Effects of Repetitive Peripheral Magnetic Stimulation on Upper Extremity Function after Stroke: A Systematic Review and Meta-analysis

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Abstract

1) *Introduction:* There are many neurorehabilitation interventions added to routine rehabilitation to promote recovery in post-stroke patients. Repetitive peripheral magnetic stimulation (rPMS) is a painless intervention that has been increasingly used in recent decades. 2) *Objective:* The objective of this study is to evaluate the effects of rPMS on upper extremity functions after stroke. 3) *Methodology:* Literature search was carried out in PubMed, Scopus, the Physiotherapy Evidence Database (Pedro), and the Cochrane Central Register of Controlled Clinical Trials databases from their beginning to July 2022. Randomized controlled trials in which stroke patients received rPMS plus conventional rehabilitation compared to conventional rehabilitation with or without sham rPMS were identified and included. The outcomes of interest were upper extremity function measured by the Fugl-Meyer Assessment (FMA), activities of daily living (ADL) and spasticity. Mean differences (MD) were pooled with a fixed-effect model. 4) *Results and Discussion:* FMA was higher in the rPMS group compared to controls (MD 5.48, 95% confidence interval [CI] 3.89, 7.06; $I^2 = 0\%$). Amongst acute to subacute stroke patients in particular, FMA was also higher in the rPMS group (MD 5.53, 95% CI 3.91, 7.15; $I^2 = 0\%$). There were insufficient data to pool on the ADL and spasticity outcomes. 5) *Conclusion:* The results of this systematic review and meta-analysis support the advantage of rPMS in improving upper extremity functions in post-stroke patients. However, there is not enough information to conclude the effects of rPMS on ADL and spasticity in post-stroke patients.

Keywords**:** *Stroke, Repetitive Peripheral Magnetic Stimulation, Upper Extremity Function, Rehabilitation*

1. Introduction

Modern neurorehabilitation therapies, including electrical stimulation (ES), transcranial magnetic stimulation (TMS), and repetitive peripheral magnetic stimulation (rPMS), are used to supplement standard rehabilitation and support neuroplasticity and recovery in post-stroke patients. While the ES could have some negative effects like skin irritation and burn (Nussbaum et al., 2017), TMS may have several unintended consequences, including headache, discomfort (Dobek, Blumberger, Downar, Daskalakis, & Vila-Rodriguez, 2012; Graef, Dadalt, Rodrigués, Stein, & Pagnussat, 2016), and unintentional seizures (frequency < 0.1%) (Dobek et al., 2012).

rPMS has become more popular recently due to its lack of the negative consequences of ES and TMS (Kanjanapanang & Chang, 2022). rPMS is a non-invasive, painless approach that offers convenience and requires no mechanical touch (Asao, Nomura, & Shibuya, 2022; Beaulieu & Schneider, 2013; Beaulieu & Schneider, 2015).

The first systematic review and meta-analysis (Momosaki, Yamada, Ota, & Abo, 2017) as well as its revised version published in 2019 (Sakai, Yasufuku, Kamo, Ota, & Momosaki, 2019), concluded that the evidence from the available studies was insufficient to draw any conclusions on the routine use of rPMS for stroke survivors. However, current research from 2019 to 2022 indicates that rPMS can enhance upper extremity function (X. Chen et al., 2020; Jiang et al., 2022; Ke et al., 2022; Obayashi & Takahashi, 2020). Therefore, a meta-analysis was carried out to assess the effects of rPMS on upper extremity functions after stroke.

2. Objectives

1) To evaluate the effects of rPMS on upper extremity functions after stroke
2) To evaluate the effects of rPMS on activities of daily living (ADL) and spasticity after stroke

3. Materials and Methods

Search strategy

Relevant studies were identified from electronic databases including MEDLINE via PubMed, Scopus, the Physiotherapy Evidence Database (PEDro), and the Cochrane Central Register of Controlled Clinical Trials from their inception to July 2022. Search terms were constructed based on the patient and intervention domains as follows: "stroke," "hemiparesis," "hemiplegia," "cerebrovascular accident," "repetitive peripheral magnetic stimulation," and "peripheral repetitive magnetic stimulation."

Selection of studies

This research included randomized control trials (RCTs) of adult stroke patients that had rPMS intervention at the upper extremity in addition to conventional rehabilitation compared with sham rPMS, or conventional rehabilitation with or without sham rPMS, and the outcomes were upper extremity functions, ADL, and spasticity. Because of the limited number of studies, mixed participant groups that included stroke patients and patients with other diseases were included if at least one half of them were stroke patients.

The exclusion criteria included studies with insufficient data for pooling after three attempts of contacting authors every two weeks, and studies published in languages that reviewers could not translate.

Interventions

The intervention of interest was rPMS. rPMS was the use of magnetic stimulation on the paretic upper limb of any regimen. The intensity of rPMS was the one that produced minimal muscle contraction. The control intervention was any type of conventional rehabilitation, for example physical therapy or occupational therapy, with or without sham rPMS.

Outcomes of interest

The outcomes of interest were upper extremity functions, ADL, and spasticity. Upper extremity functions were measured by the Fugl-Meyer Assessment (FMA) (Fugl-Mayer et al., 1975). The possible range of FMA is 0 to 66 points. A higher score means better performance in the upper extremity. ADL was measured by Barthel Index (BI) (Mahoney & Barthel, 1965), of which the possible range is from 0 to 100. A higher score corresponds to more independence in doing ADL. Spasticity was measured by the Modified Ashworth scale (MAS) (Bohannon & Smith, 1987) or the Modified Tardieu scale (MTS) (Boyd & Graham, 1999). Both scales show higher spasticity with a higher score.

Data extraction

The data extraction process was performed independently by two reviewers (AK and MS) using a standardized data extraction form. The data extraction form comprised six major parts: general information, characteristics of study, participants, interventions, outcomes, and results for pooling.

Risk of bias assessment

Risk of bias (RoB) was assessed independently by two reviewers (AK and MS) following the Cochrane Risk of Bias Tool for Randomized Trials (RoB 2.0) (Sterne et al., 2019). The following five domains were assessed: the randomization process, deviations from the intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. Each domain was rated as "low risk," "some concerns," and "high risk" RoB. If at least one of these domains was rated as high risk, the study was considered to have high RoB; if all domains were rated as low risk, the study had low RoB; otherwise, the study had some concerns on the RoB. Any disagreement was discussed to reach a consensus between the reviewers.

Statistical analysis

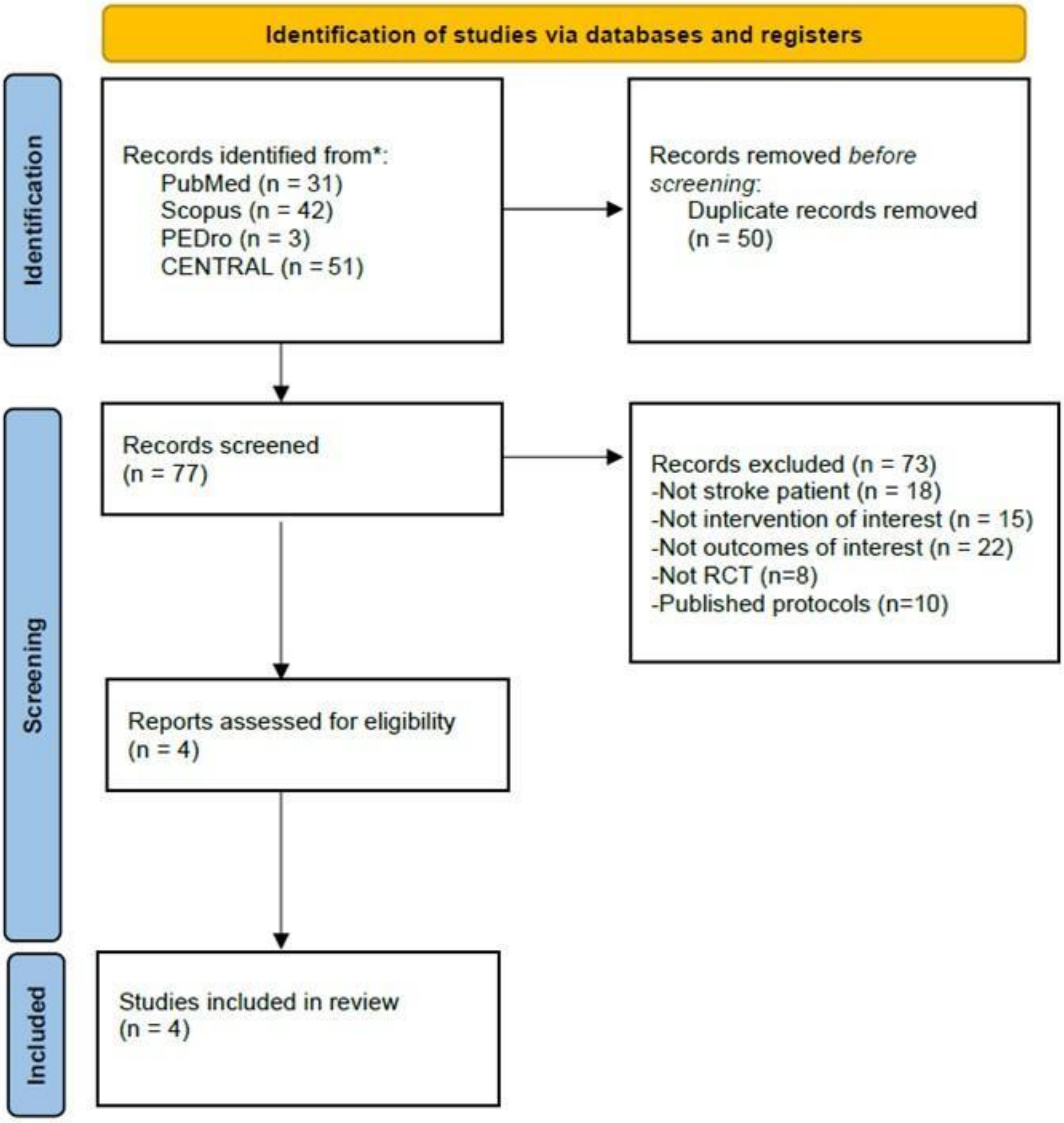
Stata software version 17.0 (StataCorp. 2022. Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC) was used for the meta-analysis. Mean differences (MD) and their 95% confidence intervals (CI) were used to assess the outcomes. Meta-analysis was conducted when three or more trials reported the same outcome. Heterogeneity was assessed by Cochrane's Q test and I^2. A fixed-effect model by the inverse variance method was used because the result showed no heterogeneity (p-value of Cochrane's Q test > 0.1 and $I^2 < 25\%$). Subgroup analysis was performed according to the duration of stroke (acute-subacute and chronic stroke).

4. Results and Discussion

4.1 Results

A total of four RCTs (El Nahas et al., 2022; Jiang et al., 2022; Ke et al., 2022; Krewer, Hartl, Müller, & Koenig, 2014) were eligible for the meta-analysis. The selection process was shown in Figure 1 and the characteristics of the studies were shown in Table 1.

The four studies included 174 patients and were published between 2014 and 2022. The patients' mean age ranged from 45.96 to 57 years. The mean duration of disease ranged from 0.46 to 46.35 months. Two studies were done in acute to subacute stroke patients (less than three months from stroke onset) (Jiang et al., 2022; Ke et al., 2022), and two studies were done in chronic stroke patients (more than three months from stroke onset) (El Nahas et al., 2022; Krewer et al., 2014). Percentage of male patients ranged from 53.85 to 75%. The mean FMA score ranged from 2.82 to 12.35.



PEDro, the Physiotherapy Evidence Database; CENTRAL, the Cochrane Central Register of Controlled Clinical Trial; RCT, randomized controlled trial

Figure 1 PRISMA Flow diagram

In terms of the details of rPMS intervention that was applied to the hemiplegic upper extremity, three studies used figure-of-eight coil (El et at., 2022; Ke et at., 2022; Krewer et al., 2014), and one study used circular coil (Jiang et al., 2022). Total pulses of rPMS ranged from 600 to 5,000 pulses per session. The frequency ranged from 20 to 50 Hz. Two studies reported the intensity of rPMS as a percentage of maximum output, which ranged from 15 to 60 % of maximum output (Jiang et al., 2022; Ke et al., 2022), one study used an intensity of 110% of motor threshold (Krewer et al., 2014); and the other study (El Nahas et al., 2022) used an intensity supramotor threshold as shown in Table 1.

According to the five domains of the RoB 2.0, one study showed low risk of bias (Krewer et al., 2014), and three studies showed some concern about the risk of bias (El Nahas et al., 2022; Jiang et al., 2022; Ke et al., 2022), as shown in Figure 2.

Table 1 Characteristics and details of intervention of the included studies

Study	Age (year)	Duration of disease (months)	Intervention, type of coil	Control	Duration of intervention (days)	Intensity	Pulses	Frequency (HZ)	On/off time (sec)	Number of sessions
Ke, 2022	57	0.54	rPMS, figure-of-eight	Sham rPMS, pt, usual care	10	40-60% of maximum output	1,800	20	1/19	10
Jiang, 2022	55.29	0.46	rPMS, circular	pt	14	15-30% of maximum output	2,400	20	0.5/2	14
Krewer, 2014	54.49	7.15	rPMS, figure-of-eight	Sham rPMS, pt, ot	10	110 % motor threshold	5,000	25	1/2	20
El Nahas, 2022	45.96	46.35	piTBS, figure-of-eight	Sham	8	Supra motor threshold	600	50	-	8

rPMS, repetitive peripheral magnetic stimulation; piTBS, peripheral intermittent theta burst stimulation; pt, physical therapy; ot occupational therapy

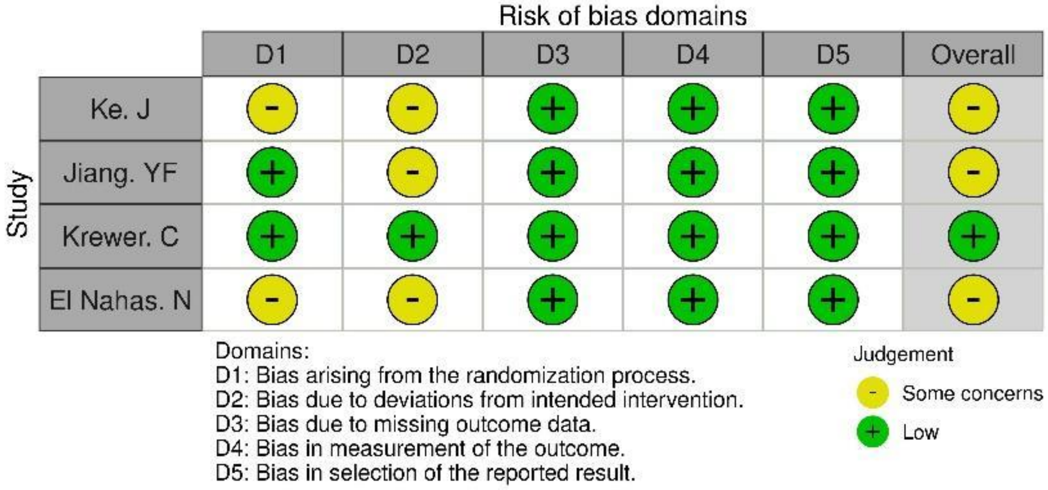


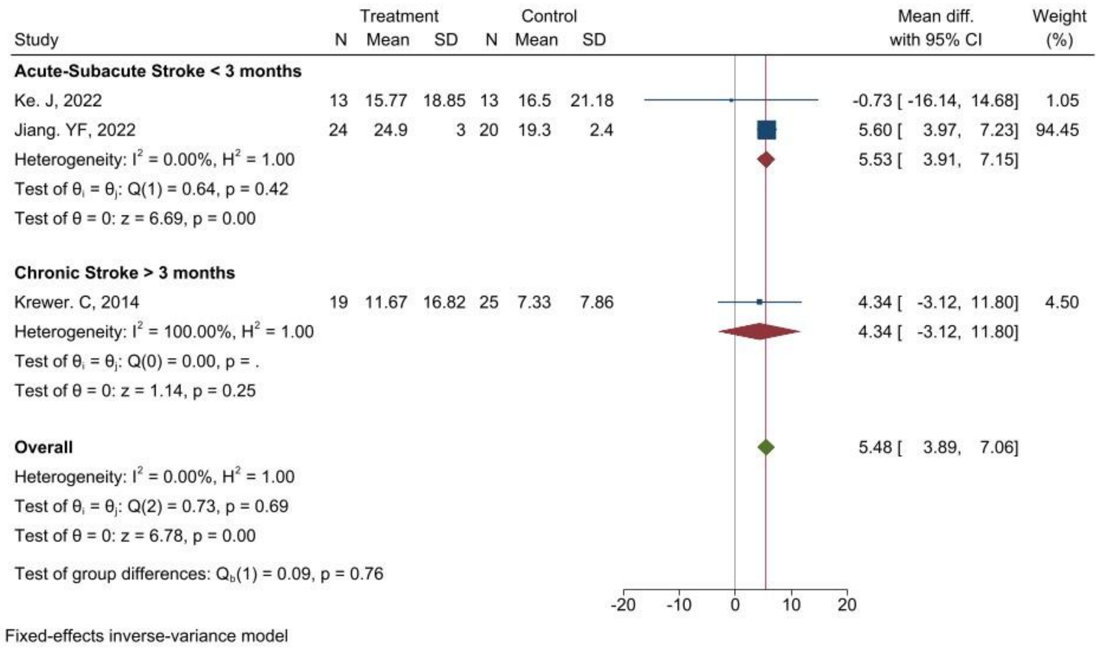
Figure 2 Risk of bias assessment

Upper extremity function

Three studies (Jiang et al., 2022; Ke et al., 2022; Krewer et al., 2014) used the FMA to evaluate upper extremity function. Results of the meta-analysis of these studies are shown in Figure 3. Data pooling using a fixed-effect model found that the rPMS group had higher upper extremity function than the conventional rehabilitation group, with a pooled MD (95% CI) of 5.48 (3.89, 7.06), with no evidence of heterogeneity (I^2 = 0%, Q-test chi^2 = 0.73, df = 2, p-value = 0.693). Subgroup analysis by the duration of stroke (acute–subacute, and chronic stroke) was also done, as shown in Figure 3. In acute–subacute stroke, the rPMS group had a higher FMA with a pooled MD (95% CI) of 5.53 (3.91, 7.15), with no evidence of heterogeneity (I^2 = 0%, Q-test chi^2 = 0.64, df = 1, p-value = 0.420).

ADL

One study (Jiang et al., 2022) used the BI to report ADL. Jiang et al. (2022) showed that the rPMS group had a more significant improvement (p-value < 0.001) in BI than the control group, with a mean (standard deviation [SD]) of 45 (5) in the rPMS group and 40 (10) in the control group.



N, number of participants; SD, standard deviation; Mean diff., mean difference; CI, confidence interval

Figure 3 Forest plot of upper extremity functions using Fugl-Meyer Assessment at the end of intervention

Spasticity

Two studies (El et al., 2022; Krewer et al., 2014) reported the spasticity outcome. El Nahas et al. (2022) used the MAS while Krewer et al. (2014) used the MTS. El Nahas et al. (2022) found that intermittent theta burst stimulation (iTBS), a pattern of using fewer pulses and shorter duration than typical rPMS, had a statistically significant difference in MAS in the upper limb compared to the sham group (mean [SD] of 0.26 [0.20] in the iTBS group, 0.11 [0.17] in the sham group, p-value 0.002). Krewer et al. (2014) showed that there was no significant effect of rPMS on decreasing spasticity after the end of intervention.

4.2 Discussion

This meta-analysis was performed to investigate the efficacy of adding rPMS to conventional rehabilitation on upper extremity function in post-stroke patients. Our results found statistically significant improvements in FMA in the rPMS group compared with conventional rehabilitation alone (MD of 5.48, 95% CI 3.89, 7.06). However, there was insufficient data in ADL and spasticity outcomes for pooling in meta-analysis.

The mechanism of rPMS in promoting recovery in stroke patients is unclear. It may be because rPMS can recruit peripheral afferents, potentially influencing cerebral activation and neuroplasticity, which may help improve motor control in stroke patients (Beaulieu, Massé-Alarie, Camiré-Bernier, Ribot-Ciscar, & Schneider, 2017; Heldmann, Kerkhoff, Struppler, Havel, & Jahn, 2000; Kaelin-Lang et al., 2002; Sato, Liu, Torii, Iwahashi, & Iramina, 2016).

Because this research included newer studies (Jiang et al., 2022; Ke et al., 2022), the results changed from those of the last systematic review and meta-analysis, which found no significant difference in improvement of upper extremity function at the end of treatment (Sakai et al., 2019). The researchers found studies that cannot be pooled in the meta-analysis because of the non-random allocation to the rPMS and control groups (S. Chen et al., 2020; Obayashi & Takahashi, 2020). These studies also found that adding rPMS to standard rehabilitation had a beneficial effect on the improvement of upper extremity function. Moreover, an ongoing study about rPMS and upper extremity function also found that rPMS can be added to the meta-analysis in the future (Kinoshita et al., 2020).

Subgroup analysis showed significant results only in the acute to subacute stroke group, with better improvement in FMA in the rPMS group than the conventional rehabilitation group, with a MD (95% CI) of 5.53 (3.91, 7.15). It could be due to greater brain plasticity in the acute to subacute stage than in the chronic stage (Joy & Carmichael, 2021).

The strength of this study was that it focused on the use of rPMS for the treatment of stroke patients, which is increasingly used recently because it is noninvasive and painless. This study's findings may provide new evidence for the use of rPMS in stroke patients in improving upper extremity functions. However, there were also limitations on this study. First, there were still a small number of studies included. Future systematic reviews and meta-analyses may yield more informative results. Second, in this study, the researchers focused on some aspects of the outcomes. Future studies may explore other outcomes of rPMS in stroke patients, such as lower extremity function. Lastly, this review did not study the long-term effects of rPMS in stroke patients. Future studies may be conducted, focusing not only on the short-term but also the long-term effects of the rPMS in stroke patients.

5. Conclusion

The results of this systematic review and meta-analysis support the advantage of rPMS in improving upper extremity functions in post-stroke patients. However, there is not enough information to conclude the effects of rPMS on ADL and spasticity in post-stroke patients.

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