6 m	Correlation Baseline EIH to predict $\Delta$ NRS $\Delta$ NRS to predict $\Delta$ CPM and $\Delta$ EIH $\Delta$ CPM and $\Delta$ EIH to predict $\Delta$ NRS	$\downarrow$ NRS = improved CPM ( $r = 0.67$ , $P < 0.008$ ) $\downarrow$ NRS = improved EIH ( $r = 0.68$ , $P < 0.008$ )	Baseline better CPM = $\downarrow$ NRS ( $r = 0.57$ , $P < 0.04$ ) Baseline better EIH = $\downarrow$ NRS ( $r = 0.53$ , $P < 0.05$ ) Improved CPM = $\downarrow$ NRS ( $r = 0.67$ , $P < 0.008$ ) Improved EIH = $\downarrow$ NRS ( $r = 0.68$ , $P < 0.008$ )
Wilder-Smith et al. <sup>60</sup>	Disk herniation	/ Only evolution of sensation DT, PPT & PTT	1 h, 2 h, 4 h, 6 h, 24 h, 5 d	/	/	/

preoperative, perioperative, and postoperative predictors for an improvement or persistence of disturbed SPS signs after surgery. Regarding the first aim, results are all very divergent and heterogeneous. However, worsening of some SPS signs was only seen at a follow-up of  $<3$  months after surgery, conclusions are stronger with a follow-up of  $\geq 3$  months after surgery, and in general more positive results are seen regarding dynamic QST. An explanation could be that after 3 months the pain in most patients was resolved. Regarding the second aim, only a change in pain-related variables over time and baseline lower PPT predicted an improved PPT over time, a change in pain-related variables over time predicted an

improved CPM and EIH over time, and being a woman predicted an improved CSI score over time. Accordingly (because correlation analyses work in 2 directions), also a change in PPT, CPM, and EIH over time predicted an improvement of pain-related variables over time.

There is no consistent pattern in the evolution of SPS signs when comparing results presurgery and postsurgery. A possible explanation could be the fact that none of the included studies compared a group in which the pain persisted or pain resolved after

Table 10

## Level of recommendation table predictors for change of somatosensory processing system sign

SPS change	Predictor	MSK disorder	Method of predictor	Result	Level of recommendation
Improved PPT	Change pain-related variable	Hip OA	↓VAS in rest [3]	Influence	Moderate for influence
		Knee OA	↓VAS peak pain [8] ↓VAS after 30min walking [8] ↓number of body sites with pain [8]		
		Closed lock TMJ	↓NRS [19] ( <b>only widespread PPT</b> )		
	Baseline pain-related variable	Knee OA	High/low baseline painDETECT [37] High/low baseline VAS [52]	No influence	Moderate for no influence
		Knee OA	Lower baseline PPT [8]		
Improved PPT	Change inflammatory-related variable	Hip OA	↑IP-10 [11] ( <b>only widespread</b> ) ΔIL-8 [11] ΔFlt [11] ΔMCP-1 [11]	Influence No influence	Conflicting
	Change inflammatory-related variable	Hip OA	↑IL-8 [11] ΔIP-10 [11] ΔFlt [11] ΔMCP-1 [11]		
	Baseline pain-related variable	Knee OA	High/low baseline painDETECT [37]	No influence	Weak for no influence
	Change pain-related variable	Closed lock TMJ	ΔNRS [19]	No influence	Weak for no influence
	Change pain-related variable	Closed lock TMJ	ΔNRS [19]	No influence	Weak for no influence
Improved Temporal summation	Change inflammatory-related variable	Hip OA	ΔIP-10 [11] ΔIL-8 [11] ΔFlt [11] ΔMCP-1 [11]	No influence	Weak for no influence
	Change inflammatory-related variable	Hip OA	↑Flt [11] ΔIP-10 [11] ΔIL-8 [11] ΔMCP-1 [11]		
Improved CPM	Baseline pain-related variable	Knee OA	High/low baseline painDETECT [37]	No influence	Weak for no influence
	Change pain-related variable	Knee OA	↓NRS [64]	Influence	Moderate for influence
Improved EI	Change inflammatory-related variable	Hip OA	↑IP-10 [11] ΔIL-8 [11] ΔFlt [11] ΔMCP-1 [11]	Influence No influence	Conflicting
	Change inflammatory-related variable	Hip OA	↑IP-10 [11] ΔIL-8 [11] ΔFlt [11] ΔMCP-1 [11]		
Improved CSI	Baseline pain-related variable	Knee OA	High/low baseline painDETECT [37]	No influence	Weak for no influence
	Pain catastrophizing	Knee OA	High/low pain catastrophizing [38]	No influence	Weak for no influence
Improved EI	Change pain-related variable	Knee OA	↓NRS [64]	Influence	Moderate for influence
Improved CSI	Sex	Knee OA	Being a woman [28]	Influence	Weak for influence

Abbreviations: SPS, somatosensory processing system; PPT, pressure pain threshold; VAS, visual analogue scale; IL-8, interleukin 8; IP-10, Interferon gamma-induced protein 10; Flt-1, Fms related tyrosine kinase 1; MCP-1, monocyte chemoattractant protein 1; PTT, pressure pain tolerance threshold; CPM, conditioned pain modulation; CSI, central sensitization index; EI, exercise induced analgesia; NRS, numeric rating scale.

surgery. Two studies categorized patients according to more or less preoperative pain,<sup>32,46</sup> but found no differences in SPS signs in the long term between groups. This could be explained by the fact that they did not analyze the groups according to pain

improvement (they only focused on the preoperative pain values). It is known that higher preoperative pain scores are a risk factor for developing chronic postsurgical pain; however, not all patients with a high preoperative pain score will experience chronic postsurgical

Table 11

Level of recommendation table somatosensory processing system change-related predictor for postsurgical outcome.

PROM outcome	Method outcome	MSK disorder	SPS-related predictor	Result	Level of recommendation
Improvement of pain-related variables	VAS pain in rest <sup>3</sup>	Hip OA <sup>3</sup>	↑PPT	Influence	Moderate for influence
	VAS peak pain <sup>8</sup>	Knee OA <sup>8</sup>			
	VAS after 30 min walking <sup>8</sup>				
	No. of body sites with pain <sup>8</sup>				
	NRS <sup>18</sup> (only widespread PPT)	Closed lock TMJ <sup>18</sup>			
	NRS <sup>59</sup>	Knee OA	Improved CPM	Influence	Moderate for influence
	NRS <sup>59</sup>	Knee OA	Improved EI <sup>H</sup>	Influence	Moderate for influence

CPM, conditioned pain modulation; EI<sup>H</sup>, exercise induced analgesia; NRS, numeric rating scale; PPT, pressure pain threshold; SPS, somatosensory processing system; VAS, visual analogue scale.

pain.<sup>28,37</sup> Findings of previous systematic reviews are also in line with this theory because they also mainly focused on preoperative SPS signs and the link with postoperative pain and found as such no fully consistent conclusions.<sup>12,44,47,50,51,61</sup> A recent review indicates the importance of performing more studies focusing on the evolution of SPS signs in combination with or without pain improvement,<sup>4</sup> and also our review reveals that the improvement of pain-related variables over time is a predictor (according to correlation analyses) for an improvement of PPT, CPM, and EI<sup>H</sup> over time and vice versa, which also strengthens this theory. It is possible that disturbed SPS signs are present preoperatively, but if they normalize after surgery in combination with pain relief, it is postulated that the driving factor for the disturbed SPS sign was the nociceptive source itself (chronic secondary MSK pain).<sup>6,22</sup> On the other hand, if disturbed SPS signs appear or remain present after surgery in combination with chronic pain, it is postulated that the driving factor is primary chronic MSK pain.<sup>45</sup> Phenotyping of patients remains thus highly necessary to make clear predictions of patients experiencing chronic postsurgical pain.

In addition to previous theory, it is also possible that SPS signs were not disturbed before surgery. If these were not disturbed before surgery, it is also obvious that no positive evolution could be found. The same theory applies for a negative or positive evolution of SPS signs, one could expect a positive or negative evolution after surgery if SPS signs were disturbed or not disturbed before surgery, respectively. However, to date, it is still challenging to decide whether a certain SPS sign is disturbed at a certain time point because a clear guideline for normative values is lacking.<sup>59</sup>

Stronger conclusions were found at a follow-up of  $\geq 3$  months after surgery, which is logical, because of the MSK population and surgeries of the included studies. Most studies focused on TKA of THA surgeries, and research has shown that most of the pain improvement is seen 3 to 6 months after surgery.<sup>1,15,22,34</sup> Patients are still recovering from the surgery at a follow-up of  $< 3$  months, and as such, very divergent patterns can be assumed. A cutoff of 3 months after surgery was chosen, based on the definition of chronic postsurgical pain of the ICD-11.<sup>25</sup>

It is also remarkable that stronger and more positive results are seen regarding dynamic QST. The difference with static QST could be the fact that dynamic QST is related to a more centrally driven pain hypersensitivity, while static QST can reflect both a combination of more peripherally (local thresholds) and centrally driven pain hypersensitivity (widespread thresholds).<sup>9,19</sup> However, caution is advised because this research is limited to THA and TKA surgery. The results are also characterized by stronger conclusions after TKA compared with after THA because more studies with lower RoB were found in the knee OA population.

Finally, apart from patients with knee OA, hip OA, and spinal pain, research about this topic in other MSK pathologies is scarce. Only 1 study studied patients with shoulder OA and closed lock TMJ pain and only 3 studied patients with spinal pain. This is remarkable because persistent pain is present around 20% after shoulder TKA<sup>17,48</sup> and around 15% after TMJ discectomy,<sup>2,4</sup> of which a part could be possibly due to disturbed SPS signs based on the presence of prolonged nociception (for explanation see the Introduction).

#### 4.2. Limitations of the included studies

First of all, it is remarkable that more than half of the studies reported a high RoB, which is accounted for in the interpretation of the conclusion (lower evidence and as such weaker conclusions). Many conclusions (level of recommendations) were weak because conclusions could only be made based on the findings of solely 1 study that reported high RoB. So, it is advised to take caution in interpreting these findings. Second, only 10 studies did investigate some kind of predictor for the normalization of the SPS sign and were mainly focused on PPT. Of these 10 studies, only 3 reported a real prediction based on regression analyses. Finally, as mentioned earlier, studies focusing on subgroups correcting for the potential change in pain are lacking.

#### 4.3. Clinical implications for future research and clinical practice

Future research should focus on the stratification of patient groups, preferably based on pain improvement in which a group of patients with pain normalization or disappearance will be compared with a group with persistent pain after 3 months or more after surgery, and investigate the evolution of the SPS signs. It is also important for future studies to examine predictors for the (non-) normalization of SPS signs because this could give us a clearer explanation for the findings. This way, it could be possible to reveal different subgroups based on chronic postsurgical pain (eg, primary chronic and secondary chronic postsurgical pain), making decisions about whether to perform surgery or first to focus on the disturbed SPS signs is more convenient.

#### 4.4. Strengths and limitations of the review

This review has a couple of strengths because this is the first review to summarize and analyze all studies that investigated the evolution of SPS signs after MSK surgery. Thereupon, the triple-blind screening, the data extraction, and the RoB assessment strengthen the power of this article. In addition, the systematic

approach gives the reader a nice overview covering all MSK patients undergoing surgery.

This review also presents with some limitations, so conclusions should be interpreted with caution. Eight studies (one-third of total included studies) were retrieved by hand-search methods. A possible explanation could be that in the PICO term, only variation of “MSK disorders” was used, not specifying which MSK disorders. In addition, our search was restricted to studies including QST or questionnaires to measure SPS signs; future research could go further and also add more invasive SPS measurements (eg, magnetic resonance imaging, electromyography, etc). Finally, no meta-analysis was performed; however, this was impossible due to the heterogeneity of the MSK population and SPS signs measured.

## 5. Conclusion

In general, no consistent evolution of SPS signs comparing preoperative and postoperative values and predictors for this evolution in MSK disorders could be found. In most cases, static QST did not change or conflicting results were found. On the other hand, dynamic QST mostly improved after surgery. Worthfully mentioning is that worsening of some SPS signs was only seen at a follow-up of <3 months after surgery, that conclusions are stronger when evaluating dynamic QST with a follow-up of ≥3 months after surgery, and that pain improvement over time was an important predictor for improvement of SPS signs. Future high-quality research should focus on the evolution of SPS signs after nociceptive targeted surgery, accounting for pain improvement patient groups and focusing on preoperative, perioperative, and postoperative predictors of this evolution.

## Conflict of interest statement

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