Efficacy, Efficiency and Safety of rTMS Applied More Than Once a Day in Depression: A Systematic Review and Meta-Analysis

Leo Chen[1,2,3], Abdul Rahman-Hudaib[2], **Kate E. Hoy**[1,2], **Paul B. Fitzgerald**[1,2]

1. Epworth Centre for Innovation in Mental Health, Epworth HealthCare, Melbourne, Australia
2. Monash Alfred Psychiatry Research Centre, Central Clinical School, Monash University, Melbourne, Australia
3. Alfred Mental and Addiction Health, Alfred Health, Melbourne, Australia

CONTACT INFORMATION

Dr Leo Chen
Epworth Centre for
Innovation in Mental Health
Epworth HealthCare
E: Leonard.Chen@monash.edu

Introduction

Repetitive transcranial magnetic stimulation (rTMS) is an effective treatment for treatment-resistant major depression but a standard, 4-6 week treatment course is time-consuming and logistically taxing.

We present the first systematic review and meta-analysis of studies that investigated high- (10Hz) or low- (1Hz) frequency rTMS applied more than once a day to treat depression. So called 'accelerated' rTMS's efficacy, efficiency and safety were reviewed. Quantitative meta-analysis was performed to determine accelerated rTMS's treatment effect size relative to standard, once-daily rTMS.

Aims

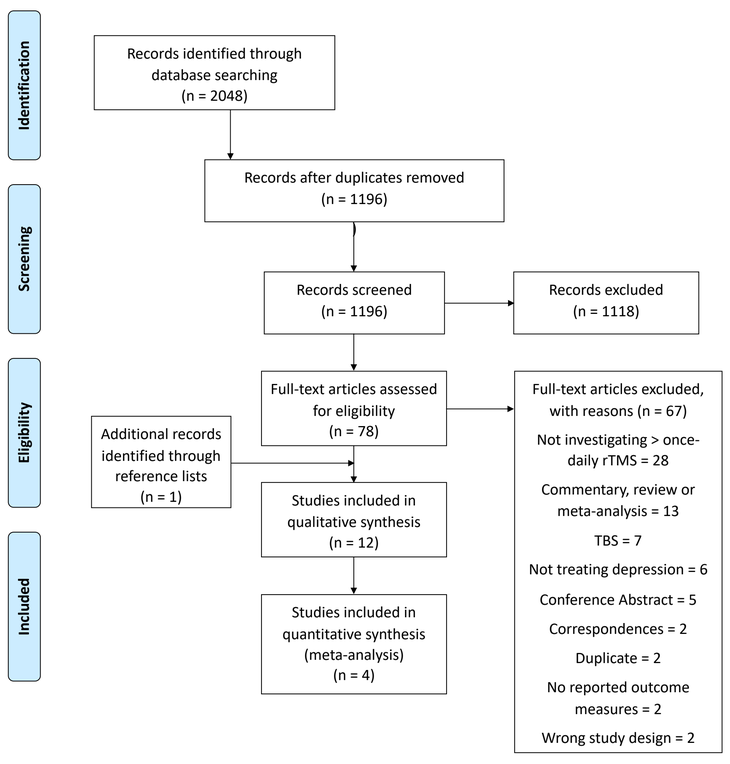
Establish evidence for therapeutic and safety outcomes of accelerated rTMS in depression.

Methodology

Electronic literature searches were conducted on 23 November 2018 across MEDLINE, CINAHL Plus, EMBASE, PsycINFO and the Cochrane Database of Systematic Reviews using defined inclusion criteria.

Antidepressant effect size (Hedge's *g*) of accelerated rTMS over standard, once-daily rTMS was calculated from standardised mean differences (Effect size Hedge's *g*) of individual studies.

Figure 1. PRISMA Flow Diagram of Literature Search



Results

Open-label accelerated rTMS studies demonstrated antidepressant efficacy. Response rates ranged 36-56%. In sham-controlled studies, accelerated rTMS was superior to sham in reducing depression severity.

Accelerated rTMS resulted in marginally faster antidepressant responses than standard rTMS. This was more apparent in open-label and smaller studies.

rTMS applied at various accelerated schedules were mostly well-tolerated.

Quantitative Analysis of Accelerated vs. Standard rTMS

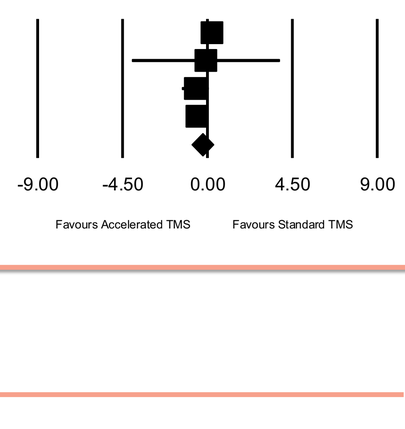
Depression treatment outcomes for 333 patients from 4 trials were analysed. There was minimal publication bias. Moderate heterogeneity existed across studies.

Overall **pooled effect size (Hedge's *g*) of accelerated vs. standard rTMS in treating depression was -0.26 (95% CI: -0.83-0.31)**, p=0.37.

Our results showed a small antidepressant effect size favouring accelerated over standard rTMS that did not approach statistical significance.

Figure 2. Forest Plot of Effect Size Analysis of Accelerated vs. Standard rTMS

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Fitzgerald et al	0.242	0.186	0.035	-0.123	0.607	1.301	0.193
Schulze et al	-0.081	1.997	3.989	-3.996	3.834	-0.041	0.968
Modirrousta et al	-0.641	0.358	0.128	-1.343	0.061	-1.791	0.073
Theleritis et al	-0.553	0.279	0.078	-1.100	-0.006	-1.982	0.047
	-0.260	0.292	0.085	-0.832	0.312	-0.892	0.372



Conclusions

- This is the first meta-analysis exclusively comparing the antidepressant efficacy of accelerated 10Hz rTMS with standard, once-daily rTMS in treating depression.
- Accelerated rTMS scheduling appeared equally effective as once-daily scheduling.
- Accelerated rTMS was overall safe and well-tolerated.
- Paucity of studies preclude definitive conclusions regarding accelerated rTMS's clinical utility and readiness.