Systematic Review and Meta-Analysis

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Effects of percutaneous neuromodulation in neuromusculoskeletal pathologies

A systematic review

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Abstract

Background: Percutaneous neuromodulation (PNM) consists in using electrical stimulation on a peripheral nerve by using a needle as an electrode in order to lessen the pain and restore both neuromuscular and nervous system functions. The aims of the present study were to evaluate the current scientific evidence of the effects of PNM on pain and physical capabilities in neuromusculoskeletal injuries.

Methods: Data sources: There was used the PRISMA protocol. In order to do the literature research, there were used the PubMed, Cochrane, Scopus, and Web of Science databases. Study selection or eligibility criteria: There were also included experimental clinical trials published between 2010 and nowadays, tested on humans, which feature treatment based on needles with electrical stimulation in order to treat neuromusculoskeletal injuries. Study appraisal and synthesis methods: A quality assessment was performed according to the PEDro scale and reviewed the impact factor and quartile of the journal

Results: The treatment resulted in significant improvement in terms of pain intensity, pressure pain threshold, balance, muscular endurance, functionality/disability, subjective improvement, function of the descending pain modulatory system, and intake of drugs. Limitations: the lack of previous research studies on the subject and the lack of data on opioid intake in the selected studies.

Conclusion: Treatment based on PNM may be an alternative when treating injuries in soft tissues without significant side effects. However, there are few articles investigating the effects of PNM so more evidence is needed to draw solid conclusions.

Abbreviations: BDNF = brain-derived neurotrophic factor, DN = dry needling, Hz = Hertz, PNM = percutaneous neuromodulation, ROM = range of motion, tDCS = transcranial direct current stimulation.

Keywords: invasive physiotherapy, percutaneous electrical nerve stimulation, percutaneous neuromodulation, PNM

1. Introduction

Neuromodulation is a quality of the nervous system that regulates or modifies electrical impulses, by enhancing or inhibiting them.[1] Even though its mechanism of action is yet to be fully determined, it is known that it lies on the ascending and descending pathways and the supraspinal regions of the central nervous system. The chronic effect of said neurophysiological process may cause central nervous system plasticity, with lasting clinical effects.[2,3] Neuromodulation is part of the treatment for multiple pathologies with few side effects.[4]

Nowadays, there are described the following neuromodulation procedures, classified according to the area of application[5,6]: at the brain level, cortical stimulation[7] and deep brain stimulation,[8] at the spinal level, stimulation of the dorsal column of the spinal cord,[9] nerve root stimulation[10] and dorsal root ganglion stimulation[11] and at the level of the peripheral nervous system, the stimulation of the peripheral nerve,[12] the stimulation of the receptive field of the peripheral nerve[13] and the stimulation of the muscular motor point.[5]

Peripheral nerve and muscle level neuromodulation (percutaneous neuromodulation [PNM]) consists in percutaneous electrical stimulation of a peripheral nerve, along its pathway or in a muscle, through a puncture needle with electric current of low or medium frequency. Even though the mechanism of action is not fully known, the PNM spans the ascending and descending pathways, as well as the supraspinal regions of the central nervous system, regulating or modifying the electrical impulses transmitted through said pathways, and thus inhibiting or exciting them.[3,14]

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The main objective of the application of PNM is to provoke a motor and/or sensitive response that eases pain and restores the usual functioning of the nervous system. Thus, on the one hand, it may relieve central sensitization and hyperexcitability (hyperalgesia or allodynia) related chronic pain and neuropathic pain, and, on the other hand, it may improve the neuromuscular function, muscle recruitment patterns and motor control.[5,14,15] In this line, recent studies suggests PNM could relieve central sensitization by improving conditioned pain modulation, reducing motor-evoked potential and increasing intracortical inhibition.[16–18] Additionally, the effects of this technique are being investigated for the improvement of some physical qualities such as elasticity, strength, balance and muscular endurance.[15,19–25]

An injury does not only produce changes in an anatomical level; it also may unfold changes within the nervous system, such as increase in the motoneuron excitability, decrease in the sense of position, movement and strength, decrease in the acetylcholine receptors, decrease in the cholinergic/non-cholinergic muscle stimulation, decrease in voluntary activation, decrease in corticospinal excitability, and central sensitization.[26] Central sensitization, on the other hand, represents an intensification when it comes to the activity of circuits and neurons in the nociceptive pathways, due to the enhancement of the excitability of the membrane and the synapses. In patients with central sensitization, the cortex suffers an aberrant reorganization, and the pain increases drastically. In addition, the perception of any other sensory experience reaches a higher amplitude, duration, and spatial extent, which results in a reduced excitation-inhibition balance.[16]

Therefore, considering the changes that take place in the nervous system after an injury, and the mechanism of action of PNM, some authors used said technique to treat soft tissue injuries.

The objective of this study was to evaluate the effects of PNM on pain and physical capabilities when it comes to neuromusculoskeletal injuries.

2. Methodology

2.1. Design

Systematic review on the effects of PNM. There was used the PRISMA protocol[27] and the research question was stated according to the PICO strategy.[28] This article does not contain any studies with human participants or animals performed by any of the authors. The medical ethics committee approval is not required for this type of study.

2.2. Identification and selection of articles

The literature research was performed between April and June 2020. In order to do so, there were used the PubMed, Cochrane, Scopus, and Web of Science databases. The searching phrase was created by combining keywords and Medical Subject Headings that defined the use of electrically stimulated needles and treatments or therapies were not wanted in the search, by using them with the Boolean operators OR and NOT. ("percutaneous electric nerve stimulation" OR "PNM therapy" OR "PNM therapies" OR "percutaneous electrical neuromodulation") OR ("electrical dry needling [DN]") OR ("intramuscular electrical stimulation") NOT ("spinal cord stimulation") NOT ("transcutaneous electric nerve stimulation") NOT ("transcranial direct current stimulation [tDCS]") NOT ("implanted" OR "surgery" OR "surgical"). The search was limited to articles published between 2010 and 2020, both in English and Spanish. The first selection of articles was screened by removing those that were not related to the topic. After fully reading the articles, a second screening was performed. Finally, the selected articles had to comply with some inclusion and exclusion criteria:

2.3. Inclusion criteria

Clinical trial tested on humans; and at least one of the experimental groups should receive treatment based on DN or acupuncture with electrical stimulation.

2.4. Exclusion criteria

Use of the PNM in non-neuromusculoskeletal pathologies; treatments based on surgery of electrostimulation devices; not using needles as a conducting electrode; treatment based on tDCS; treatments based on Chinese traditional medicine, which treats another region, far from the region in pain and with no direct relationship between the region receiving the treatment and the pathological region: auriculotherapy, digit puncture, acupuncture…

2.5. Evaluation of the characteristics of the articles

A quality assessment was performed by two authors (I.F.-M., J.J.R.-Á.) according to the PEDro scale[29] and reviewed the impact factor and quartile of the journal.

The independent variables of the study were the following: target tissue; treatment time; number of sessions; current type; current frequency; pulse width, and current intensity. On the other hand, the dependent variables were: pain intensity; range of motion (ROM); maximal isometric strength; balance; muscular endurance; muscle contractile properties; functionality/disability; quality of life; intake of drugs; sleep quality; subjective improvement; adverse effects; cortical excitability, and brain-derived neurotrophic factor (BDNF).

3. Results

3.1. Selection of articles

Through the literature search in said four databases, we found 176 potential articles for this review by all authors (I.F.-M., J.J.R.-Á., R.M.-L., and E.S.R-L). Among those, we selected 24 and narrowed it down to 15,[14,16–25,30–33] since 9 were duplicates. After reading the 15 articles, we did not discard a single one and we used them to make the bibliographical review (Fig. 1)

3.2. Types of study

Among the selected 15 articles, 14 were randomized studies[16–25,30–33] and the last one was a prospective observational study.[14]

3.3. Methodological quality of the selected articles

The articles obtained an average score of 7.06 ± 1.84 on the PEDro scale[29] (Table 1).

3.4. Pain intensity

All articles that analyzed the effect of PNM on pain found significant improvements. The studies made by Hadizadeh et al[23] in patients with trigger points in upper trapezius, Botelho et al[16] in patients with myofascial pain syndrome, da Graca-Tarragó et al 2016[17] in patients with knee osteoarthritis, and Raphael et al[33] in patients with chronic pain and hyperalgesia obtained a significant improvement when it came to pain intensity ($P \leq .048$; $P < .001$; $P = .001$, and $P < .0005$, respectively). Likewise, García-Bermejo et al 2020 found a significant improvement on PNM based treatment when treating unilateral anterior knee pain, regardless using it in a contralateral or homolateral manner ($P = .01$ in both groups).[22]

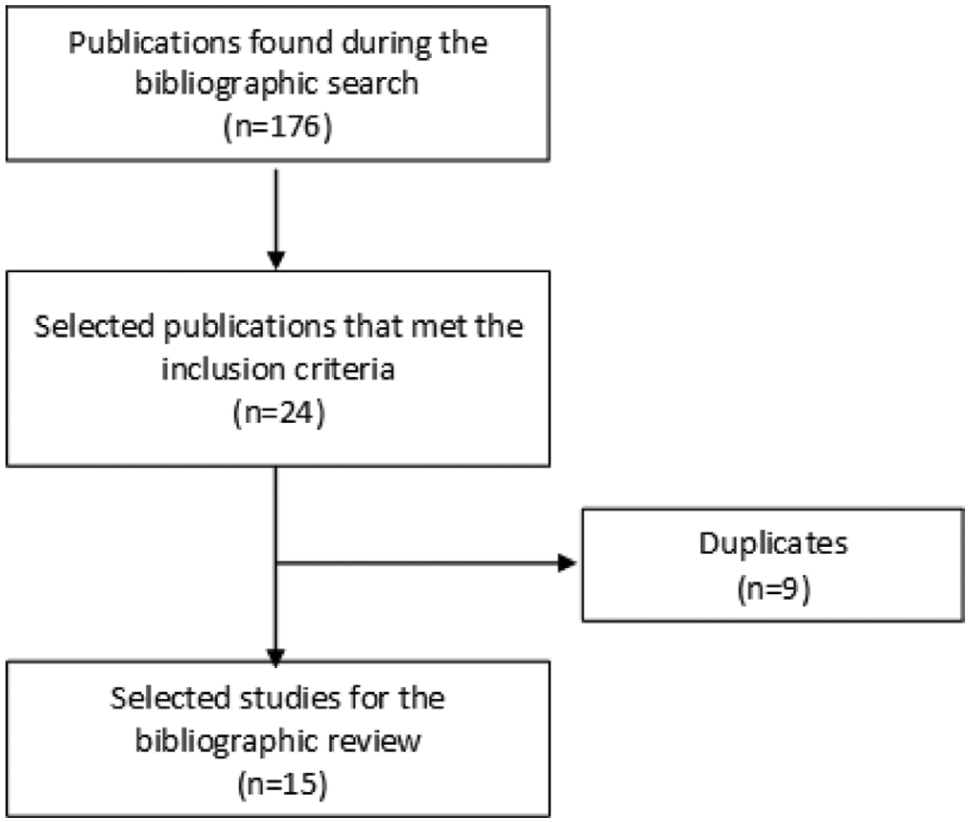

Figure 1. Flowchart.

Table 1

Methodological quality according to PEDro scale.

Artículo	1	2	3	4	5	6	7	8	9	10	11	Total
Rossi M et al 2016[14]	YES	NO	NO	NO	NO	NO	NO	YES	YES	YES	YES	4
Botelho L et al 2018[16]	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	9
da Graca-Tarragó M et al 2016[17]	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	9
da Graca-Tarragó M et al 2019[18]	YES	YES	YES	YES	YES	NO	YES	YES	YES	YES	YES	9
De-la-Cruz-Torres B et al 2019[19]	YES	YES	NO	YES	NO	NO	NO	YES	YES	YES	YES	6
De-la-Cruz-Torres B et al 2020[20]	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
De-la-Cruz-Torres B et al 2019[21]	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
García-Bermejo P et al 2020[22]	YES	YES	NO	YES	NO	NO	YES	YES	YES	NO	YES	6
Hadizadeh M et al 2017[23]	YES	YES	NO	YES	YES	NO	YES	YES	YES	YES	YES	8
León-Hernández JV et al 2016[24]	YES	YES	NO	NO	NO	NO	YES	YES	YES	YES	YES	6
Sumen A et al 2015[25]	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
Dunning J et al 2018[30]	YES	YES	YES	YES	NO	NO	YES	YES	YES	YES	YES	8
Dunning J et al 2018[31]	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
Pérez-Palomares S et al 2010[32]	YES	YES	NO	YES	NO	NO	YES	YES	YES	YES	YES	7
Raphael JH et al 2011[33]	YES	YES	YES	NO	YES	YES	YES	YES	YES	YES	YES	9

1.Eligibility criteria were specified.
2.Subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received).
3.Allocation was concealed.
4.The groups were similar at baseline regarding the most important prognostic indicators.
5.There was blinding of all subjects.
6.There was blinding of all therapists who administered the therapy.
7.There was blinding of all assessors who measured at least one key outcome.
8.Measures of at least one key outcome were obtained from >85% of the subjects initially allocated to groups.
9.All subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by "intention to treat".
10.The results of between-group statistical comparisons are reported for at least one key outcome.
11.The study provides both point measures and measures of variability for at least one key outcome.

Table 2

Type of study, subjects, target tissue, duration of the treatment, current parameters, and groups.

Article	Type of study	Subjects	Target tissue	Duration of the treatment	Current parameters	Groups
Rossi et al 2016[14]	Multicenter, prospective, observational study	Patients with peripheral neuropathic pain (n = 76)	MTP and/or hyperalgesic/allodynic area of different regions (occipital, trigeminal, maxilla, lower limb, ilioinguinal, peroneal, saphenous, lateral femoral cutaneous nerve, upper limb…)	**NUMBER OF SESSIONS:** 1 **STIMULATION DURATION**: 25 min	**CURRENT TYPE:** Unspecified **FREQUENCY:** 2–100 Hz (automatic change every 3 s) **PULSE WIDTH:** Unspecified **INTENSITY:** 0,5 V **DEVICE:** Neurostimulator PENS therapy	1 Group: -PNM G. (n = 76)
Botelho et al 2018[16]	Randomized clinical trial (double-blind, sham-controlled)	Right-handed female, 19–65 yr old, diagnosed with MPS on the upper body (n = 23)	Cervical paraspinal region (C2–C3 and C3–C4) and accessory nerves both ways	**SESSIONS:** **10** **TREATMENT DURATION:** 20 min **TREATMENT FREQUENCY:** Unspecified **TREATMENT PERIOD:** Unspecified	**CURRENT TYPE:** Unspecified **FREQUENCY:** 2 Hz **PULSE WIDTH:** Unspecified **INTENSITY:** Unspecified **DEVICE:** Sikuro (São Paulo, Brazil)	2 Groups: -PNM G. (n = 11) -Placebo G. (n = 12)
da Graça-Tarragó et al 2016[17]	Randomized clinical trial	Right-handed females, older than 50 yr old, with moderate or severe pain due to knee osteoarthritis, with at least 6 mo evolution (n = 25)	Vastus medialis, rectus femoris, vastus lateralis, tibialis anterior, pes anserinus bursae muscle, and dermatomes on L1, L2, L3, L4, L5, S1, and S2 (paravertebral)	**SESSIONS:** **1** **TREATMENT DURATION:** **30**	**CURRENT TYPE:** Unspecified **FREQUENCY:** 2 Hz **PULSE WIDTH:** Unspecified **INTENSITY:** Unspecified **DEVICE:** Sikuro (São Paulo, Brazil)	2 Groups: -PNM G. (n = 12) -Placebo G. (n = 13)
da Graca-Tarragó et al 2019[18]	Randomized clinical trial	Right-handed women, 50–75 yr old with knee osteoarthritis (n = 59)	L1-S2, vast medial, rectus femoris, vast lateral, anterior tibialis muscles, and the pes anserine bursae.	**SESSIONS:** **5** **TREATMENT DURATION:** 30 min **TREATMENT FREQUENCY:** Daily	**CURRENT TYPE:** Unspecified **FREQUENCY:** 2 Hz **PULSE WIDTH:** Unspecified	4 Groups: -a-tDCS/a-PNM G. (n = 14) -a-tDCS/s-PNM G. (n = 15) -s-tDCS/a-PNM G.

(Continued)

Table 2

(Continued)

Article	Type of study	Subjects	Target tissue	Duration of the treatment	Current parameters	Groups
				TREATMENT PERIOD: 5 d	**INTENSITY:** Depending on patient tolerance **DEVICE:** Sikuro, São Paulo, Brazil	(n = 15) -s-tDCS/s-PNM G. (n = 15)
de la Cruz et al 2019[19]	Randomized clinical trial	Professional ballet dancers (n = 45)	Muscle belly of the flexor hallucis longus muscle	**NUMBER OF SESSIONS**: 1 **STIMULATION DURATION** 90 s	**CURRENT TYPE:** Biphasic square **FREQUENCY:** 10 Hz **PULSE WIDTH:** 250 microseconds **INTENSITY:** Maximum tolerable with muscle contraction **DEVICE:** Physio Invasiva	3 Groups: -S G. (n = 15) -Ecc G. (n = 15) -PNM G. (n = 15)
de la Cruz et al 2020[20]	Randomized clinical trial without control group	Patients with hamstring shortening syndrome (n = 80)	Sciatic nerve (perineurium)	**NUMBER OF SESSIONS:** 1 **STIMULATION DURATION:** 90 s	**CURRENT TYPE:** Biphasic square **FREQUENCY:** 10 Hz **PULSE WIDTH:** 250 microseconds **INTENSITY:** Maximum tolerated **DEVICE:** Physio Invasiva	4 Groups: -S G. (n = 20) -Neurodynamic G. (n = 20) -Needle G. (n = 20) -PNM G. (n = 20)
de la Cruz et al 2019[21]	Randomized clinical trial	Professional ballet dancers (n = 32)	Muscle belly of the flexor hallucis longus muscle	**NUMBER OF SESSIONS:** 1 **STIMULATION DURATION** 90 s	Same parameters and current type for PNM G. and TENS G. **CURRENT TYPE:** Asymmetrical biphasic square **FREQUENCY:** 10 Hz **PULSE WIDTH:** 250 microseconds **INTENSITY:** Maximum tolerable that produces sudden muscle contraction **DEVICE:** Physio Invasiva	2 Groups: - TENS G. (n = 17) -PNM G. (n = 15)
García-Bermejo et al 2020[22]	Randomized clinical trial	Patients with unilateral anterior knee pain (n = 30)	Femoral nerve	**SESSIONS:** **1** **TREATMENT DURATION:** 90 s	**CURRENT TYPE:** biphasic square **FREQUENCY:** 10 Hz **PULSE WIDTH:** 250 microseconds **INTENSITY:** tolerable, able to produce muscle contraction **DEVICE:** Physio Invasiva	2 Groups: -HOMO. PNM G. (n = 15) -CONTR. PNM G. (n = 15)
Hadizadeh et al 2017[23]	Randomized clinical trial	Patients with active MTP in upper trapezius (n = 16)	Active MTP in upper trapezius	**NUMBER OF SESSIONS:** 1 **STIMULATION DURATION** 90 s	**CURRENT TYPE:** Burst **FREQUENCY:** 2 Hz **PULSE WIDTH:**	2 Groups: -PNM G. (n = 8) -Placebo G. (n = 8)

(Continued)

Table 2

(Continued)

Article	Type of study	Subjects	Target tissue	Duration of the treatment	Current parameters	Groups
					200 microseconds **INTENSITY:** Until forming a visible pain-free muscle contraction, the intensity was increasedtoavoid getting comfortable. **DEVICE:** ITO ES-160	
León-Hernández et al 2016[24]	Randomized clinical trial	Patients 18–48 yr old with chronic neck pain (n = 62)	MTP in upper trapezius	**SESSIONS:** **1** **TREATMENT DURATION:** 15 min	**CURRENT TYPE:** Compensated symmetrical pulsed biphasic current of low frequency **FREQUENCY:** 2 Hz **PULSE WIDTH:** 120 microseconds **INTENSITY:** Tolerable and non-painful	2 Groups: -DN G. (n = 31) -DN + PNM G. (n = 31)
Sumen et al 2015[25]	Prospective randomized clinical trial	Patients with active MTP in upper trapezius and diagnosed with MPS (n = 45)	MTP in upper trapezius	**SESSIONS:** 10 **TREATMENT DURATION:** 20 min **TREATMENT FREQUENCY:** Unspecified **TREATMENT PERIOD:** 2 wk	**CURRENT TYPE:** Unspecified **FREQUENCY:** 80 Hz **PULSE WIDTH:** Unspecified **INTENSITY:** Enough to feel it, without provoking muscle contraction **DEVICE:** IC-4107	3 Groups: -S + LLLT G. (n = 15) -S + PNM G. (n = 15) -S G. (n = 15)
Dunning et al 2018[30]	Multicenter randomized clinical trial	Patients with plantar fasciitis (n = 111)	MTP, periosteal and perineural 1- Plantar fascia in medial tubercle of the calcaneus. 2- Abductor hallucis muscle, distal (MTP and perineural for the medial plantar nerve) 3- Abductor hallucis muscle, proximal (MTP and perineural for the medial plantar nerve) 4- Two fingerbreadths inferior to the inferior apex of the medial malleolus (bifurcation point of the tibial nerve and posterior tibial artery) 5- Depression between the prominence of the medial malleolus and the Achilles tendon (tibial nerve in the ankle)	**SESSIONS:** 4–8 **TREATMENT DURATION:** 20 min **TREATMENT FREQUENCY:** 1–2/wk	**CURRENT TYPE:** Biphasic continuous **FREQUENCY:** 2 Hz **PULSE WIDTH:** 250 microseconds	2 Groups: -MT + E + US + PNM G. (n = 58) -MT + E + US (n = 53)

(Continued)

Table 2

(Continued)

Article	Type of study	Subjects	Target tissue	Duration of the treatment	Current parameters	Groups
			6- Muscle bellies of the flexor digitorum brevis and the quadratus plantae muscles (MTP and perineural for the lateral plantar nerve)	**TREATMENT DURATION:**	**INTENSITY:**	
			7- Plantar fascia	4 wk	Mild or moderate (sensation of the patient)	
			8- Abductor hallucis muscle, medial (MTP and perineurium of the medial plantar nerve)		**DEVICE:** ITO ES-160	
Dunning et al 2018[31]	Randomized, single-blinded, multicenter, parallel-group clinical trial	Patients with knee osteoarthrosis	Muscles and periosteum under it, of the following:	**NUMBER OF SESSIONS:**	**CURRENT TYPE:**	2 Groups:
		(n = 242)	-Popliteus -Adductor magnus	8–10 **FREQUENCY OF TREATMENT:**	Biphasic square **FREQUENCY:**	- MT + E G. (n = 121)
			-Tibialis anterior -Quadriceps tendon	1–2 times per wk **STIMULATION DURATION**	2 Hz **PULSE WIDTH:**	- PNM G. (n = 121)
			-Vastus lateralis -Vastus medialis	20–30 min **TREATMENT PERIOD:**	250 microseconds **INTENSITY:**	
			Periosteum: -Tibiofemoral joint margin within the medial infrapatellar sulcus -Tibiofemoral joint margin within the lateral infrapatellar sulcus	6 wk	Maximum tolerated **DEVICE:** ITO ES-160	
Pérez-Palomares et al 2010[32]	Randomized clinical trial	Patients with chronic low back pain for 4 mo or more (n = 112)	L2-L5 paraspinals (2–2, 5 cm depth) and gluteus medius (bilateral)	**SESSIONS:** **9** **TREATMENT DURATION:** 30 min **FREQUENCY:** 3 sessions/wk on alternate days **TREATMENT PERIOD:** 3 wk	**CURRENT TYPE:** Unspecified **FREQUENCY:** 4 Hz **PULSE WIDTH:** 30 microseconds **INTENSITY:** Unspecified **DEVICE:** Carin TNS 190 portable	2 Groups: -PNM G. (n = 64) -DN G. (n = 61)
Raphael et al 2011[33]	Randomized clinical trial (multicenter, double-blinded, crossover, placebo-controlled)	Patients with chronic pain and hyperalgesia (n = 30)	Most painful region and hyperalgesia	**SESSIONS:** **1** **TREATMENT DURATION:** 25 min	**CURRENT TYPE:** Unspecified **FREQUENCY:** 2–100 (alternating every 3 s) **PULSE WIDTH:** Unspecified **INTENSITY:** Unspecified **DEVICE:** Neurostimulator (Algotec Ltd., Haywards Health, UK)	2 Groups: -a-PNM G. (n = 30) -s-PNM G. (n = 30)

a/s = active/shame, CONTR = contralateral, DN = dry needling, E = exercise, Ecc = eccentric, G = group, HOMO = homolateral, LLLT = low-level laser therapy, MPS = myofascial pain syndrome, MT = manual therapy, MTP = myofascial trigger point, N = nerve, PNM = percutaneous neuromodulation, S = stretching, tDCS = transcranial direct current stimulation, TENS = transcutaneous electrical nerve stimulation, US = ultrasounds.

Table 3

Results.

Articles	Results
Pain intensity	
Hadizadeh et al 2017[23]	Significant improvement ($P \leq 0.048$)
Dunning et al 2018[30]	Significant decrease, higher after 6 wk ($P < .001$) and 3 mo ($P < .001$) of the MT + E + PNM G.
Rossi et al 2016[14]	Significant improvement after 60 minutes ($P < .001$), which remained constant over 6 mo
Botelho et al 2018[16]	Significant improvement ($P < .001$)
da Graça-Tarragó et al 2016[17]	Significant decrease ($P = .001$)
Pérez-Palomares et al 2010[32]	No significant difference between ($P = .94$) PNM G. and DN G.
Sumen et al 2015[25]	Significant decrease with both laser treatment ($P = .016$) or PNM ($P = .001$)
García-Bermejo et al 2020[22]	Significant improvement (pre vs post) in both groups ($P = .01$).
León-Hernández et al 2016[24]	There was a significant difference ($P < .05$) when measuring immediately after the treatment, on favor of the DN + PNM G., but not after 72 hours or the post-puncture soreness ($P < .05$)
Dunning et al 2018[30]	The PNM G. improved significantly pain intensity of the first step ($P < .001$), pain intensity while resting ($P < .001$), and pain intensity during the activity ($P = .007$)
da Graça-Tarragó et al 2019[18]	The a-tDCS/a-PNM G. obtained a higher decrease compared to the other groups ($P < .0001$). All groups obtained a significant decrease in pain intensity ($P < .03$). The group that received both types of treatment actively obtained the highest decrease in pain intensity, with a big effect (d = 1.86). The a-tDCS/a-PNM obtained a greater effect (34,4% greater than the s-tDCS/a-PNM G.).
Raphael et al 2011[33]	The a-PNM G. obtained an average of pain intensity that changed from 7.5 to 0.5 before and after the treatment ($P < .0005$). There was a significant statistic difference between both groups in terms of change of pain intensity ($P \leq 0.0001$), in favor of the active treatment
Pressure pain threshold	
da Graça-Tarragó et al 2016[17]	Increased significantly ($P = .01$)
Pérez-Palomares et al 2010[32]	No significant difference ($P > .05$)
Sumen et al 2015[25]	Significantly bigger than the PNM G. ($P = .017$) after 3 mo, when comparing with S G.
León-Hernández et al 2016[24]	No significant differences
da Graça-Tarragó et al 2019[18]	All groups that received some kind of active treatment had a significant statistic rise in terms of pressure pain threshold, compared to s-tDCS/s-PNM G. ($P = .02$)
Raphael et al 2011[33]	In the a-PNM G., the average pressure pain threshold (pre vs post) changed from 202 grams to 626 grams ($P < .0005$). There was a significant statistic difference between both groups in terms of change of the pressure pain threshold ($P = .007$), in favor of the active treatment.
ROM	
de la Cruz et al 2019[19]	No significant improvement ($P > .05$)
de la Cruz et al 2019[21]	No significant improvement
Hadizadeh et al 2017[23]	Significant improvement ($P \leq 0.048$)
de la Cruz et al 2020[20]	Improved significantly ($P < .01$)
Sumen et al 2015[25]	The 3 groups improved significantly compared to the beginning
García-Bermejo et al 2020[22]	Improved significantly (pre vs post) in both groups ($P = .001$)
León-Hernández et al 2016[24]	No significant differences
Balance	
de la Cruz et al 2019[19]	Significant improvement ($P < .001$)
de la Cruz et al 2019[21]	Significant improvement ($P \leq 0.001$)
Muscle endurance	
de la Cruz et al 2019[19]	Significant improvement ($P < .001$)
de la Cruz et al 2019[21]	Significant improvement ($P \leq 0.001$)
Functionality/disability	
Dunning et al 2018[30]	**Disability:**significant improvement, better after 6 wk ($P < .001$) and 3 mo ($P < .001$) of the MT + E + PNM G. **Physical function:** significant improvement, ($P < .001$) of the MT + E + PNM G.
García-Bermejo et al 2020[22]	Improved significantly (pre vs post) in both groups ($P = .001$)
León-Hernández et al 2016[24]	No significant differences
Dunning et al 2018[30]	Improved significantly ($P < .001$)
da Graça-Tarragó et al 2019[18]	The score on the WOMAC scale decreased significantly in those groups that received any kind of active treatment, compared to s-tDCS/s-PNM G. There was a considerable improvement in the WOMAC scale in a-tDCS/a-PNM G., with a significant statistic difference when compared to other groups ($P = .03$)
Quality of life	
Pérez-Palomares et al 2010[32]	No significant difference ($P > .05$)
Sleep quality	
Botelho et al 2018[16]	There was no significant improvement without interaction between time and intervention (12,5%; $P = .004$)
Pérez-Palomares et al 2010[32]	No significant difference ($P = .68$)
Intake of drugs	
Dunning et al 2018[30]	MT + E + PNM G. was more prone to quit the intake of drugs altogether after 3 mo ($P = .001$)
Rossi et al 2016[14]	11 patients quit and 19 reduced the intake
Botelho et al 2018[16]	It decreased significantly (69.4% vs 30.6%; $P < .01$), with a relative risk of intake of drugs of the PNM G. (2.95 times less than the Placebo G.)
Dunning et al 2018[30]	Significantly ($P = .023$) more patients that received PNM (n = 47; 81%) quit the intake of drugs altogether 3 mo after treatment (n = 37; 69%)

(Continued)

Table 3

(Continued)

Articles	Results
da Graça-Tarragó et al 2019[18]	The intake of drugs of 74% of patients was at least 3 times/wk, in the s-tDCS/s.PNM G., 45% in the a-tDCS/a-PNM G., 69.2% in the a-tDCS/s-PNM G., and 49.3% in the s-tDCS/a-PNM G. The groups that received a-PNM were the ones with the biggest decrease in the intake of drugs, regardless of receiving a-tDCS or s-tDCS.
Subjective improvement	
Dunning et al 2018[30]	Significantly ($P < .001$) more patients (n = 91; 75%) of the MT + E + PNM G. achieved a successful result when compared to the MT + E G. (n = 23; 19%).
Rossi et al 2016[14]	Significant improvement 6 mo later ($P < .001$)
Function of the descending pain modulatory system	
Botelho et al 2018[16]	After 10 sessions, there was a significant improvement ($P \leq 0.01$)
da Graça-Tarragó et al 2016[17]	**CPM:** Improved significantly ($P = .01$).
da Graca-Tarragó et al 2019[18]	The group that received both treatments actively obtained an increase in the function of the descending pain modulatory system statistically significant, when compared to the placebo group ($P = .03$), but the effect of a single active treatment did not produce significant differences
Cortical excitability	
Botelho et al 2018[16]	**Motor evoked potential:** decreased significantly ($P = .02$). **Cortical silent period:** increased significantly ($P = .005$). **Short intracortical inhibition:** no significant changes. **Intracortical inhibition:** no significant changes
da Graca-Tarragó et al 2016[17]	**Motor evoked potential:** decreased significantly ($P = .03$) from the average MEP of 31.61%. **Short intracortical inhibition:** no significant changes ($P = 66$). **Cortical silent period:** improved significantly ($P = 0001$). **Intracortical facilitation:** improved significantly ($P = .02$). **Function of the descending pain modulatory system:** improved significantly ($P = .01$).
BDNF	
Botelho et al 2018[16]	The Placebo G. obtained a serum BDNF significantly lower ($P < .01$) than the PNM G. There was an interaction between the groups and the serum BDNF ($P < .05$), which suggests that the rise of BDNF was due to the intervention
da Graca-Tarragó et al 2016[17]	It did not correlate with the MEP, but it did so negatively and marginally ($P = .05$) with the pressure pain threshold
da Graca-Tarragó et al 2019[18]	No significant differences among the four groups before or after the treatment (Pre: $P = .56$; Post $P = .58$)

a/s = active/shame, BDNF = brain derived neurotrophic factor, CPM = conditioned pain modulation, DN = dry needling, E = exercise, G = group, MEP = motor evoked potential, MT = manual therapy, PNM = percutaneous neuromodulation, S = stretching, tDCS = transcranial direct current stimulation, WOMAC = Western Ontario and McMaster Universities Arthritis Index.

On the other hand, Rossi et al[14] observed a significant improvement in patients with neuropathic pain ($P < .001$), which began 60 minutes post-treatment and lasted for 6 months.

Some studies compared the effects of PNM to other techniques. Pérez-Palomares et al found no significant difference ($P = .94$) between PNM and DN in patients with chronic low back pain when it came to mid-term effect.[32] Nonetheless, León-Hernández et al did find significant differences when combining PNM with DN against only using DN on patients with chronic neck pain ($P < .05$), with a significant decrease in the post-needling soreness intensity 72 hours after using PNM ($P < .05$).[24] Dunning et al[30,31] observed a significant decrease in pain thanks to the PNM treatment, compared to manual therapy, in patients with knee osteoarthritis and plantar fasciitis. Said decrease lasted for 3 months. Sumen et al[25] compared PNM treatment to low-level laser therapy in patients with an active trigger point in upper trapezius and diagnosed with myofascial pain syndrome. Both treatments improved symptomatology ($P = .016$ and $P = .001$, respectively).[25]

Finally, da Graca-Tarragó et al 2019 observed that patients with knee osteoarthritis that received transcranial direct currents and PNM, regardless of being simulated or not, showed a significant improvement ($P < .03$), with a higher reduction of the pain intensity when combining both techniques.[18]

3.5. Pressure pain threshold

All articles found a significant improvement in the pressure pain threshold when using PNM or DN, with no significant differences between them.[17,18,24,25,32]

3.6. Range of motion

There was a significant improvement in three out of six articles that analyzed this parameter. In patients with trigger points in upper trapezius ($P = .048$),[23] patients with bilateral reduced hamstring syndrome ($P < .01$),[21] and patients with anterior knee pain ($P = .001$).[22] Nonetheless, de la Cruz et al 2019 found no significant improvement in ballet dancers,[19,21] nor did Sumen et al in patients with trigger points in upper trapezius.[25]

3.7. Balance and muscle endurance

Two studies evaluated balance and muscle endurance and observed a significant improvement in ballet dancers ($P < .001$ in both cases).[19,21]

3.8. Muscle contractile properties

Only one study evaluated the effects of PNM on muscle contractile properties through tensiomyography and found no significant differences ($P > .05$).[20]

3.9. Functionality/disability

Five studies analyzed the effects of PNM on functionality/disability[18,22,24,30,31] and all of them found significant improvements. In patients with knee osteoarthritis ($P < .001$ and $P = .03$)[18,31] in patients with plantar fasciitis ($P < .001$),[30] in patients with anterior knee pain ($P = .001$),[22] and in patients with neck pain, if they combined the treatment with DN.[24]

3.10. Quality of life

The only study that analyzed the quality of life compared PNM and DN, and found no significant differences.[32]

3.11. Intake of drugs

The 5 studies that analyzed intake of drugs reported that there was a reduction in the use of analgesics and non-steroidal anti-inflammatory drugs after PNM based treatment. In chronic neuropathic pain,[14] in plantar fasciitis (P = .001),[30] in knee osteoarthritis (P = .023 and P < .019)[18,31] and in myofascial pain syndrome.[16]

3.12. Sleep quality

Two studies evaluated the sleep quality. In the myofascial pain syndrome, Botelho et al found an improvement in said parameter (P = .04).[16] Nonetheless, Pérez-Palomares et al[32] found no major differences when it came to chronic low back pain (P = .68).

3.13. Subjective improvement

The three articles that analyze subjective improvement after PNM found a significant improvement in patients with neuropathic pain,[14] knee osteoarthritis,[31] and plantar fasciitis[30] (P < .001 in all three cases).

3.14. Function of the descending pain modulatory system

Three articles analyze the effect of PNM on the function of the descending pain modulatory system, obtaining significant improvements. Those three articles made the analysis based on myofascial pain (P = .01)[16] and osteoarthritis (P = .01).[17,18]

3.15. Cortical excitability

Two articles analyzed the effects of PNM on cortical excitability and found a significant decrease in the motor evoked potential in myofascial pain (P = .02)[16] and osteoarthritis (P = .03).[17] In terms of the cortical silent period, both studies agree on the significant increase in said parameter (P = .005 and P = .001, respectively). Finally, none of those studies found significant differences when it came to short intracortical inhibition.

3.16. Brain derived neurotrophic factor

Three articles studied the effect of PNM on BDNF, with conflicting results. The BDNF is a protein associated with nerve growth factor who is secreted by astrocytes and glial cells and produces spinal cord neurons sensitization, facilitates the activation of N-Methyl-d-asparyaye and increases the excitability of gamma-aminobutyric acid-ergic neurons.[16] Botelho et al obtained significantly higher results of BDNF (P < .01) than the placebo when it came to myofascial pain.[16] Nonetheless, da Graca-Tarragó et al 2019 found no effect on BDNF when treating knee osteoarthritis.[18] On the other hand, in the study by da Graca-Tarragó et al 2016, they observed that BDNF had no correlation with the motor evoked potential, but it had a negative and marginal correlation (P = .05) with the pressure pain threshold.[17]

3.17. Adverse effects

Nine articles informed of the possible adverse effects of the PNM; two of them found no such effects after applying treatment[19,33] and three of them had no unspecified significant, severe or moderate adverse effects.[16–18] In three articles, patients reported frequent post-needling soreness and/or hematomas,[14,30,31] and two studies reported occasional somnolence, headache, and nausea.[30,31] All articles that showed there were adverse effects after treatment coincide that said effects disappeared spontaneously within 1 to 4 days.

4. Discussion

Among the articles selected for this review, there is a consensus on the fact that PNM produced significant improvements in pain intensity,[14,16–18,22–24,30,31,33] pressure pain threshold,[17,18,25,33] balance and muscle endurance,[19,21] functionality/disability,[18,22,30,31] subjective improvement,[14,30,31] and the function of the descending pain modulatory system.[16–18] Some articles also agree on the effect it has on the intake of drugs after treating with PNM,[14,16,18,30,31] producing a significant change in three of them.[1–3,16,30,31]

On the other hand, there was no significant improvement when it came to muscle contractile properties[20] or the quality of life of the patients.[32] The study by de la Cruz et al in 2020[20] was the only one that showed the effect of said technique on muscle contractile properties. Thus, it is hard to draw solid conclusions on the matter. Nonetheless, not finding any significant changes leads us to think that we can use this technique before physical exercise or sport, in case of confirming said findings.

On the other hand, the study that analyzed the quality of life of patients after receiving PNM treatment[32] compared its effect to DN, from which we can conclude that none of them obtained better results. In order to establish a direct cause-effect between PNM and the improvement of the quality of life, the study should have a control group.

In terms of the ROM, only 50% of the articles that studied this parameter found a significant improvement thanks to the PNM.[20,22,23] The adverse results on the ROM may be conditioned because of the characteristics of the studied sample. In two of the articles, they studied the ROM of ballet dancers, since their activity involves a lot of ROM and, therefore, it is unlikely to improve due to this intervention.[19,21] In the third article, they used PNM only in the trapezius.[25] Evidently, this is not the only muscle involved in neck ROM, which is way the intervention would be insufficient to evaluate said parameter.

There is little research when it comes to the improvement of strength by using PNM; as far as we know only one article evaluates this parameter,[15] and even though it obtained good results, it had no control group and it is not published at an indexed journal. It would be necessary to have more studies to confirm that PNM is useful when it comes to restoring strength. We obtain the same conclusion in parameters such as sleep quality, since only two articles have studied it, with conflicting results.[16,32]

When it comes to the effects of PNM on cortical excitability, the two articles that analyzed it[16,18] obtained a significant decrease in the motor evoked potential, and a significant increase in the cortical silent period, with no significant differences on the intracortical inhibition. Intracortical facilitation seemed to improve only when combined with tDCS, a form of top-down neuromodulation through constant, low and direct current delivered via electrodes on the head that modulates the thalamocortical synapses within pain pathways and it might change in thalamic inhibitory pathways, cingulate cortex, and periaqueductal gray matter.[18] Thus, said effect may be the result of the last technique or because of the combination of both. When it comes to BDNF, the results obtained are unalike[16–18] which is why we cannot draw conclusions and need more research. The crossed effect observed by de la Cruz et al 2020[20] and García-Bermejo et al 2020[22]on the untreated limb suggests that PNM

does not only produce distal-level effects on the homolateral region, but also may act on the central nervous system, causing bilateral effects.

Some studies compared the effect of PNM with DN,[24,32] resulting in both being equally effective techniques in short-term, with DN having a better benefit-cost ratio. Nonetheless, the worst post-needling soreness of DN went together with the highest rate of treatment abandonment.[32] However, the combination of both techniques obtained better short-term results, improving post-needling soreness.[4,24] This suggests that it may be a good idea to combine both techniques, but there should be more studies to prove that suggestion. Likewise, combining PNM and tDCS may improve the results rather than using those techniques separately.[18] All the same, only one study considers that possibility.

Finally, choosing the optimal current parameters was a controversial topic, due to the bibliographical variety. However, it seems that frequency is the most important parameter and with more options in terms of application.[5]

There is a huge disparity between the frequency used in the articles within this bibliographical review, with a range between 2 and 100 Hertz (Hz).[14–25,30–33] In relation to the frequency, there are various hypotheses to explain the action mechanisms of the technique. The first hypothesis suggests that electrical impulses modulate in a peripheral manner. According to the second hypothesis, it may be possible to explain their effect by stimulating the release of endogenous opioids, through electric current. Finally, the last hypothesis has observed mechanisms of synaptic plasticity.[14,34,35]

Paying attention to the mechanism of release of endogenous opioids, they found out that low frequencies (2–5 Hz) activate small-diameter motor fibers. Consequently, they cause a release of enkephalins and endorphins, which cause extra-segmental analgesia, with longer lasting effects. On the other hand, higher frequencies (50–100 Hz) may selectively activate big diameter nonnociceptive Aβ fibers, which cause a release of dynorphins and thus produce a decrease in the activity and sensitization of the nociceptive cells on the segment-level in the central nervous system. The analgesia mechanism produced by high frequencies produce shorter-lasting effects. Nonetheless, its application seems interesting in patients with tolerance towards opioids, since the main mechanism of low frequencies is the release of endogenous opioids, as opposed to the higher frequencies, which seem to be segmental.[14,35–38]

The best choice of frequencies may be a combination of both high and low frequencies, since it seems that the therapeutic effect of the combination is more effective than applying them separately.[39]

The best application time seems to be 30 minutes, since Hamza et al used 15, 30, and 45 minute intervals and obtained best results when using it for 30 minutes instead of 15 minutes. There was no difference between applying it for 30 or 45 minutes.[40]

Moreover, there are two types of applications when it comes to the effect of PNM on synaptic plasticity. According to said classification, there are long-term potentiation and long-term depression processes. Long-term potentiation is a form of use-dependent plasticity which can be produced using high frequency stimulation trains of 100 Hz for 1 second repeated five times at 10 seconds intervals. As a result, the synaptic transmission improves persistently. On the other hand, long-term depression, using a low frequency, non-interrupted and long lasted stimulation (17 minutes at 1 Hz) reduces the effectiveness of the synaptic transmission.[9,41,42] Repairing to this, we could adjust the parameters of the application to potentiate Aβ fibers or depress C fibers.

Besides, recent studies suggests that spinal cord stimulation could be effective for treating allodynia and neuropathic pain by attenuating wide dynamic range neurons hyperexcitability, releasing gamma-aminobutyric acid and decreasing neurotransmitters as glutamate and activating dorsal column fibers in an orthodromic manner, furthermore these authors propose as a promising therapeutic target the dorsal root ganglion.[11,43,44] This finding evidences a new possible therapeutic target in PNM.

Most of the articles selected in this review have notified adverse effects, even though they were mild and disappeared in 4 days at most. These facts imply that the technique is safe.

For this review, we established a minimum score of 5 in the PEDro scale in order to include the articles. Nonetheless, we chose one article with a score of 4, since it was the only ones that evaluated the effects of PNM on neuropathic pain.[14]

5. Limits of the study

The main limitations of the study were the lack of previous research studies on the subject and the lack of data on opioid intake in the selected studies.

6. Conclusion

The use of PNM seems useful when treating neuromusculoskeletal injuries. However, results may not be conclusive, since there are few articles published currently and we cannot confirm that the results obtained with PNM to be applicable to all neuromusculoskeletal injuries.

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