

Repetitive Peripheral Magnetic Stimulation (rpMS) in Combination with Muscle Stretch Decreased the Wrist and Finger Flexor Muscle Spasticity in Chronic Patients after CNS Lesion

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Abstract

Objective: The study assessed the effect of a single session of repetitive peripheral magnetic stimulation (rpMS) combined with manual stretch on wrist and finger flexor muscle spasticity.

Methods: Forty chronic patients after CNS lesion with a severe wrist and finger flexor spasticity with a Modified Ashworth Score (MAS, 0-5) of either 2, 3 or 4 participated and formed two groups. A single session of rpMS (A) or sham (B) (5 Hz, Intensity 60% or 0%, 3s trains, 750 stimuli delivered within five minutes) was applied in an A-B (group I) or B-A (group II) design. A 30 min baseline (90 min follow-up) preceded (followed) A or B. During the intervention, the wrist and metatarsophalangeal (MCP) joints were stretched manually. Primary variable was the wrist and finger flexor spasticity, assessed with the help of the Modified Ashworth Score (MAS, 0-5), by a rater blinded to treatment allocation. A- and B-data were pooled irrespective of group assignment.

Results: At study onset, both groups were homogeneous. Following rpMS but not sham, the wrist and finger MAS significantly decreased over time. Accordingly, the MAS of the rpMS group was significantly less at t+5 min (wrist $p=0.002$, MCP joints $p<0.001$) and at t+90 min (MCP joints $p=0.002$). No side effects occurred.

Conclusion: A single session of rpMS but not sham in combination with manual stretch significantly reduced the wrist and finger flexor muscle spasticity in chronically CNS-lesioned patients. Long-term studies including an rpMS group only should follow.

Keywords: CNS lesion; Muscle spasticity; Repetitive peripheral Magnetic stimulation; Spasticity; Stroke

Introduction

The treatment of wrist and finger flexor muscle spasticity after CNS lesion is a major issue in upper limb neurological rehabilitation. Spasticity is defined as a velocity-dependent increased muscle tone and resistance to stretch. It results on one hand from neurogenic spasticity and on the other hand from immobility-related changes of the mechanical muscle properties including sarcopenia and contracture [1,2]. It is rapidly evolving within a time period of 12 weeks after CNS lesion. A severe wrist muscle extensor paresis and immobility are additional predictors [3]. Three months after stroke for instance, 25% of the surviving stroke patients present an upper limb flexor muscle spasticity impeding the activities of daily living and the restoration of arm function [4].

Conventional treatment of wrist flexor muscle spasticity after CNS lesion includes passive mobilization, physical therapy, oral antispastic medication, Botulinum toxin injections (BTX), serial casting and surgery. Among them, only BTX has been proven to be effective to reduce wrist flexor muscle spasticity in controlled trials and meta-analysis [5,6]. The neurolytic agent BTX, however, has a limited effectiveness in severely affected chronic patients where the

immobility-related changes of the mechanical muscle properties are prevailing. Furthermore, the BTX-treatment is expensive and needs to be repeated every three to four months.

The non-invasive repetitive peripheral magnetic stimulation (rpMS) of nerves, muscles or spinal roots may be an alternative. It has been successfully applied in neurologically impaired adults and CP children to reduce muscle spasticity, to improve range of motion, motor function and perceptual cognitive tasks [7-12]. Struppler et al. reported positive effects of rpMS on upper limb spasticity, range of motion and motor recovery in chronic stroke subjects [7-9]. Flamand et al applied multiple sessions of rpMS of the tibial and common peroneal nerve in CP children, which affected in a sustained reduction of lower limb spasticity and improved motor control and gait at the same time [10-12].

The present work intended to study the effect of single, low-frequency rpMS vs. sham stimulation of the wrist and finger flexors in combination with a continuous manual muscle stretch in chronic patients after stroke or traumatic brain injury (TBI).

Methods

Patients were allocated to two groups, they either followed an A-B or a B-A design (A: rpMS, and B: sham). The stimulation frequency was 5 Hz; 750 stimuli per target muscle group were applied in trains of

3 seconds within a time period of five minutes. The chosen frequency and intensity were rather low when compared to other protocols, but helped to prevent an overheating of the coils [11,12]. The low-intensity rpMS could have been less effective regarding muscle tone regulation; therefore the authors combined the stimulation with a continuous manual muscle stretch, a method commonly applied by therapists to reduce muscle tone [13].

Subjects

All participating patients fulfilled the following inclusion criteria:

- Patients with a single history of CNS lesion due to stroke or traumatic brain injury
- Lesion interval >12 months
- Increased muscle tone, i.e. 1, 2, 3 or 4 in the Modified Ashworth Score (0-5) in the affected wrist or finger joints (14)
- No volitional distal motor function of the affected arm, except for mass flexion
- No metal implants or /and open wounds in the stimulation area
- No deep vein thrombosis
- No relevant edema
- No pacemaker
- No preceding Botulinum toxin injection within the last six months
- Signed written informed consent (approved by the local ethic committee)

Please note that most of the patients (n=17 in each group) received a Botulinum toxin A injection six months or longer ago, with a dosage and muscle selection according to national guidelines. All patients reported a non-relevant muscle tone reduction after the injection.

The patients were randomly allocated either to group I (n=20) or group II (n=20) with the help of a computer-generated lot (www.randomizer.at). The experimental design was a randomized-controlled study with two blocks, A and B. Block A signified rpMS and block B sham stimulation. The order was A-B in group I-, and B-A in group II-patients (Figure 1). Each block (A and B) lasted 120 min, it included a 30 min baseline, 5 min of rpMS of the forearm flexor muscles in combination with a continuous stretch of the forearm flexor muscles, and a subsequent 85 min observation period. A 24-hours wash-out phase separated each block (Figure 2). A Magstim rapid2 device with a round coil (diameter 8 inches) provided rpMS. An optically similar sham coil provided the sham stimulation, meaning that the typical clicking sound was delivered but without releasing any energy. The therapists, applying the stimulation and muscle stretch, were not aware, whether the used coil was the one intended for rpMS or sham. Prior to therapy onset, the subinvestigator of the study either attached the rpMS or sham coil according to the group assignment.

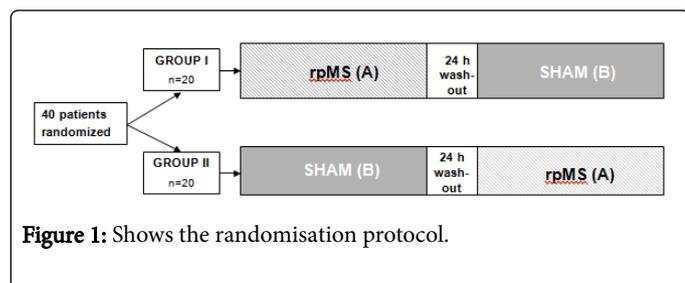


Figure 1: Shows the randomisation protocol.

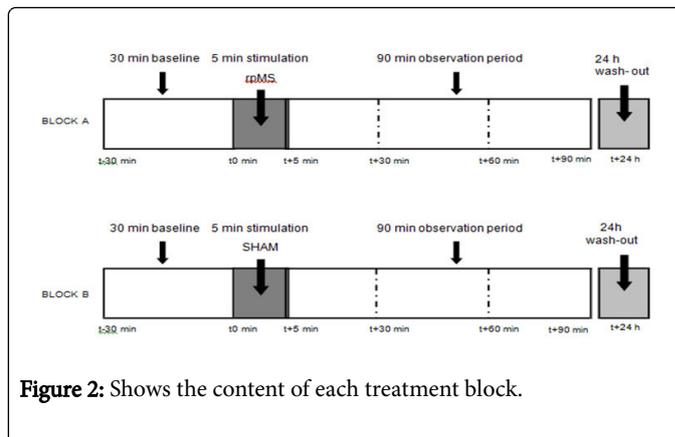


Figure 2: Shows the content of each treatment block.

Intervention

The patient was positioned on a height-adjustable chair that stood next to a mat table. The forearm was positioned on the table with the elbow 120° to 150° flexed and supinated without eliciting pain. A supportive pillow helped the patient to hold his arm in position. Before rpMS onset, one therapist applied a firm and continuous stretch on the wrist and finger flexor muscles. This supramaximal stretch was kept throughout the rpMS (sham) application; it means that the strength first exceeded the pain level and was then gradually released to a level tolerable by the patient. The therapists were instructed to exert a comparable force throughout the intervention.

For the stimulation (rpMS or sham), another therapist placed the coil on the forearm and moved it in parallel to the skin covering the forearm flexor muscles from the proximal to the distal insertion point and return. The coil was placed on the skin and no pressure was ensured (Figure 3). The stimulation setting revealed the following parameters: Frequency 5 Hz, and train duration 3 seconds; accordingly 15 stimuli per train was applied. Rest between trains was also set to 3 seconds. In total, 750 stimuli per block were applied, either A (rpMS) or B (sham).

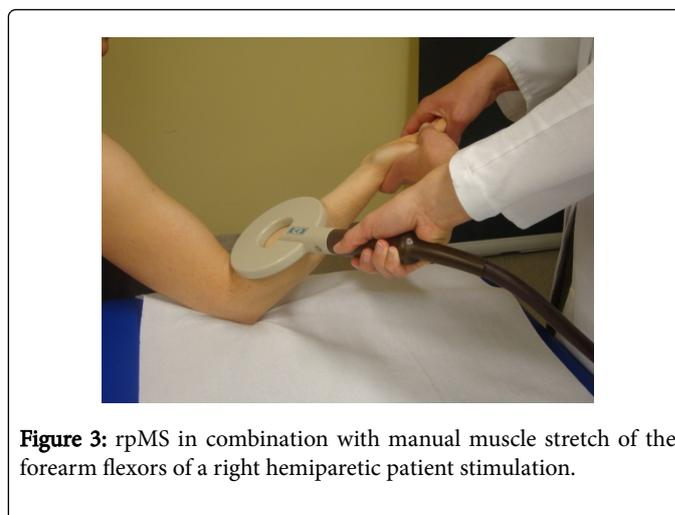


Figure 3: rpMS in combination with manual muscle stretch of the forearm flexors of a right hemiparetic patient stimulation.

After rpMS, the arm was put back on the mat table with a pronated forearm (the elbow was flexed 90° to 100°). The patient was instructed to keep the arm in the most relaxed position until the next measurement.

Assessment

The primary outcome measure was the muscle tone of the wrist (Mm. flexor carpi radialis et ulnaris) and finger flexor muscles (MM. flexor digitorum superficialis, profundus et lumbricales). The muscle tone was assessed using the Modified Ashworth Score (MAS, 0-5, 0=no increase in muscle tone, 5=affected part(s) rigid in flexion or extension) [14]. For the assessment of the muscle tone, the physiotherapist stabilized the forearm just proximal to the wrist joint and the other hand grasped the patient's hand. The wrist was moved from maximum possible flexion to maximum possible extension. The same technique was applied for the MCP; here the physiotherapist stabilized the wrist with the forearm in neutral position and with her thumb in the palm of the hand, the other hand of the therapist grasped the MCP II-V between the middle and distal phalanx [15].

Secondary outcome measures were the passive extension deficit to neutral of the wrist and metacarpophalangeal II-V joints (MCP), assessed with the help of a goniometer. For the MCP, the goniometer was laid alongside the ulnar edge of the hand from the Os pisiforme to the distal phalanx of finger V. The measurement of the extension deficit followed the tonus assessment in such a way that the last rapid extension was kept and then measured. For the MCP measurement the wrist was kept manually to its maximum extension. The ability (yes or no) to volitionally extend the wrist (metacarpophalangeal) joints for at least 10 degrees without gravity was another secondary outcome measure. The extension deficits of the wrist and MCP II-V joints to

neutral were calculated relatively to the maximum anatomical joint flexion, which allowed a comparison irrespective of the anatomical conditions. The wrist joint was assumed to reach a maximum flexion of 80°, accordingly an extension deficit of 20° to neutral was converted into an extension deficit of 25%. For the MCP joints a maximum flexion of 90° was taken.

Measurement points were t-30 min, t0 min, t+5 min, t+30 min, t+60 min, t+90 min and t 24 h in every block. A rater, blinded to treatment allocation, assessed the patients. The rater was kept constant throughout the study.

Statistics

For the primary variable, the MAS, a Wilcoxon test confirmed initial homogeneity of the groups at study onset, and helped to detect any improvement in the time periods t0 to t+5 min and t0 to t+90 min for each group. In a second step, the non-parametric Mann-Whitney test for unpaired samples helped to detect any between group differences at t+5 min and t+90 min. The global alpha was set for this purpose at alpha=0.025 (Bonferroni measurement due to two end points). The secondary parameters were used descriptively only.

Results

Forty patients with a single history of CNS lesion participated in the study. Table 1 shows the clinical data of the participants.

Parameter	GROUP I A-B (rpMS-sham stim)	GROUP II B-A (sham-rpMS stim)
n	20	20
Diagnosis	12=ischemic stroke 8=traumatic brain injury	13=ischemic stroke 7=traumatic brain injury
Paresis	15=hemiparesis 5=tetraparesis	15=hemiparesis 5=tetraparesis
Lesion interval [months]	22.7 (± 8.8)	23.8 (± 6.4)
Age [years]	47.9 (± 8.5)	55.4 (± 8.6)
Sex	9= ♀ ; 11= ♂	7= ♀ ; 13= ♂
Barthel Index [0-100]	54.1 (± 11.4)	54.2 (± 10.6)

Table 1: Shows the clinical data of all patients according to their group assignment.

Side effects did not occur. The two groups were homogeneous at study onset regarding clinical parameters and the primary and secondary variables.

The MAS of the wrist and MCP did not change to a relevant extent during the baseline (time period t-30 to t0) in both groups (Figures 4 and 5). In the time interval t0 to t+5 min, the MAS of the wrist and MCP joints significantly decreased over time following rpMS (p=0.001 for both joints). In the time interval t0 to t+90 min, only the MAS of the MCP joint remained significantly decreased following rpMS (p=0.003). Following sham no significant changes were detected over time. At t+24 hours the effects had waned. Consequently, the between group comparison revealed significantly less muscle tone following rpMS as compared to sham at t+5 min for the wrist (p=0.003) and for the MCP joints(p<0.001). At t+90 min only the MAS of the MCP

joints was still significantly decreased in the rpMS group (p=0.002) as compared to sham.

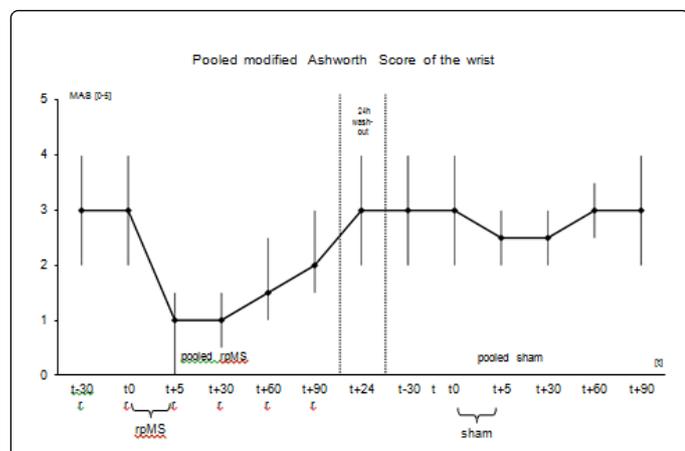


Figure 4: Median (IQR) of the Modified Ashworth Score (MAS, 0-5) of the wrist flexor muscles before and after rpMS or sham in combination with manual muscle stretch, applied within the time interval t0 min to t+5 min. rpMS and sham data were pooled.

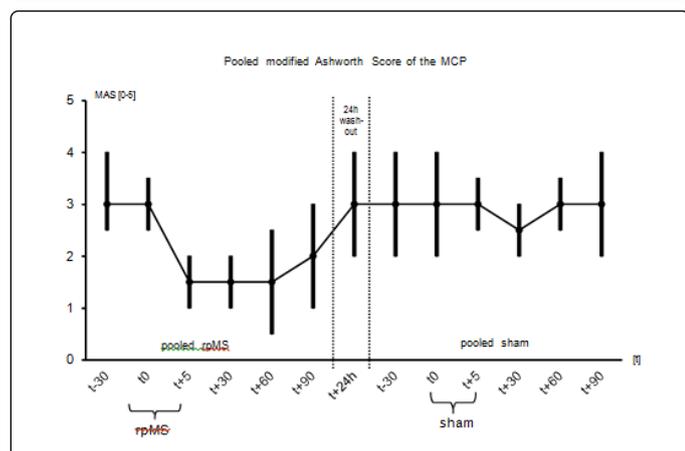


Figure 5: Median (IQR) of the Modified Ashworth Score (MAS, 0-5) of the finger flexor muscles before and after rpMS or sham in combination with manual muscle stretch, applied within the time interval t0 min to t+5 min. rpMS and sham data were pooled.

The mean relative extension deficit of the wrist and MCP joints to neutral showed a similar behavior, i.e. no change during baseline and a larger decrease of the relative extension deficit following rpMS as compared to sham (Figure 6 and Table 2).

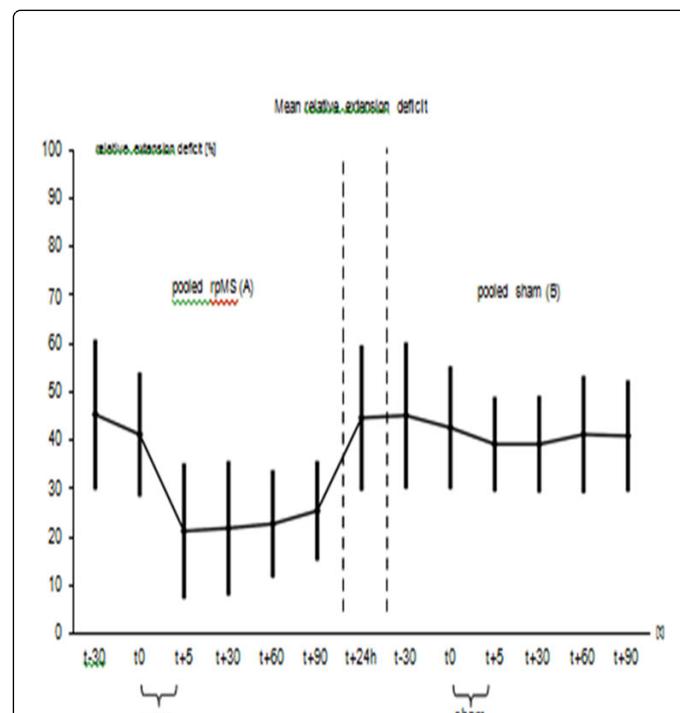


Figure 6: Mean (SD) extension deficit (%) of the wrist joints during before and after rpMS or sham in combination with manual muscle stretch, applied within the time interval t0 min to t+5 min. rpMS and sham data were pooled.

Group	Mean value (± SD) of the differences for each group	95% Confidence interval of the difference		p-value for the difference between groups
		upper	lower	
rpMS t+5 min-t0 min sham	19.9 ± 9.8 3.5 ± 4.7	14.0 0.6	25.8 6.3	P=0.001
rpMS t+90 min-t0 min sham	15.7 ± 9.4 1.7 ± 3.7	10.0 0.5	21.4 3.8	P=0.006

Table 2: shows the 95% confidence interval of the differences of the MCP joints between t+5 min – t0 min and t+90 min-t0 min for each group (rpMS and sham), as well as the level of significance for the group differences.

None of the patients of both groups was able to volitionally extend his wrist or metacarpophalangeal joints before and after any kind of intervention.

Discussion

A single session of rpMS but not sham of the wrist and finger flexors in combination with a continuous muscle stretch significantly decreased the wrist and finger flexor muscle spasticity and improved the passive range of motion of the wrist and MCP joints in chronic patients after stroke and TBI. The positive effect lasted up to 90 minutes. Unwanted side effects did not occur. The motor control remained unchanged in both groups.

All patients were in the chronic stage, i.e. spasticity in the sense of an altered muscle activity level and immobility-related muscle contractures with sarcopenia both contributed to the clinical picture of inherent and reflex mediated forearm flexor muscle stiffness and limited range of joint mobility [1,2]. Less tendon and joint capsule elasticity were probably also contributing to the clinical picture.

The patients had not profited to a larger extent from conventional treatment including passive mobilization, oral antispastic medication, and the i.m. injection of Botulinum toxin. Although the toxin proved effective both in chronic upper and lower limb spasticity [5,6]. The forearm flexor muscles of the chronic patients studied were probably too inherently spastic to respond to the toxin and its neurolytic effect. Surgeries, e.g., muscle and tendon lengthening, had not been regarded as a therapeutic option by most of the patients due to their invasive and irreversible nature.

The positive effects of a single session of rpMS on muscle spasticity and range of motion were in correspondence to preceding reports in chronic stroke patients and CP children [7-12]. Compared to other protocols, the chosen frequency and intensity were rather low, Struppler et al., for instance had applied 2000 stimuli per target muscle group with a frequency of 20 Hz [7-9]. The chosen lower frequency and intensity helped to prevent an overheating of the coil. On the other hand, a less antispastic effect of low-intensity rpMS, applied in the present study, could not be ruled out [11,12]. The authors therefore combined rpMS with a continuous muscle stretch, a method commonly applied by therapists [13].

Irrespective of the stimulation protocol, the degree of spasticity at baseline seems to be a major predictor of the response to the rpMS intervention. Struppler et al., had studied chronic stroke patients with spasticity values by means of the Modified Ashworth Scale between 3 and 5, corresponding to the values of the present study [7-9]. In less spastic patients with initial modified Ashworth scores of 1 or 2 Krewer et al., following the protocol of Struppler et al., did not find a relevant effect on muscle tone in stroke patients following two weeks of 20 min rpMS twice daily [16]. Flamand et al., performed a bilateral theta-burst stimulation of the tibial and common peroneal nerves with 900 pulses per minute in children with CP and mild to moderate plantarflexor muscle spasticity. They also described a stronger effect of the stimulation on muscle tone and ankle range of motion on the more affected side [10].

To explain the positive effect of rpMS in patients with a severe muscle spasticity, both Struppler et al., and Flamand et al., discussed an induction of a proprioceptive inflow, primarily acting on the cortical level. A long term stimulation may even induce plasticity changes in the CNS [7-12], as improvements on muscle tone and motor control in

chronic hemiparetic subjects were associated with a significant increase of neural activation within the superior posterior parietal lobe and the pre-motor cortex areas [9]. Increased cortical motor evoked potentials following rpMS in healthy subjects also hinted at a facilitatory effect [17]. The continuous manual muscle stretch itself could not explain the results on muscle spasticity, as the muscle tone did not change following sham in combination with continuous muscle stretch. Although commonly applied in daily routine, it seems not to be a very effective method. Vattanasilp et al., for instance, had studied the contribution of thixotropy, the primary target of muscle stretch, to ankle spasticity after stroke. They did not find that it was a major contributor to long term muscle spasticity [18].

Electrotherapy, vibration and shock wave therapy are potential alternatives among the physical rehabilitation methods. Electrical stimulation of agonist and antagonistic muscles in an alternate fashion could reduce spasticity but had the disadvantage of potentially eliciting pain which in turn triggered spasticity [19]. By comparison rpMS are almost painless. For muscle vibration and shock wave therapy, recent studies have reported a positive effect on muscle tone in various patient groups, the future may see comparative studies [20,21].

Major limitation of the study was the lack of a third group receiving rpMS only. It would have allowed distinguishing between effects due to rpMS and effects due to the combination of rpMS and stretch. Further limitations were the assessment of a single r-PMS application only, the results do not warrant any statement on its long term effect. One may speculate whether the MAS were the right tool to assess the muscle tone. The papers of Ansari and Naghdi questioned its reliability and validity. They suggest assessing the muscle tone with the help of the modified modified Ashworth Scale [22,23]. Also, the manual force exerted during muscle stretch was not standardized so that it could have varied between subjects and during single interventions.

In summary, a single session of verum r-PMS in combination with manual muscle stretch effected in a significantly larger decrease of the wrist and finger muscle spasticity in chronic patients as compared to sham in combination with manual muscle stretch. Long-term studies should follow.

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Conflict of Interest

None

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