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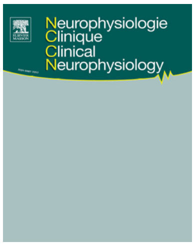

REVIEW/MISE AU POINT

Repetitive peripheral magnetic stimulation to reduce pain or improve sensorimotor impairments: A literature review on parameters of application and afferents recruitment

Stimulations magnétiques répétitives périphériques pour réduire la douleur ou améliorer les désordres sensorimoteurs : une revue de la littérature sur les paramètres d'application et le recrutement des afférences

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KEYWORDS
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Stimulation parameters;
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Musculoskeletal pain

Summary
Introduction. — Repetitive peripheral magnetic stimulation (rPMS over spinal root, nerve or muscle belly) is a promising technology in physiopathology research. As compared to electrical stimulation, rPMS is deemed to activate deep conductive structures and produce strong muscle contractions and massive proprioceptive afferents with minimal cutaneous recruitment. RPMS may thus act differently on neural plasticity involved in pain reduction and motor recovery in musculoskeletal or neurological conditions. However, literature is very scant and still controversial concerning afferents recruited by rPMS, thus no consensus is reached yet for its clinical use.
Study aim. — This review dealt with stimulation parameters reported in any scientific research that applied rPMS as an intervention to improve somatosensory or motor disorders with a view of proposing recommendations for future applications. Also, controversy on afferents recruitment was discussed.

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Results. — The literature search resulted in 24 studies. Literature is scant on the topic but our review presents the rationale and the experimental data that may underlie the selection of parameters in future studies using rPMS as an intervention. Although controversy remains, the review presents that the specific recruitment of sensory afferents by magnetic stimulation may offer advantages and disadvantages depending on the pathology.

Conclusions. — The review proposed recommendations to improve rPMS application in clinical research. However, the development of guidelines still requires methodological and clinical studies enrolling larger samples and with randomized sham-controlled designs.

MOTS CLÉS
Stimulation magnétique périphérique répétitive ;
Paramètres de stimulation ;
Afférences proprioceptives ;
Problèmes neurologiques ;
Douleur musculosquelettique

Résumé

Introduction. — La stimulation magnétique périphérique répétitive (rPMS de racine spinale, nerf ou muscle) est une technologie prometteuse en recherche clinique. Comparée à la stimulation électrique, la rPMS produirait de fortes contractions musculaires avec recrutement massif des afférences proprioceptives et recrutement minimal des fibres cutanées. La rPMS pourrait ainsi agir différemment sur la plasticité neuronale à l'origine de la baisse de douleur et de la récupération motrice après lésion ou maladie affectant le système musculosquelettique ou nerveux. La littérature est cependant limitée et toujours controversée quant aux afférences recrutées. Aucune recommandation n'existe quant à l'utilisation de la rPMS en recherche clinique.

But de l'article. — La revue s'est intéressée aux paramètres de stimulation rapportés dans toutes les études scientifiques utilisant la rPMS pour améliorer les désordres somatosensoriels et moteurs et propose des recommandations pour applications futures. Aussi, la controverse concernant les afférences recrutées a été discutée.

Résultats. — La recherche littéraire a permis d'obtenir 24 articles. Malgré un manque d'évidences scientifiques, les données expérimentales et le rationnel présentés dans la revue pourraient aider à la sélection de paramètres appropriés dans les études futures, utilisant la rPMS comme une intervention. Quoique certaines controverses persistent, la spécificité de recrutement des afférences par la stimulation magnétique semble offrir des avantages et inconvénients, dépendant de la pathologie.

Conclusions. — La revue propose des recommandations pour améliorer l'application de la rPMS en recherche clinique. Cependant, le développement de guides de pratique requiert plus d'études méthodologiques et cliniques sur un plus grand nombre de participants et présentant un plan d'analyse randomisé contrôlé avec placebo.

Introduction

Non-invasive peripheral stimulation refers to the use of an external device that can produce muscle contractions and sensory afferents via the depolarisation of conductive structures within the peripheral nervous system. For example, transcutaneous electrical stimulation (TES) and peripheral magnetic stimulation (PMS) create voltage differences and ion flows, thus activating conductive structures beneath the stimulated region [5]. Repetitive trains of TES and PMS stimuli are used in clinical research, with varying parameters, for reducing pain or promoting sensorimotor recovery [7,12,15,62,63,65]. The mechanisms potentially involved include local changes of muscle and nerve function, synaptic strengthening in the ventral horn of spinal cord [13], and also remote changes in fronto-parietal activation between sensory and motor cortices and in corticospinal and intracortical motor excitability regulation [13,33,61,68]. These mechanisms of action were discussed in our last review, especially for the after-effects of PMS (named repetitive peripheral magnetic stimulation, rPMS), a novel easy-to-administer approach in neurological conditions affecting sensorimotor control [7] and in pain conditions affecting the musculoskeletal system [55,65]. Conversely to TES, rPMS is considered a painless method deemed to preferentially recruit proprioceptive afferents with minimal activation of cutaneous fibers [67,68]. However, rPMS popularity and applicability are limited owing to missing evidence and recommendations on parameters of application, conversely to TES whose guidelines are already published [15,62]. Furthermore, the preferential recruitment of cutaneous vs. proprioceptive afferents by rPMS over nerves and muscles and whether this preferential activation is beneficial in pathological conditions are still controversial topics [38,77,78]. The present work included all papers using rPMS as an intervention to improve somatosensory or motor disorders with limitations of musculoskeletal function. The primary objective was to review some selected parameters to refine rPMS application in future protocols. The work also discusses which afferents are preferentially recruited by rPMS and whether this basic knowledge has a potential clinical impact.

RPMS parameters

Methods

The literature search was undertaken in 3 databases (Pubmed, CINAHL and SPORTDiscus) with no time restriction using the following search strategy: (peripheral magnetic stimulation) OR (spinal magnetic stimulation) AND (repetitive OR Hz OR Hertz) NOT ''repetitive transcranial magnetic stimulation'' NOT ''transcranial direct current stimulation''. Additional relevant studies were also hand-searched in the references list of the papers selected for the review. Articles that met the following selection criteria were retained for full-length examination: full-text original papers written in English, which used rPMS as an intervention to improve somatosensory or motor disorders that limit the musculoskeletal function.

Results

The literature search was ended in March 2015 and included 24 papers (Fig. 1). Sixteen studies had administrated rPMS in order to improve sensorimotor impairments caused by several neurological pathologies: multiple sclerosis [34,49—51], spinal cord injury [32], stroke [8,22,23,29,37,66,68], traumatic brain injury [37,66], cerebral palsy [19,20], traumatic brachial plexopathy [30] and Parkinson's disease [4]; eight studies used rPMS to reduce pain caused by various pathological conditions: musculoskeletal injuries [55], myofacial pain syndrome [64,65], complex regional pain syndrome [35], lumbosacral spondylotic pain [40] chronic low back pain [46], neuroma/nerve entrapment [39] and pudendal neuralgia/sciatica [60]. RPMS parameters were retrieved along with authors' justifications in each study, including coil design and location, coil orientation and current direction, duty cycle, duration, frequency and intensity (Table 1). Furthermore, because rPMS was used for two main purposes across the included studies (i.e. sensorimotor improvements or pain), a secondary analysis was performed to verify whether parameters differed between these therapy goals. Also, details concerning the use of sham stimulation in the included studies were reported.

Coil design and location

The information regarding the type of coil was provided in 22 of the 24 papers. The round coil (RC) and the figure-of-eight coil (Fof8) were respectively used in 7 and 12 studies. The three remaining studies used both Fof8 and RC, alternatively. The effects of coil design or location of stimulation were addressed in a few studies. Krause et al. [32,34,35] selected RC to stimulate lumbar and cervical spinal roots with higher magnetic strength, whereas Struppler's group [66,68] used Fof8 to selectively stimulate the superficial paretic muscles. Smania et al. [64,65] used Fof8 and RC over the superior trapezius muscle in alternation due to coils overheating, but they acknowledged that each coil presented specific advantages: Fof8 was better for accurate targeting of painful trigger points whereas RC enabled stimulation of deeper and larger painful muscle areas. In that vein, out of the 12 studies that used Fof8, 11 intended to stimulate superficial muscles or nerves and out of the 7 studies that used RC, 7 intended to reach deeper conductive structures such as spinal roots. Table 1 shows that this dichotomous use of Fof8 vs. RC was true either in studies focusing on sensorimotor improvements and in studies tackling pain reduction. The choice made by the authors on whether which coil to use relay on the impact of the between-coil differences of focality and depth of penetration on their objectives. The electric field induced in the tissue by RC and Fof8 can be visually inspected for focality in Figure 8 of [52] and for depth of penetration in Figure 7 of [44] and Figure 14 of [28]. RC is the less focal with a stimulated area equivalent to its diameter because electrical currents are produced along the whole winding [5]. Currents are in opposite directions in the two windings of Fof8, thus passing the coil's center in the same direction and the periphery in opposite directions. The resulting magnetic field is thus weaker at the periphery and 2—3 times stronger at the center [5] with a focus (called virtual cathode) that is relatively accurate (2.5—3.0 cm from coil's center to handle, Table 2) [52,58]. Fof8 thus enables the selective stimulation of nerves without co-activation of surrounding structures that often occurred with RC [53]. Nevertheless, RC focality can be significantly improved by tilting the coil 45° from the skin surface (see section ''Coil orientation and current direction'') [42] or by using smaller diameters [18], e.g. 7 cm diameter instead of 14 cm. Manufacturers must however respect a minimal size of coils to avoid unsafe heat dissipation produced by the large current flows [17]. Fof8 is therefore a better choice to selectively stimulate a specific muscle or a distal nerve, at least at weak intensities of stimulation [28]. Small peaks of half the amplitude of the center peak can be produced on either side of the windings and could depolarize conductive structures at greater intensities [28].

A recording probe in restricted and unrestricted volume conductors was used to study depth of penetration and it showed that fall-off of magnetic field with distance was faster with Fof8 than with RC [44], thus indicating that RC should be preferentially used to stimulate deeper structures. Indeed, a large-diameter RC was shown to be more suitable to depolarize deep structures such as spinal nerve roots at weaker intensities, especially if the edge of the coil coincides with the neuro-foramina [43]. For example, Chokroverty et al. [14] stimulated the L5/S1 nerve roots with RC and from the latencies of the direct motor response (direct recruitment of alpha-motor neurons) and spinal reflex loops (recruitment of 1a-fibers) recorded in the soleus muscle, they calculated that both afferent and efferent fibers were depolarized near the spine exit at the intervertebral foramina (20 cm from the anterior horn cells). In line with this, the laws of physics teach that the magnetic field, even if bypassing bones, will follow the path of less resistance, i.e. the electric current generated by magnetic stimulation concentrates at the entrance of the narrow channel formed by high-resistance structures of bones (foramina) [72].

Recommendations. Evidence suggests that RC is more efficient for stimulating the deep conductive structures. However, due to large diameter of action, if co-activation of other nerve roots is unwanted, a meticulous EMG monitoring of multiple muscles is recommended to adjust coil position for the specificity of stimulation. This procedure was already

Table 1 Parameters of rPMS application.

Reference	Population	Coil type	Coil location	Coil orientation/Current direction	ON/OFF (s)	Duration (min)	Number of pulse	Frequency (Hz)	Intensity (T)
Sensorimotor impairments									
Nielsen et al., 1995	MS, $n = 12$	RC	Caudal part of the coil at T8	NM/NM	8/22	30	5760	12	0.95—1.2, above SMT
Nielsen et al., 1996	MS, $n = 38$	RC	Caudal part of the coil at T8	NM/NM	8/22	25	10,000	25	1.05—1.26, above SMT
Nielsen and Sinkjaer, 1997	MS, $n = 11$ HS, $n = 9$	RC RC RC	Caudal part of the coil at T8, C7 and L3	NM/NM	NA Continuous 5/5	NM NM 5	1 16 3750	NA 25 25	1.26, above SMT 1.26, above SMT 1.26, above SMT
Heldmann et al., 2000	SK, $n = 14$ HS, $n = 7$	Fof8	Finger and hand extensors	NM/NM	NM	NM	NM	NM	Above MCT
Havel and Struppler, 2001	SK, $n = 1$	Fof8	Extensor indices proprius	NM/NM	1.5/NM[a]	NM	∼2100	20	Above MCT
Kerkhoff et al., 2001	SK, $n = 14$ HS, $n = 7$	NM	Hand's dorsal palm	NM/NM	NM	20	NM	NM	NM
Struppler et al., 2003	SK, $n = 47$ TBI, $n = 5$	Fof8	Extensor indices proprius	NM/NM	1.5/4	∼15	4500	20	Above MCT
Krause et al., 2004	VSP, $n = 15$ HS, $n = 16$	RC	2 cm paravertebral between L3 and L4	TE/NM	10/40	∼8.3	2000	20	20% above SMT
Krause and Straube, 2005	SCI, $n = 1$	NM	Over lumbar nerve roots	NM/NM	10/NM 10/NM 10/NM	∼20 ∼30 ∼40	2000 2000 2000	20 15 10	20% above SMT 20% above SMT 20% above SMT
Struppler et al., 2007	SK, $n = 8$	Fof8	Finger/hand extensors	Adjusted/NM	1.5/4	∼15.3	5000	20	1.2, above MCT
Khedr et al., 2012[b]	TBP, $n = 34$	Fof8	Superior trapezius	NM/NM	10/20 10/30	∼3.5 ∼33.3	1050 1500	15 3	Below MCT 1.54, above MCT
Flamand et al., 2012	CP, $n = 5$	Fof8	Tibial nerve Common peroneal nerve	FL/NM	Continuous 2/8	1 5	900 900	TB (15) TB (15)	Above MCT
Arii et al., 2014	PD, $n = 37$	RC	Over thoraco-lumbar vertebras[c]	ST/NM	1/10	∼1.3	40	5	1.0, above SMT

Table 1 (*Continued*)

Reference	Population	Coil type	Coil location	Coil orientation/Current direction	ON/OFF (s)	Duration (min)	Number of pulse	Frequency (Hz)	Intensity (T)
Flamand and Schneider, 2014	CP, *n* = 1	Fof8	Sciatic nerve Tibial nerve Common peroneal nerve	FL/NM	Continuous Continuous 2/8	3 1 5	2700 900 900	TB (15)	Above MCT
Krewer et al., 2014	SK, *n* = 60 TBI, *n* = 3	Fof8	Arm muscles[d]	NM/NM	1/2	~10	5000	25	10% above MCT
Beaulieu et al., 2015	SK, *n* = 18	Fof8	Tibialis anterior	FT/NM	2/8	3.33	600	TB (15)	1.47, above MCT
Pain conditions									
Pujol et al., 1998	MKI, *n* = 30	Fof8 RC	Various painful musculoskeletal structures	NM/NM	5/25	40	8000	20	Below MCT
Sato and Nagai, 2002	PN, *n* = 4 Sciatica, *n* = 1	RC	Over S2—S3	TE/NM	Continuous	1—2	30—50	< 0.5	1.5, above MCT
Smania et al., 2003	MPS, *n* = 18	Fof8 RC	Most painful superior trapezius trigger point	NM/NM	5/25	20	4000	20	Below MCT
Smania et al., 2005	MPS, *n* = 53	Fof8 RC	Most painful superior trapezius trigger point	NM/NM	5/25	20	4000	20	Below MCT
Krause et al., 2005	CRPS, *n* = 12 HS, *n* = 10	RC	Over C7—C8	NM/NM	10/NM	~10	NM	20	20% above SMT
Lo et al., 2011	LSD, *n* = 20	Fof8	Over cauda equina (T12—L1)	FL/NM	0.5/4.5	~16.7	1000	10	Below MCT
Massé-Alarie et al., 2013	CLBP, *n* = 13 HS, *n* = 9	Fof8	Transversus abdominis/obliquus internus	NM/NM	2/8	10	1800	TB (15)	1.16, above MCT
Leung et al., 2014	N/NE, *n* = 5	Fof8	Over the site of N/NE	NM/NM	Continuous	~13.33	400	0.5	NM

ON: phase of active stimulations; OFF: phase of rest (no stimulation); T: Tesla; MS: multiple sclerosis; RC: round coil; C7—C8—T8—T12—L1—L3—L4—S2—S3: refer to either cervical (C) — thoracic (T) — lumbar (L) or sacral (S) vertebrae; NM: not mentioned; SMT: spinal motor threshold; HS: healthy subject; NA: not applicable; SK: stroke; Fof8: figure-of-eight; MCT: muscle contraction threshold; TBI: traumatic brain injury; VSP: various spinal disorders; TE: flat tangential edge; SCI: spinal cord injury; TBP: traumatic brachial plexopathy; CP: cerebral palsy; TB: theta-burst frequency; FL: flat longitudinal; PD: Parkinson disease; ST: symmetrical-tangential; FT: flat transverse; MKI: various musculoskeletal injuries; PN: pudendal neuralgia; MPS: myofacial pain syndrome; CRPS: complex regional pain syndrome; LSD: lumbosacral spondylotic pain; CLBP: chronic low back pain; N/NE: neuroma/nerve entrapment.

[a] The authors applied approximately 70 cycles of 1.5 sec each.

[b] Two different rPMS interventions were separated by a 10-min resting period.

[c] Adaptation of coil placement helped target the largest spinal anteflexion in standing posture for each participant (photograph or spinal X-ray films).

[d] Stimuli were distributed among arm/forearm extensor and flexor muscles.

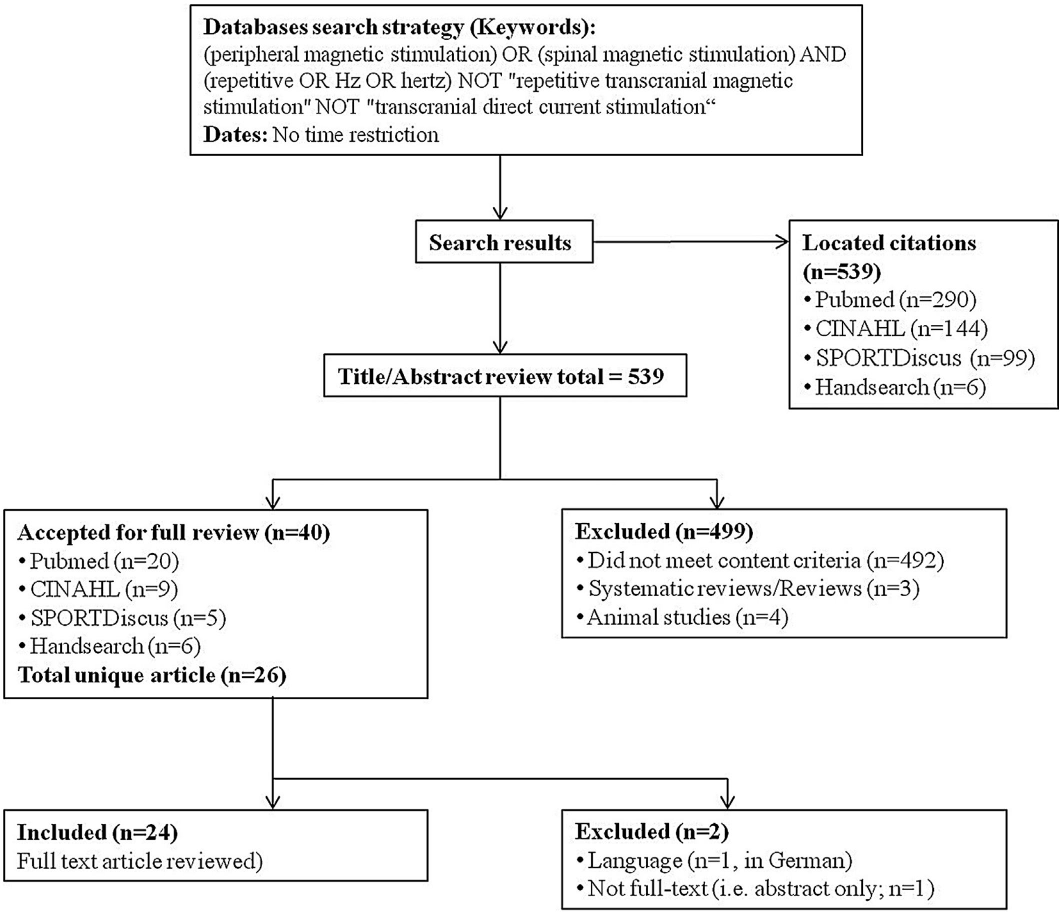

Figure 1 Flow chart of the review's research strategy. CINAHL: cumulative index to nursing and allied health literature.

Table 2 Pros and cons of magnetic stimulation applied at the periphery.

Advantages	Disadvantages
Painless[a] [3,5,6,10,14,16,17,21,26,36,41,54,56,71,73,77]	Locus of stimulation not well-defined[a] [3,5,6,11,17,38,42,56,73]
Non-invasive [3,5,6,10,14,16,17,41,54,56,73,77]	Slowed by overheating of the coil[a] [5,6,10,11,38,42,56]
Deeper penetration[a] [3,5,6,14,16,17,41]	Larger area stimulated with increased intensity [3,6,17,52,56,74]
Easy administration [3,5,6]	Bulky and expensive equipment[a] [5,6]
Induces higher muscle torque[a] [21,26,36]	Muscle contractions uncomfortable at higher intensities [11,17]
Useful in children stimulation [3]	Time-consuming for positioning because site of stimulation and orientation more critical[a] [11]
Separate stimulation of a variety of different muscles[a] [77]	Coil often displaced by muscle contractions [11]
Induces better torque output, smoothness, and symmetry of pedaling movement on a cycling ergometer in patients with stroke, SCI or MS and with partially or completely preserved sensitivity[a] [70,71]	Induces lesser torque output and power of pedaling movements on a cycling ergometer in patients with complete SCI[a] [70]

M-responses: muscle contraction evoked by the direct depolarisation of the α-motor neuron axons in the stimulated nerve; H-responses: Hoffmann reflexes; SCI: spinal cord injury; MS: multiple sclerosis.

[a] As compared to electrical stimulation.

followed to target a nerve root [34,35,45]. Conversely, Fof8 is appropriate for selective recruitment of superficial structures, such as muscles and nerves, without co-activation of surrounding tissues. Future studies will have to compare the effectiveness and selectivity of different coil designs at different sites of stimulation.

Coil orientation and current direction

Seven studies provided sufficient details on the specific orientation of the coil relative to the target structure but none informed on current direction within the coil (Table 1). Four studies used basic data to support coil orientation over spinal roots [34], nerve trunks [19,20] and muscle [8]. Another study performed pilot testing to determine the optimal coil position/orientation over spinal roots [4]. The two last studies did not justify their coil orientation [40,60]. Interestingly, one study reported that coil orientation was adapted per participant to induce the strongest contraction/movement [68]. The following paragraphs depict the basic knowledge underlying the selection of coil's orientation and current direction for rPMS application.

In the late 1980s, basic studies tested how different orientations of coil and direction of electrical current in the coil impacted on the effectiveness of magnetic stimulation to depolarize peripheral conductive structures. Maccabee et al. [42,44] reported six RC orientations relative to the longitudinal axis of a conductive structure, as follows, from the most to the lesser effective to induce large amplitudes of electrical current: flat tangential edge (0° to horizontal/0° to axis); tilted (45° to horizontal/0° to axis); orthogonal-longitudinal (90° to horizontal/0° to axis); orthogonal-rotated (90° to horizontal/45° to axis); symmetrical-tangential (0° to horizontal/90° to axis); transverse (90° to horizontal/90° to axis) (see Figure 3 in [42] and Figure 9 in [44]). The three former orientations produced strong muscle contractions but the tilted and orthogonal-longitudinal were more accurate with minimal loss of effectiveness [17,42,44]. Two orientations were tested for Fof8 coil with the flat longitudinal (0° to horizontal/0° to axis) more effective than the flat transverse (0° to horizontal/90° to axis) (see Figure 5 in [44]). Higher effectiveness was explained in all cases by the optimal location of virtual cathode and anode along the course of the conductive structure [44].

It was also questioned whether reversing the current direction, i.e. interchanging the cathode/anode virtual position along the nerve without changing coil orientation, could influence the effectiveness of stimulation [1,17,42,48,76]. Over cervical spinal roots, motor latencies are relatively unaffected by current direction because the depolarization site remains similar at the low threshold region near neuro-foramina [72,76]. Over a nerve, when the virtual cathode is proximal (further from muscle) and the anode distal (closer to muscle), the current is directed toward the muscle (see Figure 6 in [42]). In this case, given that fibers are depolarized under the cathode, muscle response latencies are slightly longer and amplitudes slightly lower [1] or unaffected [42,48] as compared to a current directed toward the spine (distal cathode, proximal anode) and for which stronger muscle contractions are induced at lower intensities [76]. In order to explain why muscle action potentials were smaller when the cathode was located proximally, Tuday et al. [75] used EMG recordings (muscle action potentials) and electroencephalography (sensory evoked potentials) and showed that the cathodal depolarization triggered bidirectional action potentials along the nerve and that propagation to the anode was blocked or attenuated by local hyperpolarization (anodal block). Finally, the impact of coil orientation and current direction on muscle belly stimulation has not yet been thoroughly studied. Theoretically, nerve endings roughly follow muscle fiber orientation, especially for long parallel and fusiform muscle shapes; thus this may be a starting point for selection of coil orientation/current direction. However, recent evidence with the Fof8 coil suggested that even a flat transverse orientation relative to the tibialis anterior muscle axis is effective in inducing contractions and movements [8]. Also, it was impossible to predict which orientation/current direction would be more effective to activate a peripheral structure with no longitudinal axis (for example, the trigger point of painful trapezius muscle [64,65]).

Recommendations. Basic knowledge is sufficient to select a coil orientation that will efficiently stimulate a nerve trunk or spinal root. However, there is limited evidence for other peripheral conductive structures (such as muscles) where fibers orientation varies between individuals. Also, the choice of the most efficient coil current direction remains hypothetical (anodal block). Thus, care should be taken at the onset of future rPMS studies for testing the combination of coil orientation and current direction that will best respond to the objectives of the intervention. Researchers should be aware of the fact that different combinations may be required to induce either stronger muscle contractions [68] or better-tolerated sensations when stimulating injured musculoskeletal structures [55,75].

Duty cycle

Seventeen papers used intermittent stimulation and provided details on the duration of ON (active stimulation) and OFF periods (pause) of rPMS application, two studies used continuous stimulation (i.e. no OFF), two studies combined intermittent and continuous stimulation, one study used only ON periods and the information was missing in two studies (Table 1). In intermittent protocols, OFF periods were overall 4.4 ± 2.2 times longer than ON periods. More specifically, OFF periods were longer in studies using rPMS to reduce pain (mean ratio OFF/ON: 5.7 ± 1.8%) than in studies focusing on sensorimotor impairments (mean ratio: 3.9 ± 2.2%). However, no rationale supported between-study differences thus this result might be fortuitous. Anecdotally, it was mentioned that pilot testing in myofacial pain syndrome (four participants) helped determine that 5 s ON duration had better therapeutic effects than 1 s or 3 s [64]. Also, the specific duty cycle of theta-burst frequency protocol (2 s ON/8 s OFF) was used in four studies but no rationale was proposed to support this choice [8,19,20,46]. The choice of longer OFF periods was however related in several studies to coil overheating which is a major problem in repetitive magnetic stimulation protocols (see Table 2) especially in former rPMS studies [50,51]. Most authors used a coil-implemented cooling device while others prevented overheating by using two coils in alternation

[32,34,55,64,65]. However, despite the advent of improved devices for rapid-rate stimulation, repetitive magnetic stimulation cannot yet be conducted for long durations without a parallel adjustment of intensity, frequency or OFF duration. Seven studies postulated that intermittent ON/OFF periods of rPMS above muscle contraction threshold (rather than continuous) produced physiological contraction/relaxation of muscles and generated massive proprioceptive inflows to sensorimotor networks by ascending pathways, thus influencing neuroplastic mechanisms [8,19,20,46,66,68] and avoiding unnecessary fatigue of paretic muscles [8]. They did not however justify the ON and OFF durations chosen. Specifically, Flamand et al. [19,20] applied intermittent ON/OFF rPMS over the common peroneal nerve to mimic contraction/relaxation of the paretic ankle dorsiflexors in cerebral palsy just after the application of continuous stimulation (no OFF) over the tibial nerve [19,20] and the sciatic nerve [19] to reduce the reflex hyperactivity of the triceps surae and hamstrings circuits. They hypothesized that continuous rPMS could best induce transient saturation (i.e. inhibition) of hyperactive spinal circuits of spastic muscles.

Recommendations. The selection of a specific ON duration seems arbitrary whereas applying longer OFF periods depends on technological limitations related to magnetic stimulators. Although the choice of protocols relies on interesting hypotheses, no study has yet evaluated the specific after-effects of continuous (ON with no OFF) versus intermittent rPMS protocols (ON/OFF) in physiopathology. Two pilot studies [19,20] proposed a rationale for each protocol (intermittent to improve motor control of the paretic muscles; continuous to down-regulate spinal circuits of spastic muscles), but applied them in combination, thus challenging the detection of a specific influence. When repetitive magnetic stimulation is applied over the skull, intermittent protocols may help minimize the risk of tissue heating, magnetic field exposure and side effects: this safety issue was recently dealt by the International Federation of Clinical Neurophysiology [57]. Although this knowledge cannot be directly transferred to rPMS application (at the periphery), the question remains whether longer continuous protocols could increase the risk of adverse events. Table 3 shows that rPMS side effects are not often reported and insights on rPMS safety remain insufficient. Future studies should thus test the after-effects of ON vs. ON/OFF protocols and report any side effect. If rPMS are to be administrated over a long period of time or with short OFF periods, then a minimal safety measure should be the use of a coil-implemented cooling device.

Duration/total number of stimuli

Twenty-two studies reported on the total duration of rPMS application or gave sufficient details on frequency, ON/OFF repetitions, number of stimuli, etc., to infer the information. Twenty-one studies reported on the total number of stimuli. Given inconsistent length of OFF periods across studies, the total number of magnetic pulses appeared to be a more relevant parameter and more readily comparable between studies. This parameter is also considered a determining factor of effectiveness in brain stimulation studies [57]. Results from rPMS duration and number of stimuli are discussed together because they were not different between studies on sensorimotor impairments (mean ± SD = 13.5 ± 9.5 min and 2979 ± 2527 stimuli) and studies on pain reduction (13.1 ± 7.5 min and 2749 ± 2814 stimuli).

Overall, duration of stimulation and number of stimuli are highly variable across studies (13.4 ± 8.8 min and 2914 ± 2552 stimuli). Their choice missed rationale, although some authors relay on evidences from previous studies with rPMS [45,64] or protocols published for repetitive transcranial magnetic stimulation [8,19,20,46]. One study tested three different rPMS frequencies (20, 15 and 10 Hz) and durations (20, 30 and 40 min) but with always the same number of stimuli [32] thus did not investigate the effect of changing rPMS duration/number of pulses per se. Another study tested how different numbers of rPMS stimuli above thoraco-lumbar spinal roots, thus with different durations and always the same frequency (25 Hz), influenced the soleus spinal excitability measured by H-reflex (electrical analogue of stretch reflex) [49]. It was reported that increasing the number of stimuli decreased more H-reflex and for a longer time, especially in multiple sclerosis where 5-min rPMS (3750 stimuli) down-regulated H-reflex during 28 min [49]. Also, spasticity of lower limbs (assessed by ordinal scale) decreased more in multiple sclerosis when the total number of stimuli was almost twice higher (i.e. from 5760 [51] to 10,000 [50] pulses). However, although the two previous studies used the same coil type, location and duty cycle, the latter used higher frequency and intensity of rPMS thus mitigating the interpretation of results. Recent works with theta-burst frequency showed that short rPMS durations (3—10 min) applied on lower limb muscles in stroke [8] and cerebral palsy [19,20] and over deep abdominal muscles in combination with manual therapy in chronic low back pain [46] improved spasticity, corticomotor control and pain. The total number of stimuli in a theta-burst session was similar to longer classic repetitive protocols, i.e. between 600—4500 pulses. Interestingly, two studies reported that a single rPMS session with a total of only 30—50 magnetic pulses induced significant long lasting pain reduction in pudendal neuralgia or sciatica [60] and improvement of postural abnormality in Parkinson's disease [4].

Recommendations. The scarce data available tend to show that longer rPMS durations or larger numbers of stimuli may better impact on sensorimotor systems. However, this is not yet clear because significant and long lasting improvements could have been obtained recently after short lasting application of rPMS with either a small number of pulses or instead, a high number of stimuli (available in complex stimulation patterns such as theta-burst stimulation). Clinical studies are warranted to test the efficiency of such protocols in terms of time-consumption, persistence of effects, improvement of function and quality of life, before any knowledge transfer.

Frequency

Eleven studies applied rPMS at a frequency of 20—25 Hz (Table 1), six studies used 15 Hz or less, one study used different frequencies, four studies used theta-burst stimulation (5 Hz trains of three pulses elicited at 50 Hz, see Figure 1a in [24]) and the information was missing in two papers. Very low frequencies (≤ 0.5 Hz) were used only in

Table 3 Side effects of magnetic stimulation applied at the periphery.

Reference	Side effects
Sensorimotor impairments	
Nielsen et al., 1995	No major side effects. All reported a ''tight feeling as if wearing a narrow ring around the midthoracic level during stimulation''. One participant had a single episode of brief dizziness
Nielsen et al., 1996	Two participants complained of irregular heartbeats 2 hours after stimulation, but showed a normal rhythm on electrocardiogram. One participant complained of low cost-benefit ratio, mostly because of long transportation time. All reported a ''tight feeling as if wearing a narrow ring around the midthoracic level during stimulation''. Two episodes of brief dizziness were reported immediately after rPMS
Nielsen and Sinkjaer, 1997	All reported a ''tight feeling as if wearing a narrow ring around the midthoracic level during stimulation''. This feeling was well tolerated, except for one who refused to participate to the final study part applying a longer stimulation duration
Heldmann et al., 2000	NM
Havel and Struppler, 2001	NM
Kerkhoff et al., 2001	NM
Struppler et al., 2003	Two participants developed a slight rigidity in the stimulated arm
Krause et al., 2004	NM
Krause and Straube, 2005	NM
Struppler et al., 2007	NM
Khedr et al., 2012	RPMS was well tolerated by all participants, without any adverse effects
Flamand et al., 2012	No side effects reported. The children ''demonstrated curiosity and enjoyment from one session to another, laughing with their parents when the foot on the stimulated side was moving on its own''
Arii et al., 2014	No major safety issues. No participant reported pain during rPMS, but two reported mild discomfort 1—3 hours after rPMS that disappeared by the next day
Flamand and Schneider, 2014	NM
Krewer et al., 2014	RPMS and sham were well tolerated by all participants. None reported pain or uncomfortable feeling during or after the treatments
Beaulieu et al., 2015	NM
Pain conditions	
Pujol et al., 1998	RPMS was well tolerated by all participants. None reported excessive discomfort or pain during and immediately after the treatments
Sato and Nagai, 2002	RPMS was well tolerated by all participants without any adverse effects
Smania et al., 2003	NM
Smania et al., 2005	High intensity rPMS did not cause any significant discomfort
Krause et al., 2005	NM
Lo et al., 2011	RPMS was well tolerated by all participants without any adverse effects
Massé-Alarie et al., 2013	No adverse effect reported after rPMS
Leung et al., 2014	NM

RPMS: repetitive peripheral magnetic stimulation; NM: not mentioned.

studies focusing on pain reduction [39,60], thus results from sensorimotor impairments and pain conditions are discussed separately.

Sensorimotor impairments. Three studies [8,19,20] applied the theta-burst frequency without providing a sound rationale. Two studies compared the effectiveness of different frequencies, and their results questioned whether rPMS frequency influenced the outcomes. They showed that frequency used for paravertebral rPMS did not actually impact on the reduction of spinal excitability (assessed by soleus H-reflex in three healthy subjects) [49] or of muscle tone (assessed by the Modified Ashworth Scale and the Wartenburg's Pendulum Test in a case of spinal cord injury) [32]. Precisely, Nielsen and Sinkjaer [49] showed that the only difference was a more pronounced H-reflex inhibition at 10 and 25 Hz than at 1 Hz but Krause and Straube [32] did not reproduce any difference between 10, 15, and 20 Hz. A sixth study [66] reported longer lasting improvements of spasticity and motor control with 20 Hz rPMS. This result differed from the authors' previous German-written study (not included in the review) where better improvements were obtained with 40 Hz in about half of their participants with various spastic disorders. They proposed that rPMS after-effects might depend on the spastic paresis pathogenesis.

Pain conditions. As for duration/number of stimuli, some authors justified the frequency used on the basis of previous rPMS studies [64] or on results from repetitive transcranial magnetic stimulation (rTMS) literature [39,46]. Frequency below 1 Hz could have been used to reduce pain because low frequency rTMS of the motor cortex induces a transient inhibition of cortico-cortical connections [39]. It was hypothesized that low-frequency rPMS over the site of neuroma/nerve entrapment could inhibit neural hypersensitivity and thus reduce pain. In the same vein, a former study by Sato and Nagai used frequencies below 0.5 Hz in cases of painful nerve hypersensitivity caused by pudendal neuralgia or sciatica [60]. However, all other studies used frequencies higher than 10 Hz and significantly reduced pain [35,40,46,55,64,65]. This discrepancy (low vs. high frequency to reduce pain) may be related to the existence of different origins of the pain conditions, those studies with higher frequencies having not included nerve irritation/hypersensitivity. One study [46] used theta-burst frequency and refereed to Huang et al. [24] seminal work on brain stimulation but no rationale was provided to select this specific stimulation pattern at the periphery.

Recommendations. No evidence yet allows determination of whether rPMS frequency is a factor of influence for the outcomes tested. Although appealing, the rationale for using very low frequency in order to reduce pain caused by nerve hypersensitivity comes from insights on motor cortex inhibition by transcranial stimulation. No neurophysiological data can yet confirm whether this hypothesis is true with rPMS administration. Also, H-reflex hyperexcitability was best inhibited when using higher rather than lower rPMS frequencies over spinal roots. However, this knowledge is based on too small-sampled studies for any clear conclusion to be drawn. Future studies ought to test larger samples with different frequencies over the same locations. Also, no evidence tackled the impact of using lower versus higher frequencies in terms of quality of muscle contractions. Evidence from rPMS at sufficient intensity to produce muscle contractions denote that lower frequencies (for example 5 Hz and less [4]) and theta-burst frequency [8] induced muscle twitching whereas higher frequencies (for example above 10 Hz) produced sustained muscle contractions due to temporal summation of motor units recruitment [26]. When compared to sustained contraction, muscle twitching gave rise to more but weaker contractions and smaller joint movements. For example, 5 Hz rPMS-induced 5 weak contractions or small movements per second while 20 Hz induce one strong contraction or larger movement during the whole ON period. It would be of interest to address, for example, whether frequencies producing sustained contractions or muscle tetanus impact differently from those producing muscle twitching. Sustained contraction may be chosen to strengthen muscles [21,26] and muscle twitching would be a better choice to improve movement by mimicking contractions/relaxations [7] and triggering massive proprioceptive inflow towards fronto-parietal areas [68].

Intensity

Nine papers provided rPMS intensity in Tesla or in percentage of the maximal stimulator output (%MSO then transformed in Tesla if MSO value available). However, the magnetic field strength at the depth of the targeted structures cannot be estimated because it depends on the type of coil, the depth of tissue stimulated and the geometry of the area beneath the coil [28]. A solution could be the expression of rPMS intensity in percentage of muscle contraction threshold. However, accurate surface EMG determination of this threshold can be contaminated by rPMS artifacts when the coil is placed near the recording electrodes [11]. Also, visual detection of slight contractions is challenging, especially when the coil is positioned directly above the muscle. Alternatively, movement threshold and spinal motor threshold correspond to the lowest rPMS intensity eliciting respectively a joint movement detected visually and the minimal intensity to depolarize a nerve root and evoke contraction of innervated muscles. Some authors thus expressed rPMS intensity in percentage of movement threshold [37] or spinal motor threshold [32,34,35]. The present review details such information on threshold when available in papers and if not, it refers to supra-threshold versus sub-threshold stimulation when reported, i.e. intensity eliciting muscle contraction or not. Almost all papers set supra-threshold rPMS (i.e. 17 studies, Table 1), four used sub-threshold intensities, one used both supra- and sub-threshold protocols and the information was missing in two studies. Of note, all studies using sub-threshold intensities focused on pain reduction. The study with both protocols [30] was in traumatic brachial plexopathy participants: sub-threshold rPMS was used to reduce shoulder pain and rPMS inducing strong muscle contractions was used to strengthen the trapezius muscle affected. Therefore, rPMS studies aiming at improving sensorimotor impairments vs. decreasing pain are discussed separately.

Sensorimotor impairments. The rationale available in studies supports that muscle contraction and joint movement produce massive ascending flows of proprioceptive afferents thus influencing the plasticity of residual sensorimotor circuits available for recovery after lesion or disease of central or peripheral nervous system [20,23,30,68] (see Beaulieu and Schneider, 2013 [7] for a review). Two papers specifically tested how changing rPMS intensity could influence the outcomes. Nielsen and Sinkjaer [49] showed in three healthy subjects that soleus H-reflex was more depressed when rPMS intensity over spinal roots was increased from 30% MSO (minor contractions) to 45% MSO (moderate contractions) and 45—60% MSO (strong contractions), thus suggesting that the magnitude of after-effects could be intensity-dependent. In line, Krause et al. [32] compared the influence of supra-threshold (120% MSO) and 'sham' rPMS consisting of sub-threshold stimulation (50% MSO) of spinal roots in a spinal cord injury case and reported that supra-threshold rPMS reduced lower limb spasticity whereas sub-threshold did not influence.

Pain conditions. Most studies [40,55,64,65] referred to evidence from the electrical stimulation literature where intensity of pure sensory stimulation (i.e. transcutaneous electrical stimulation insufficient to induce muscle contraction) was effective to reduce pain in various disorders. However, two rPMS studies [35,60] that used supra-threshold intensities to reach deep spinal roots still observed a significant reduction of pain. The last study was on chronic low back pain [46]: the authors refereed to the influence of rPMS-induced proprioceptive afferents on cortical sensorimotor plasticity and used supra-threshold rPMS over the transversus abdominis muscle to improve lumbar spine motor control and reduce pain.

Recommendations. Intensity seems to be a determining factor for rPMS after-effects. The choice depends on the depth of the targeted structure and on the afferents recruited, thus a different rationale is used to influence sensorimotor impairments or to reduce pain. However, the section ''Preferential afferents recruitment'' of this review deals with the capacity of rPMS to strongly activate cutaneous fibers as compared to electrical stimulation and thus questions the potential of sub-threshold intensity in rPMS protocols. The expression of intensity relative to a specific threshold should help standardize the procedures and compare results between studies. Methodological studies are warranted to circumvent or reduce surface EMG recordings contamination by rPMS artifacts and enable motor threshold determination. Importantly, the use of high intensities reduce the magnetic coil's focality [1] thus a compromise between intensity and focality should help selectively recruit a muscle whose spinal and corticospinal excitability have to be influenced without co-activation of surrounding structures.

Sham stimulation

Sham-controlled protocols contribute to evidence especially for demonstrating the effectiveness of a new approach, such as rPMS. A very limited number of rPMS studies used a placebo [7] and this section details the methods they used.

Plastic or air isolation. Nielsen et al. [50] used real rPMS but with a 15-cm plastic tube inserted between the coil and the skin. A recent study rather maintained the coil away from the participant, i.e. without skin contact [30]. These two studies shared the advantage of producing the same clicking noise associated with repeated magnetic stimulation and the former [50] also ensured a same skin contact between rPMS and sham stimulation.

Coil position/orientation and stimulation parameters. Two studies tilted the round coil vertically (i.e. orthogonally relative to muscle or nerve fibers) and either reduced stimulation intensity and frequency [55], or kept the same parameters as for real rPMS [40]. Significant differences were detected between groups treated with rPMS (improvements) and sham (no effects or slight improvements). However, the orthogonal orientation of a round coil relative to fibers can reduce muscle contraction by only 25% [42] and a 45- to 90-degree orientation can even improve stimulation focality with minimal loss of magnetic strength [3,17,44,58], thus mitigating the choice of orthogonal orientation for sham stimulation. Transverse placement of the coil relative to the fibers could be less effective thus preferred for sham (see Figure 3 in Maccabee et al. [42]). The situation is relatively similar for the figure-of-eight coil whose small peripheral peaks produced around the windings are about half the amplitude of the central peak [28]. Two studies used the same position/orientation of coil between rPMS and sham series but reduced intensity in sham [32,46] in order to avoid muscle [46] or spinal root activation [32]. A recent study in stroke to improve ankle motor control [8] also used a very low intensity but with the coil positioned over the metatarsals to ensure that no muscle was beneath the sham stimulation. The tingling sensation produced by magnetic stimulation over the skin presents the advantage of more easily blinding participants but differences in sensory coding between higher (rPMS) and lower magnetic strength (sham) are unknown. Therefore, convenient orientations/parameters of rPMS coil for sham stimulation may combine a transverse and orthogonal tilting with the use of lower intensity away from nerve trunks or muscles (like in [55]).

Inactive intervention. Two studies applied an ultrasound device that was turned off [64,65]. The obvious disadvantage of using turned-off devices is the risk of nocebo effect when the participant is aware that he/she may receive a sham or a real intervention [27]. Therefore, the use of a sham coil where strength and frequency of the clicking noise was similar to rPMS but with no magnetic stimulation or other methods homogenizing sham and rPMS devices is preferred. For example, two coils could be used and hidden from the participants, one inactive positioned over the skin and one active and triggered away from the participants [2,37]. Earplugs could also be used to reduce possibilities for the participant to distinguish between rPMS and sham stimulation [9].

Recommendations. Various techniques are described for sham stimulation and it appears that the obvious sensations elicited by rPMS (i.e. tingling, muscle contractions) challenge the effectiveness of any placebo tested. It is therefore important to recruit participants with no previous experience of magnetic stimulation and who are naïve to what they receive (rPMS or sham). Amongst all techniques reported, the sham coil is preferred, as it shares the same skin contact and noise patterns with real rPMS. However, less expensive alternatives were described with minimal disadvantages and successful blinding of participants.

Preferential afferents recruitment

Understanding how peripheral magnetic stimulation recruits fibers is crucial to better tackle the pros and cons of magnetic stimulation compared to electrical stimulation, as denoted in Table 2, and to point out the potential impact in clinical research and physiopathology when administrated with a repetitive pattern (rPMS). This section on the magnetic stimulation principles of action essentially concerns the preferential recruitment of fibers as compared to electrical stimulation, even if intensities between both methods cannot be directly compared due to a distinct mode of energy transfer (magnetic vs. electrical).

Preferential recruitment over a nerve trunk

Preferential fibers recruitment when varying stimulation intensity differs between magnetic and electrical stimulation of a nerve trunk. Low intensities of electrical stimulation selectively recruit the large-diameter 1a-fibers (giving rise to H-response of the muscle via the mono- or disynaptic reflex loops between 1a-fibers and alpha-motor neurons) whereas higher intensities are required to recruit the motor neuron axons (giving rise to short-latency M-response of the muscle) [25]. Hence, at maximal electrical stimulation that gives rise to M-plateau almost all 1a-fibers are recruited too [25]. The same was not observed for magnetic stimulation, with M-response easily produced at low intensities and H-reflex being recorded at same or greater stimulus strength [41,77] or even not obtained [17]. A difference in pulse conformation and duration could underlie the different order of fiber recruitment between magnetic stimulation (0.05 ms spike) and electrical (longer square-wave, 0.2—1 ms). Indeed, M-response and H-reflex thresholds can be similar if electrical pulse is shortened to a pulse duration similar to magnetic, as already reported by Zhu and Starr [77]. Also, electrical stimulation transfers electrons to the skin and produces superficial ion flows with some ions passing through nearby axons; the resulting density of current is thus limited to the skin and efficacy of recruitment depends more on the depth and impedance of tissues beneath the coil. Conversely, the time-varying magnetic field bypasses skin without any resistance and induces a voltage difference between two virtual points thus resulting in a secondary ion flow in the tissues [31]. Theoretically, magnetic stimulation triggers an electric field in any volume (even in air or free space) but electrical current will flow only in a conductive volume, such as a nerve [5]. This illustrates why motor fibers are magnetically recruited at the same threshold as sensory fibers, which is not the case with electrical stimulation.

Given its negligible attenuation by skin impedance and depth, magnetic stimulation can activate the dorsal spinal roots with tolerable intensities (Table 2). This was confirmed by electroencephalography recordings of somatosensory evoked potentials (SEPs) in sensory areas of brain with latencies shorter for magnetic than for electrical stimulation [73,74], thus reflecting the recruitment of large-diameter proprioceptive afferents. The authors suggested that magnetic stimulation could directly activate roots whereas electrical stimulation, at tolerable intensities in their protocol, most likely depolarized the cutaneous branch of the dorsal primary ramus of spinal nerves [73,74].

Preferential recruitment over a muscle

Magnetic stimulation over a muscle belly can trigger muscle contractions at relatively low intensities with minimal cutaneous sensations. Conversely, with electrical stimulation, muscle contraction threshold can be higher than depolarization threshold of cutaneous and nociceptive receptors. In line, SEPs evoked in brain by electrical stimulation of the vastus lateralis muscle, even at high intensity, could be completely suppressed by a procaine nerve block of the lateral femoral cutaneous nerve whereas the same injection during magnetic stimulation had no effect on the early SEPs components and only modified the late components [77]. Furthermore, compared to electrical stimulation of digital nerves (using ring electrodes), magnetic stimulation over the finger pads (with no underlying motor fibers) failed to produce synchronized SEPs, even at high intensity [38]. These studies strongly suggested that magnetic stimulation, in contrast to electrical stimulation, could not depolarize the thin superficial cutaneous nerves. Therefore, SEPs induced by rPMS over a muscle may be less contaminated by cutaneous inflows [77] and depend more on muscular proprioceptive afferents [68]. However, it remains unclear whether magnetic stimulation over a muscle produces SEP via the direct activation of 1a-afferents from the spindles, or indirectly via muscle contraction and joint movement that stretch spindles or excite Golgi organs. For example, SEP latencies were compared in 14 healthy individuals between magnetic stimulation of gastrocnemius muscle and electrical stimulation of the posterior tibial nerve at the ankle and it was shown that SEPs were of similar sequential components (P40, N50, P60, N70, and P100) but peaked 0.2 to 8.9 ms earlier for electrical stimulation, even if the stimulation was elicited more distally [77]. The authors thus suggested that SEPs, induced by magnetic stimulation over the muscle belly, did not result from a direct recruitment of sensory fibers (such as 1a-afferents). These longer latencies of SEPs elicited by magnetic stimulation could alternatively be explained by the indirect recruitment of 1a-afferents from the contracting muscle, from its joint antagonist stretched by the induced movement or from the activation of 1b-afferents subsequent to fiber shortening in the contracting muscle. Kunesh et al. [38] conversely found that SEPs latencies of electrical and magnetic stimulation at the wrist were similar, thus suggesting that proprioceptive fibers were directly activated by both types of stimulations. These authors however nuanced that indirect activation of proprioceptive afferents was more likely to occur for the coil over a muscle belly far from nerve trunks, which was the case for gastrocnemius's experiment of Zhu and Starr [77] but not for wrist joint [38]. A few years later, Zhu et al. [78] replicated their earlier study on muscle paralysis but instead of local drug injection in muscle, they used intravenous administration of succinylcholine (curare) in three patients undergoing general anaesthesia for cancer surgery. They showed that SEPs, evoked by magnetic stimulation over the gastrocnemius and with electrical stimulation over the tibial nerve, were still present during paralysis. They eliminated the hypothesis of an indirect activation of muscle spindles with contractions, and rather proposed that 1a-afferents terminals can be directly activated in the muscle. However, the use of a large round coil (12-cm diameter) compared to earlier study (pointed coil of 4.1-cm diameter [77]) cannot exclude a possible recruitment of the tibial nerve near the popliteal fossae. Also, the small sample size and the specific context of the experiment (general anaesthesia, total muscle paralysis) limit the strength of this demonstration.

Recommendations for rPMS application based on preferential recruitment of afferents

The previous sections described the basic differences between magnetic and electrical stimulation owing to their preferential recruitment of afferents over nerves and muscles. Although evidence remains controversial, it is clear that the main difference between each technique is cutaneous inflow (including afferents to lemniscal and spino-thalamic pathways), being more easily and strongly recruited with electrical stimulation. The relative inability of rPMS to recruit skin afferents may share advantages and disadvantages when applied in physiopathology. For example, if the aim is to reduce pain with intensities below muscle contraction threshold in order to target the analgesic gating system [47], electrical stimulation would be a better choice [59]. However, rPMS should be preferred if the objective is rather to generate proprioceptive inflow (directly via 1a-afferents recruitment or indirectly via muscle contraction and joint movement) or to target deeper conductive structures such as spinal roots or profound muscles [7,68,73,74]. Also, when the aim is to favour brain plasticity and motor recovery via the repetitive production of muscle contractions/joint movements, then the use of electrical stimulation may be limited in the presence of painful disorders, such as post-stroke spasticity or incomplete spinal cord injury [70,71]. Indeed, painless magnetic stimulation enables the production of greater joint movements when compared to electrical stimulation [21,26,36,69].

Conclusions

This work overviewed current knowledge on use of rPMS in various pathological disorders. Literature remains very scant and no consensus yet proposes guidelines on the best parameters of rPMS application. Future rPMS studies should however rely on experimental data, rationale and hypotheses reported in the review and in relation to health problem (e.g., reducing pain with sub-threshold intensity and low frequency, improving sensorimotor disorder with supra-threshold intensity and intermittent protocols, increasing muscle strength with continuous high frequency) or in relation to the basic after-effects targeted (depth and focality of the stimulation depending on coil design, orientation, current direction). Future studies should propose more structured designs in larger samples and with the contribution of different imaging technologies to investigate whether magnetic stimulation actually generates pure proprioceptive flows (no cutaneous recruitment) and if such specificity has a real advantage to favor sensorimotor plasticity. This question is of basic clinical importance to recommend the use of magnetic stimulation in pain conditions and sensorimotor impairments for the control of musculoskeletal function.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

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