European Psychiatry 41 (2017) 75–84

Contents lists available at ScienceDirect

European Psychiatry

journal homepage: http://www.europsy-journal.com

Review

High-frequency repetitive transcranial magnetic stimulation over the left DLPFC for major depression: Session-dependent efficacy: A meta-analysis

S. Teng [a,1], Z. Guo [a,1], H. Peng [a], G. Xing [a,b], H. Chen [a], B. He [a], M.A. McClure [a], Q. Mu [a,*]

[a] The Department of Imaging & Imaging Institute of Rehabilitation and Development of Brain Function, The Second Clinical Medical College of North Sichuan Medical College Nanchong Central Hospital, 637000 Nanchong, China
[b] Lotus Biotech.com LLC., John Hopkins University-MCC, Rockville, Maryland, USA

ARTICLE INFO

Article history:
Received 13 July 2016
Received in revised form 2 November 2016
Accepted 2 November 2016
Available online 3 February 2017

Keywords:
Repetitive transcranial magnetic stimulation
Unipolar depression
Session
Pulse
Meta-analysis

ABSTRACT

Background: Depression is a major debilitating psychiatric disorder. Current antidepressant drugs are often associated with side effects or treatment resistance. The aim of this meta-analysis was to evaluate therapeutic effects of high-frequency repetitive transcranial magnetic stimulation (HF-rTMS) in major depression (MD).

Methods: The medical data bases of PubMed, Medline, Embase and Cochrane Central Register were searched for randomized controlled trials (RCTs) reporting the therapeutic effects of high-frequency rTMS for depression, which were published in English between January 1990 and June 2016. The index terms were "depress*", "depression" and "transcranial magnetic stimulation". Depression outcome data of different sessions (5, 10, 15, and 20 sessions of rTMS treatment) were extracted and synthesized by calculating standardized mean difference (SMD) with 95% confidence intervals (CI) by using a random-effect model. Within each session group, the subgroup analyses based on the number of pulses ($\leq$ 1000, 1200–1500, 1600–1800, and 2000–3000) were also conducted.

Results: Thirty RCTs with a total of 1754 subjects including 1136 in the rTMS group and 618 in the sham group were included in this meta-analysis. rTMS had a significant overall therapeutic effect on depression severity scores (SMD = −0.73, $P < 0.00001$). The five, 10, 15, 20 sessions of rTMS treatments yielded the significant mean effect sizes of −0.43, −0.60, −1.13, and −2.74, respectively. In the four groups (5, 10, 15, 20 sessions), the maximal mean effect size was all obtained in the subgroup of 1200–1500 pulses per day (−0.97, −1.14, −1.91, −5.47; $P < 0.05$).

Conclusions: The increasing of HF-rTMS sessions is associated with the increased efficacy of HF-rTMS in reducing depressed patients' symptom severity. A total number of pulses of 1200–1500 per day appear to deliver the best antidepressant effects of HF-rTMS.

1. Introduction

Major depression (MD or unipolar depression) is a global severe mental illness that can occur in all age groups including young children [1]. Due to its high prevalence and high incidence, MD is associated with a substantial loss of quality of life, and increased mortality rates as well as enormous social and economic burdens [2]. The World Health Organization (WHO) has ranked MD as the third most disabling disorder [3].

Although current treatments of MD range from pharmacological agents and cognitive behavioral therapy to electroconvulsive therapy (ECT) [4], most of the commonly available antidepressants are associated with high disability and lack of tolerance in MD patients. In addition, treatment-resistant depression persists although recent antidepressant medications seem to be able to enhance neuroplasticity mechanisms and adult neurogenesis. Except for few recent particular antidepressant medications, which seem to be able to enhance neuroplasticity mechanisms and adult neurogenesis of treatment-resistant depression, most all antidepressant drugs predominantly act through monoaminergic mechanisms [5]. Therefore, recent psychoactive compounds are of particular interest due to another alternative mechanism of action, which is able to enhance

* Corresponding author at: Imaging Institute of Rehabilitation and Development of Brain Function, The Second Clinical College of North Sichuan Medical College Nanchong Central Hospital, No. 97 South Renmin Road, Shunqing District, Nanchong, 637000 Sichuan, China. Tel.: +86 0817 2260 993.
E-mail address: muqiwen99@yahoo.com (Q. Mu).
[1] Shuai Teng and Zhiwei Guo contributed equally to this work.

http://dx.doi.org/10.1016/j.eurpsy.2016.11.002
0924-9338/

the neuroplasticity mechanism in brain areas. In the past two decades, repetitive transcranial magnetic stimulation (rTMS), as a neural modulation treatment method, has been widely used as an alternative antidepressant [6]. Numerous studies have shown that rTMS is effective for treating MD patients [7–11].

The use of rTMS is a non-invasive and safe technique that has been used to stimulate the nerve cells in superficial areas of the brain with the rapidly changing electromagnetic fields generated by a small coil placed over the scalp [12]. The electric current spreading through the coil generates a magnetic field, which can project into the brain without resistance. The effect of magnetic stimulation is dependent on the frequency, location, and intensity of the magnetic pulses [13]. Current rTMS treatment for MD has frequently followed the protocols set by early studies. The two most common protocols are the high-frequency rTMS (HF-rTMS, $>$ 1.0 Hz) to the left dorsolateral prefrontal cortex (DLPFC) and the low-frequency rTMS (LF-rTMS, $\leq$ 1.0 Hz) to the right DLPFC [14]. High-frequency stimulation activates whereas low-frequency inhibits neural activities, which underlie altered regional cortex activity, which modulate interactions of different brain regions, and the therapeutic responses on depression [15]. Meta-analysis has demonstrated that both rTMS methods have been equally effective therapies for MD [16].

Several meta-analyses have shown that HF-rTMS applied over the left DLPFC has had antidepressant effects [16,17]. However, there is still no consensus regarding the most effective HF-rTMS parameters. So far, there has been no meta-analysis devoted to study the antidepressant effects of different sessions of rTMS treatment in patients with MD. This meta-analysis was conducted to determine the antidepressant efficacy of different sessions and pulses of HF-rTMS.

2. Methods and materials

2.1. Search strategy

Clinical trials and previous studies on rTMS for MD were searched for inclusion and were identified from PubMed, Medline, Embase, the Cochrane Central Register of Controlled Trials databases, and Web of Science published between January 1990 and June 2016. The search criteria terms were "depress*", "depression", and "transcranial magnetic stimulation". Two independent reviewers (Shuai Teng and Zhiwei Guo) screened the titles and abstracts of the studies, and then checked full articles for eligibility before data extraction. Any disagreement was resolved by discussion and/or consultation with a third reviewer (Guoqiang Xing).

2.2. Quality assessment

The methodological quality of each of the included studies was assessed by using a modified checklist according to the revised Consort Statement by Moher et al. [18] that contains three aspects:

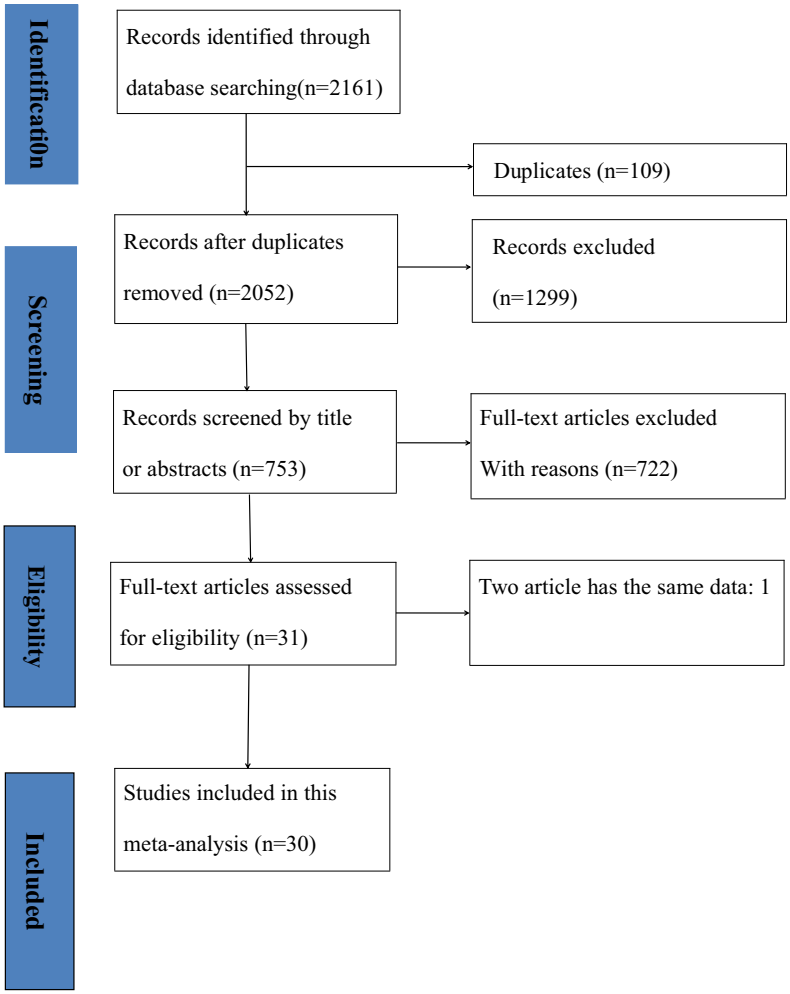

Fig. 1. Flow diagram of study selection.