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The impact of the number of sessions on response to Repetitive Transcranial Magnetic Stimulation (rTMS) therapy in Major Depressive Disorder (MDD): a naturalistic study in a tertiary psychiatric hospital, Singapore.

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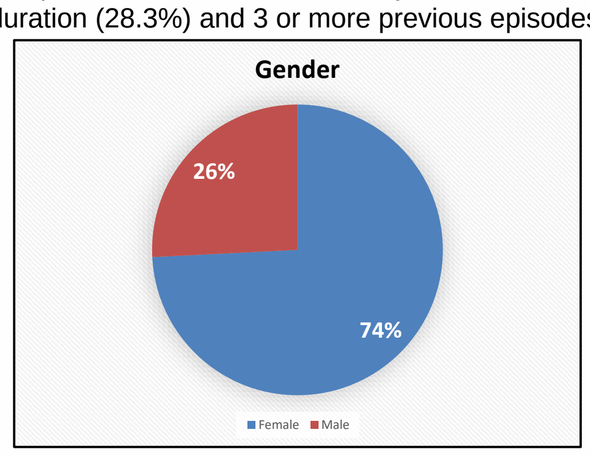
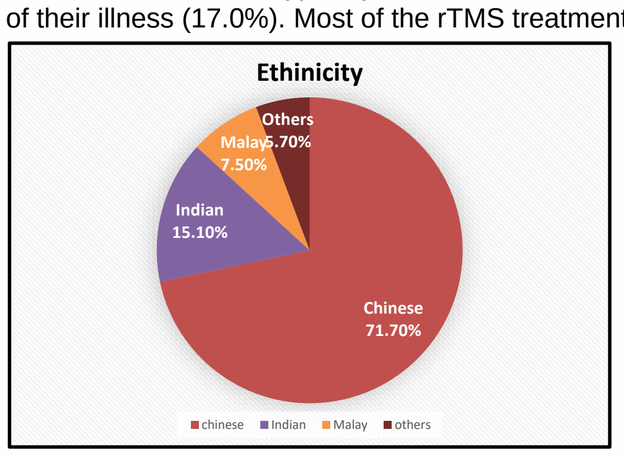
Introduction

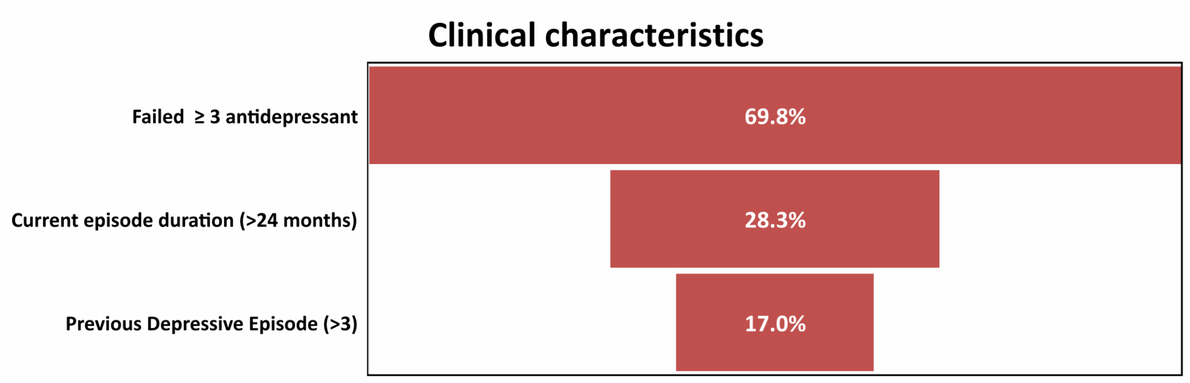
Repetitive transcranial magnetic stimulation (rTMS) is a novel and effective neuromodulation therapy for treatment-resistant major depressive disorder (MDD). [1] The aim of this paper is to attempt to answer what is the optimal dosage for effective rTMS treatment. A standard course of rTMS in USA is 30 sessions but it is unclear if this applies in Asia.[2] We aimed to compare rTMS response for patients ≤ 30 versus > 30 sessions in an Asian tertiary psychiatric hospital.

Sociodemographic & Clinical characteristics

A total of 53 patients whose average age was 34.1 (SD 15.8) on rTMS were analyzed. The data indicated more females (60%) than males. Of these patients, the largest ethnic group was Chinese 71.7% as compared to Indian 15.1%, Malay 7.5%, and others 5.7%. Patient was typically referred for rTMS due to treatment resistance to pharmacological treatment (69.8%) with more than 24 months of illness duration (28.3%) and 3 or more previous episodes of their illness (17.0%). Most of the rTMS treatments administered were left dorsolateral prefrontal cortex (DLPFC) (56.6%).







Methods

A naturalistic retrospective study of patients who received rTMS treatment between June 2018 and April 2023 of 53 inpatient and outpatient was conducted. Clinical outcomes were assessed using the clinician-rated Montgomery–Åsberg Depression Rating Scale (MADRS), Clinical Global Impression-Severity (CGI-S), and Self-rated Depression Anxiety and Stress Scale 21 (DASS-21). Patients who achieved a “>25% MADRS improvement at session 30” were offered additional treatment. The number of rTMS treatment sessions was stratified into “(≤30 sessions)” and “(>30 sessions)” for analysis.

Results

Patients treated with rTMS experienced an improvement of MADRS from 28.1 (SD 7.3) to 20.7 (SD 10.1). (P<0.0001). (Response rate 20.8% / Remission rate 17%); CGI-S mean from 4.6 (SD 0.8) to 3.3 (SD 1.2). (P<0.0001); DASS 21 total mean from 67.3 (SD 24.6) to 49.6 (SD 28.0) (P<0.0001).

rTMS associated change of clinical MDD assessment outcome before and after treatment (Table 1)

Assessment Scale	Pre-rTMS			Post-rTMS			Paired T test P value
	N	mean	SD	N	mean	SD	
MADRS	53	28.1	7.3	53	20.7	10.1	**0.0001***
CGI-S	52	4.6	0.8	52	3.3	1.2	**0.0001***
DASS 21 Total Score	51	67.3	24.6	51	49.6	28.0	**0.0001***

Independent T test*
P <0.001
Abbreviation: **MARDS,** Montgomery–Åsberg Depression Rating Scale; **CGI-S,** Clinical Global Impressions-Severity; **DASS-21**, Depression Anxiety and Stress Scale 21;

The subgroup of 35% of patients with less than 30 rTMS sessions had contributed disproportionately to non-response rate of 85.7% illustrated in Table 2.

Change of MADR score stratified by two subgroups (Table 2)

	Sessions	N	Mean	Std. Deviation	Std. Error. Mean
MADRSc *	≤ 30	19	3.8	12.3	2.8
	>30	34	9.4	9.7	1.6

Abbreviation:
MADRSc : change of MARDS score from baseline to post rTMS treatment

Patients who received longer rTMS treatment (>30 sessions) had a trend of larger improvement of MADRS score when compared to patients with (≤30 sessions) [9.4 (SD 9.7) vs 3.8 (SD 12.3) (P =0.078)] as illustrated in Table 3.

Clinical outcome associated with change of MADR score (Table 3)

		Levene's Test for Equality of Variances	t-test for Equality of Means						
		F	Sig.	T	df	Sig. (2-tailed)	Mean Difference	Std. Error Difference	95% Confidence Interval of the Difference
									Lower / Upper
MADRSc	Equal variances assumed	3.242	0.078*	-1.8	51	0.078	-5.517	3.067	-11.675 / 0.641
	Equal variances assumed			-1.68	30.69	0.103	-5.517	3.28	-12.21 / 1.176

Abbreviation:
MADRSc : change of MARDS score from baseline to post rTMS treatment

Discussion & Conclusion

As one of the largest naturalistic study reporting the impact of the number of sessions and outcomes of rTMS therapy for treating MDD in Southeast Asia. This study demonstrated that rTMS treatment was a rapid-acting, effective, safe, and well-tolerated alternative treatment option for treatment-resistant MDD. Consistent with our hypothesis, rTMS efficacy was dose - dependent. Patients who received an rTMS course of more than 30 sessions are probably more likely to have depressive symptom improvement than those having less than 30 sessions. In comparing our depression clinician-reported outcome with similar naturalist studies, the remission rate of 17% was encouraging, comparable to three studies:25.5% (HAM-D) [3] and 28% (HAMD-17), [4] lower than 37.1% (CGI-S). [5] However, the response rate of 20.8% was less robust than most studies that reported response rates of 40% (HAM-D), [3] 54% (HAMD-17), [4] and 58.0% (CGI). [5] Our treatment population displayed greater treatment resistance as evidenced by a higher proportion of failing at least 2 antidepressant trials when compared to (Carpenter *et al.,* 2012), (66.2% vs 54%). Higher baseline symptom severity and treatment refractories had been identified as a poor response to rTMS. Further in our study, the proportion of patients receiving prior ECT was higher than in the Carpenter’s sample, (18.6% Vs 5.2%). Galletly et al. (2015) found prior ECT exposure was a significant nonresponse to rTMS . The difference in outcome measurements and varying definitions of treatment response used highlight the need to have a standardized definition of treatment response to facilitate fair comparisons of treatment outcomes across clinics.

Recommendation

As rTMS efficacy was dose-dependent which was further supported with by two studies: Dosing an additional 6 sessions in non-responders after completing 20 sessions of treatment resulted in a 61% response rate. [6] Preservation rTMS was used as a safe and effective strategy to sustain positive outcomes after completing an acute course of rTMS. [7]The results of this study could help to prevent premature termination of rTMS treatment and potentially affect the clinical practice of rTMS dosing. However, not all patients had access to additional/ preservation rTMS due to travel, cost, rTMS capacity, or other constraints, such factors could confound the treatment outcome beyond 30 sessions. Future interventions, such as accelerated rTMS modalities addressed this practical issue by adding more sessions and could theoretically expedite treatment response time. More in - depth research is recommended to establish the efficacy of accelerated rTMS protocol in local naturalistic setting s with the aim of adding more treatment sessions while expediting treatment response time. This study supports revising long-term rTMS subsidies to at least 30 sessions to meet clinical needs.

References

1. McClintock SM, Reti IM, Carpenter LL, et al. Consensus recommendations for the clinical application of repetitive transcranial magnetic stimulation (rTMS) in the treatment of depression. *Journal of Clinical Psychiatry*. 2018;79(1):35-48. doi:10.4088/JCP.16cs10905
2. Hutton TM, Aaronson ST, Carpenter LL, et al. Dosing transcranial magnetic stimulation in major depressive disorder: Relations between number of treatment sessions and effectiveness in a large patient registry. *Brain Stimul*. 2023;16(5):1510-1521. doi:10.1016/j.brs.2023.10.001
3. Dowling NL, Bonwick R, Dharwadkar NP, Ng CH. Repetitive transcranial magnetic stimulation for major depression: A naturalistic observational study in an Australian private hospital. *Psychiatry Res*. 2020;291. doi:10.1016/J.PSYCHRES.2020.113275
4. Griffiths C, O’Neill-Kerr A, Millward T, da Silva K. Repetitive transcranial magnetic stimulation (rTMS) for depression: outcomes in a United Kingdom (UK) clinical practice. Int J Psychiatry Clin Pract. 2019;23(2):122-127. doi:10.1080/13651501.2018.1562077
5. Carpenter LL, Janicak PG, Aaronson ST, et al. Transcranial magnetic stimulation (TMS) for major depression: A multisite, naturalistic, observational study of acute treatment outcomes in clinical practice. Depress Anxiety. 2012;29(7):587-596. doi:10.1002/da.21969
6. Yip AG, George MS, Tendler A, Roth Y, Zangen A, Carpenter LL. 61% of unmedicated treatment resistant depression patients who did not respond to acute TMS treatment responded after four weeks of twice weekly deep TMS in the Brainsway pivotal trial. Brain Stimul. 2017;10(4):847-849. doi:10.1016/j.brs.2017.02.013
7. Wilson S, Croarkin PE, Aaronson ST, et al. Systematic review of preservation TMS that includes continuation, maintenance, relapse-prevention, and rescue TMS. J Affect Disord. 2022;296:79-88. doi:10.1016/j.jad.2021.09.040

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