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REVIEW ARTICLE (META-ANALYSIS)

Efficacy of High-Frequency Repetitive Transcranial Magnetic Stimulation at 10 Hz in Fibromyalgia: A Systematic Review and Meta-analysis

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Introduction

- **Fibromyalgia syndrome (FMS):**
- common disease
- chronic, widespread, or regional musculoskeletal pain
- general public prevalence rate is 2%
- more common in women
- The ratio of women to men in fibromyalgia is about 2:1

Chronic pain in fibromyalgia can cause:

- excessive fatigue
- mood disorders
- cognitive dysfunction
- sleep disorders
- affects the quality of daily life

etiology of FMS:

- is still unclear
- Genetic factor
- Environmental factors
- Psychological factors
- Neuropathy
- Neuromodulation
- most credible mechanism may be pain regulation and central sensitivity disorder

treatment

Drugs :

- Gabapentinoid (pregabalin, gabapentin)
- tricyclic compounds (amitriptyline, cyclobenzaprine)
- serotonin-norepinephrine reuptake inhibitors (duloxetine, milnacipran)

treatment

Nondrug:

- Education
- cognitive behavioral therapy
- exercises
- tai chi
- yoga
- chiropractic techniques
- acupuncture
- moxibustion

treatment

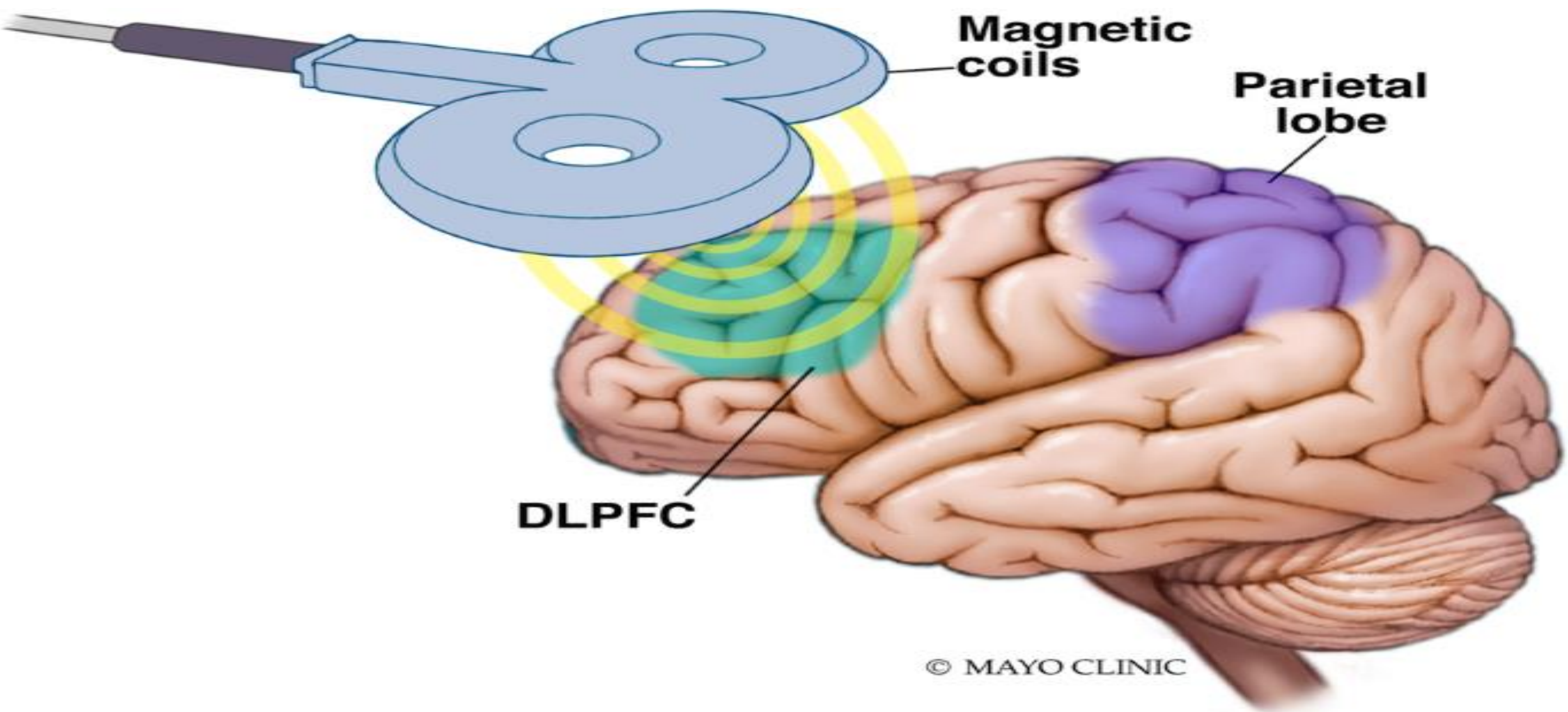
- in recent years, scholars have studied the imbalance of fibromyalgia central sensitivity and pain regulation
- Various neuroelectric stimulations
- repetitive transcranial magnetic stimulation (rTMS)

repetitive transcranial magnetic stimulation (rTMS)

- changes in brain activities and pain regulation and processing
- Low-frequency stimulation(<1Hz) :
  inhibitory effects on brain activity
- High-frequency stimulation (>5Hz): increases cortical excitability

site

- left dorsolateral prefrontal cortex (DLPFC)
- left primary motor cortex (M1)



- stimulation of (DLPFC) using low-frequency rTMS :

reduce pain and related symptoms by targeting spinal pain circuits and top-down pain modulation.

- high-frequency rTMS to stimulate the (M1) :

have an analgesic effect and high-frequency rTMS may achieve direct antinociceptive effects by activating descending pain inhibitory controls

- There is currently no consensus on the optimal parameters for rTMS in FMS treatment.
- Therefore, we systematically reviewed the available literature

Search strategy

- PubMed, Embase, Cochrane, Ovid, Web of Science
- from the beginning until November 6, 2021

Inclusion criteria

- 1. only patients diagnosed with FMS according to the American Rheumatic Society diagnostic criteria
- 2. intervention method including 10-Hz high-frequency rTMS, but the treatment site is not limited
- 3. outcome indicators must have a scale for assessing pain, depression, and quality of life, such as (VAS), (BPI), (HDRS),…
- 4. literature is original and provides sufficient information

exclusion criteria

- 1. animal experiments
- 2. nonrandomized controlled trials
- 3. non-10 Hz frequency rTMS treatment

Search results

- A total of 488 articles were searched
- 7 studies were included
- 217 patients with FMS were included
- 3 studies on the left MI
- 3 studies on the left DLPFC
- 1 study on both the left MI and the left DLPFC

Table 1 Characteristics of the included studies

Author	Age (y), Mean ± SD	Experimental Group (n)	Control Group (n)	Intervention Protocol	Stimulation Site	Outcome
Altas et al[31]	M1: 46.3±9.01 DLPFC: 47.9±7.89 Sham: 48.2±9.38	MI: 10 DLPFC:10	10	10-Hz rTMS, 90% strength; 15 times (5 times/wk)	Left M1 and left DLPFC	Pain: VAS Depression: BDI Living quality: FIQ
Tekin et al[29]	Experimental group: 42.4±7.63 Control group: 46.5±8.36	27	24	10-Hz frequency, 100% strength, and 10 consecutive treatments were performed	Left M1	Pain: VAS Depression: MADRS Living quality: World Briefing on Healthy Quality of Life
Bilir et al[32]	Experimental group: 46.70±9.06 Control group: 43.80±9.37	10	10	10-Hz rTMS, 14 sessions: 10 daily (5d/wk, 2 wk), and 4 weekly (1d/wk, 4 wk)	Left DLPFC	Pain: VAS Depression: HADS Living quality: FIQ
Fitzgibbon et al[33]	Experimental group: 45.07±11.02 Control group: 46.25±15.04	14	12	10-Hz frequency, 120% strength, daily (Monday-Friday) rTMS for 4 consecutive weeks (20 times in total)	Left DLPFC	Pain: VAS Depression: BDI Living quality: FIQ
Mhalla et al[34]	Experimental group: 51.8±11.6 Control group: 49.6±10.0	20	20	10-Hz frequency, 80% strength, 14 sessions of stimulation	Left M1	Pain: BPI Depression: BDI Living quality: FIQ
Passard et al[30]	Experimental group: 52.6±7.9 Control group: 55.3±8.9	15	15	10-Hz frequency, 80% strength, 10 sessions in 2 wk	Left M1	Pain: BPI Depression: BDI Living quality: FIQ
Short et al[9]	Experimental group: 54.20±8.28 Control group: 51.67±18.19	10	10	5 times/wk for 2 wk 10-Hz pulse train duration (on time) 5 s, power (intensity) 120% strength	Left DLPFC	Pain: average daily pain Depression: HDRS Living quality: FIQ

Abbreviations: HADS, Hospital Anxiety and Depression Scale; MADRS, Montgomery-Asberg Depression Rating Scale.

results

- **Effect of 10-Hz frequency rTMS on pain:**

significantly associated with reduced pain compared with sham stimulation in controls

results

- **Effect of 10-Hz high-frequency rTMS on depression:**

depression was not significantly better than that of the control group

results

- **Effects of 10-Hz frequency rTMS on quality of life:**

significantly improved the quality of life

result

- **Subgroup analysis:**

MI region and DLPFC region

The results showed no statistical significance

Conclusions

- significant improvement in pain and quality of life
- no significant effect was shown in depression

Conclusions

- DLPFC high-frequency rTMS appears to be more effective for analgesia.
- DLPFC low-frequency rTMS may be more promising in the treatment of depression.
- M1 high-frequency rTMS may be more effective in improving quality of life.

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REVIEW ARTICLE (META-ANALYSIS)

Effects of Transcranial Direct Current Stimulation on Poststroke Dysphagia: A Systematic Review and Meta-analysis of Randomized Controlled Trials

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Introduction

- **Dysphagia**
- common complication of stroke
- incidence of dysphagia after acute stroke is 78%
- increase the incidence of aspiration pneumonia, malnutrition and death due to asphyxia

Introduction

- **Transcranial direct current stimulation (tDCS)**

- Noninvasive brain stimulation technology
- regulates the transmembrane potential of neurons to produce hyperpolarization or depolarization by transmitting weak currents through the skull
- increase or decrease cortical excitability
- can cause motor function and psychophysiological changes

Search strategy

- PubMed, Cochrane Library (CENTRAL), Web of Science, VIP, CNKI, and Wanfang

Inclusion criteria

- 1. all patients with stroke that was confirmed by MRI
- 2. tDCS was used as the intervention
- 3. at least 1 of the following standardized, validated dysphagia scales
- 4. clinical RCT of tDCS for the treatment of dysphagia after stroke

Exclusion criteria

- (1). The article was not an RCT
- (2) the article was a repetitive literature
- (3) swallowing dysfunction was caused by other diseases
- (4) poor rating on the Physiotherapy Evidence Database Scale

Search results

- total of 273 studies

- 16 RCTs were included in the present study

Stimulation protocols

- All included RCTs were performed using anode tDCS

- 5 of them were on the unaffected hemisphere
- 7 on the affected hemisphere
- 3 included bihemispheric stimulation
- One trial used dual stimulation

(anodal tDCS to the affected and cathodal tDCS to the unaffected);

Overall summary effect

- overall,statistically significant pooled effect size in favor of tDCS on poststroke dysphagia

- Five trials had a small negative effect.
- Thirteen trials had moderate to large positive effect sizes,
- but only 7 trials were considered statistically significant

results

- The tDCS on the affected vs unaffected hemisphere revealed a moderate and significant pooled effect size for both
- tDCS in the acute vs chronic stroke phase yielded a moderate and significanteffect size for both groups

Stimulation intensity

- The 2 high-intensity stimulation studies that used 2 mA showed a small, nonsignificant effect size of 0.36 (CI, 0.19to 0.91; P=.20).
- Application of 1 mA current strength for 20 min/d, as in the 7 RCTs, revealed a moderate,significant effect size of 0.47 (CI, 0.13-0.81; P=.006).
- 2 studies that used 1.4 mA and 1 study that used 1.6 mA showed a moderate, significant effect size of 0.53 (CI, 0.07-0.99; P=.02) and 1.39 (CI, 0.69-2.08; P<.001)

Stimulation intensity

- Two studies that used 1.2 mA showed a large but nonsignificant effect size of 2.50 (CI, 0.56 to 5.56;P=.11).
- One study that used 1.5 mA showed a moderate but nonsignificant effect size of 0.57 (CI, 0.06 to 1.20; P=.08)

Stroke location

- Nine trials using tDCS to the unilateral hemisphere demonstrateda large and significant pooled effect size of 0.82 (CI,0.11-1.53; P=.02)
- Three studies on the brain stem demonstrated a large and significant pooled effect size (1.06,CI 0.58-1.53; P<.001),
- Studies using tDCS to the bulbar paralysis demonstrated a large and significant pooled effect size of 0.71 (CI, 0.18-1.25; P=.008).
- Two studies on the cerebellum and basal ganglia showed a small,nonsignificant effect size of 0.40 (CI, 0.32 to 1.12; P=.28)and 0.57 (CI, 0.06 to 1.20; P=.08).

Discusion and Conclusions:

- Our study, based on a large sample size from all RCTs, showed that tDCS improves swallowing function in patients with poststroke dysphagia.
- the excitatory stimulation of tDCS on both the unaffected and affected sides was statistically significant in the improvement of poststroke dysphagia
- **affected > unaffected**
- **chronic > acute**
- **low-intensity**(=1mA) **> high-intensity**(>1mA)