DIFFERENCES IN EFFICACY OF H1-COIL AND 8-COIL HR rTMS ON DIFFERENT DIMENSIONS OF MAJOR DEPRESSIVE DISORDER: POOLED SAMPLE FROM 2016-2022 STUDIES IN PSYCHIATRIC CLINIC SVETI IVAN

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Objectives: To compare the efficacy of HR rTMS with H1-coil and 8-coil on different dimension of major depressive disorder.

Methods: We conducted this analysis in intention-to-treat population of the pooled sample from two prospective cohort and two randomized controlled trials conducted in Psychiatric Clinic Sveti Ivan during 2016-2022. The outcome was Hamilton Depression Rating Scale-17 (HDRS-17). Allocation was concealed and outcome assessment was blinded. We conducted the analysis using adjusted within-between subject analysis of covariance. We controlled confounding effects of age, gender, diagnosis, duration of MDD and patients age at MDD onset. Using confirmatory factor analysis we tested the HDRS-17-part of the five-dimensions model derived by Uher (2012). We performed all interventions at 120% of the motor threshold, H1-coil with frequency of 18 Hz and 8-coil with 10 Hz, all in one session daily during 20 workdays (Figure 1).

Table 1. Characteristics of participants, ITT population

	H1-coil (n=125)	8-coil (n=107)
Sociodemographic characteristics		
Age (years), median (IQR)	54 (44; 60)	52 (43; 61)
Gender, n (%)		
men	56 (44.8)	52 (48.6)
women	69 (55.2)	55 (51.4)
Clinical characteristics		
Diagnosis, n (%)		
depressive episode (F32)	35 (28.0)	34 (31.8)
recurrent MDD (F33)	90 (72.0)	73 (68.2)
Duration of MDD (years), median (IQR)	9 (4; 17)	7 (3; 16)
Age at onset, median (IQR)	41 (27; 50)	42 (34; 51)
Psychiatric comorbidities, n (%)	59 (52.2)	73 (73.7)
Number of psychiatric comorbidities, mean (SD)	1.9 (1.0)	2.8 (1.2)
Neurotic, stress-related and somatoform disorders (F40-F48), n (%)	33 (26.4)	30 (28.0)
Disorders of adult personality and behaviour (F60-F69), n (%)	22 (17.6)	26 (24.3)
Organic mental disorders (F00-F09), n (%)	6 (4.8)	42 (39.3)
Mental and behavioural disorders due to psychoactive substance use (F10-F19), n (%)	10 (8.0)	10 (9.3)
Schizophrenia, schizotypal and delusional disorders (F20-F29), n (%)	6 (4.8)	2 (1.9)
Other psychiatric diagnosis*, n (%)	5 (4.0)	3 (2.8)
Severity of MDD symptoms at baseline		
HDRS-17 at baseline, median (IQR)	19 (15; 23)	17 (13; 20)
HDRS-17 at baseline, n (%)		
mild (≤13)	27 (23.7)	29 (29.0)
moderate (14-18)	28 (24.6)	34 (34.0)
severe (19-22)	30 (26.3)	20 (20.0)
very severe (≥ 23)	29 (25.4)	17 (17.0)

Abbreviations: ITT - intention-to-treat; IQR - interquartile range; MDD - major depressive disorder; SD - standard deviation; HDRS-17 - Hamilton Depression Rating Scale-17

* Other psychiatric diagnosis: Behavioural syndromes associated with physiological disturbances and physical factors (F50-F59), Intentional self-harm by sharp object (X78), Other problems related to primary support group, including family circumstances (Z63), Problems related to employment and unemployment (Z56)

Table 2. Multivariable, adjusted analysis of efficacy of HR rTMS with H1-coil and 8-coil on different dimensions of major depressive disorder symptoms, ITT population

	H1-coil (n = 125)				8-coil (n = 107)				Interaction of time x arm	
	Baseline	After intervention	Δ_{abs}	$\Delta_{\%}$	Baseline	After intervention	Δ	Δ_{abs}	p	η^2
Dimensions										
Depressed mood	6.5 (6.1; 7.0)	2.7 (2.2; 3.2)	-3.8 (-4.4; -3.3)	-59 (-67; -51)	6.0 (5.5; 6.5)	3.0 (2.5; 3.6)	-3.0 (-3.6; -2.4)	-52 (-60; -44)	0.046*	0.02
Anxiety	4.5 (4.1; 4.9)	1.9 (1.6; 2.2)	-2.6 (-3.0; -2.1)	-53 (-62; -44)	4.3 (3.8; 4.8)	1.7 (1.4; 2.1)	-2.5 (-3.0; -2.1)	-55 (-65; -45)	0.880	0.00
Pessimism	1.7 (1.4; 2.0)	0.6 (0.4; 0.8)	-1.1 (-1.3; -0.9)	-74 (-83; -65)	1.6 (1.3; 1.9)	7.0 (0.5; 0.9)	-0.9 (-1.2; -0.6)	-63 (-73; -53)	0.270	0.01
Sleep	1.9 (1.6; 2.3)	0.6 (0.4; 0.8)	-1.3 (-1.7; -1.0)	-71 (-81; -62)	1.8 (1.5; 2.2)	1.0 (0.7; 1.3)	-0.8 (-1.2; -0.5)	-59 (-70; -48)	0.054	0.02
Appetite	0.7 (0.6; 0.9)	0.3 (0.2; 0.5)	-0.4 (-0.6; -0.2)	-75 (-84; -66)	0.6 (0.4; 0.8)	0.2 (0.1; 0.4)	-0.4 (-0.6; -0.2)	-82 (-92; -72)	0.282	0.001
Factors (2nd order)										
Observed mood	11 (10; 12)	5 (4; 5)	-6 (-7; -6)	-59 (-66; -52)	10 (10; 11)	5 (4; 6)	-6 (-6; -5)	-54 (-61; -47)	0.826	0.00
Cognitive	4.3 (4.0; 4.7)	1.8 (1.4; 2.1)	-2.6 (-3.0; -2.1)	-61 (-69; -53)	4.1 (3.7; 4.5)	2.0 (1.6; 2.4)	-2.2 (-2.6; -1.7)	-55 (-64; -46)	0.497	0.00
Neurovegetative	4.3 (4.0; 4.7)	1.8 (1.4; 2.1)	-2.6 (-3.0; -2.1)	-61 (-69; -53)	4.1 (3.7; 4.5)	2.0 (1.5; 2.4)	-2.2 (-2.6; -1.7)	-55 (-64; -46)	0.500	0.00
Complete HDRS-17	19 (17; 20)	8 (7; 9)	-11 (-12; -10)	-59 (-65; -53)	17 (16; 18)	8 (7; 9)	-9 (-10; -7)	-52 (-59; -46)	0.025*	0.03

Data are presented as mean (standard deviation) in unadjusted and mean (95% confidence interval) in multivariable, adjusted analysis if not stated otherwise
Abbreviations: SD - standard deviation; Δ_{abs} - mean of absolute differences between the baseline and measurement after the treatment; CI - confidence interval; $\Delta_{\%}$ - mean of relative differences calculated as absolute difference divided by the baseline value; p - statistical significance of the difference from baseline to after the treatment within each of the two study groups, calculated using repeated measures analysis of covariance; p_I - statistical significance of the interaction of study group and change during the treatment calculated using mixed, within-between analysis of covariance; η^2 - partial eta squared standardized effect size
Data are adjusted for age, gender, diagnosis (depressive episode or recurrent MDD), duration of MDD, and age at onset
* FDR < 5%

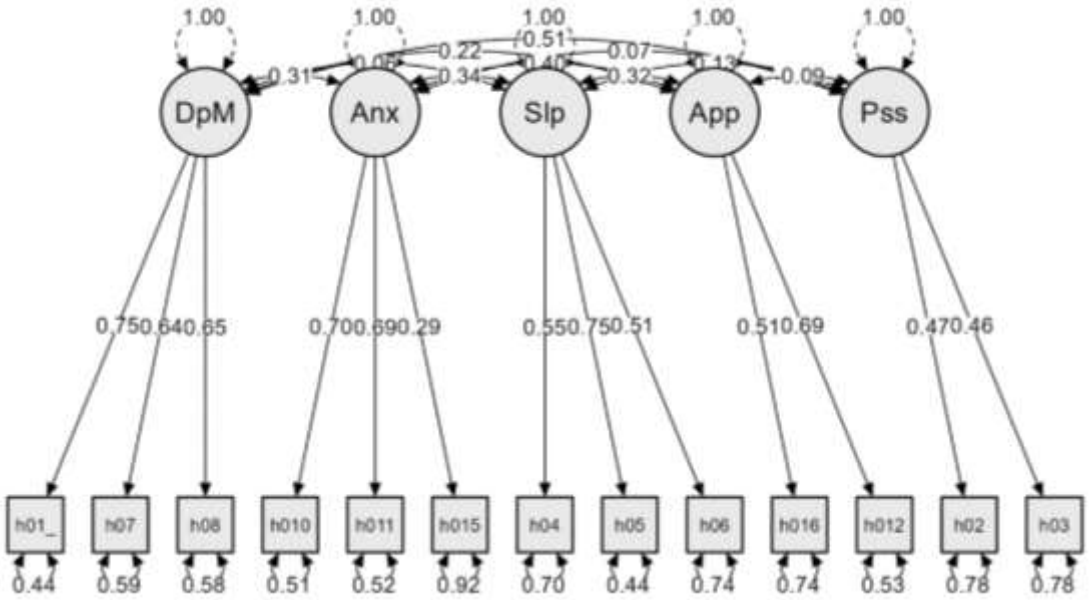

Figure 1. Hamilton depression rating scale confirmatory factor analysis model plot

Results: We analysed 125 patients treated with H1-coil, 55% women, and 107 patients treated with 8-coil, 51% women. Median (interquartile range; IQR) age was 54 (44-60) years in H1-coil arm and 52 (43-61) years in 8-coil arm. Two arms were well balanced in terms of diagnosis (depressive episode or recurrent MDD), duration and baseline severity of MDD. Patients in 8-coil arm more often had psychiatric comorbidity, primarily organic mental disorders. Five dimensions model of HDRS: depressed mood, anxiety, pessimism, sleep difficulties and changes in appetite fitted the empirical data very well (X^2=69.5, p=0.091; CFI = 0.96; TLI = 0.94; RMSEA = 0.035, 90% CI 0.000; 0.058), SRMR = 0.050).

Lowering of total HDRS-17 score was significantly larger in H1-coil, than in 8-coil arm (59% and 52% respectively; p=0.025; η^2=0.03; FDR <5%). H1-coil had significantly better effect on depressed mood dimension (p=0.046; η^2=0.02; FDR <5%). In other dimensions and 2nd order factors (mood, cognitive, neurovegetative) we have not observed significant differences between the two coils (Table 1, 2).

Conclusion: This study indicated somewhat better effect of H1-coil on total HDRS-17 score and on depressed mood dimension, but not on any other dimension or the 2nd order factor.

References:

1. *Uher R, Perlis R, Henigsberg N, Zobel A, Rietschel M, Mors O, et al.: Depression symptom dimensions as predictors of antidepressant treatment outcome: replicable evidence for interest-activity symptoms. Psychol Med 2012; 42:967–80*

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THE USE OF TMS IN TREATMENT OF GAMBLING DISORDERS

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Gambling disorder is characterized by persistent and recurrent gambling behavior that can lead to devastating consequences for those with the disorder and their families. Disorders in the prefrontal activity of the brain are mentioned as the upcoming pathophysiological substrate in the development of gambling disorders (GD). A fundamental feature of this disorder is a craving that we define as an urgent and irresistible desire to indulge in addictive behavior, which usually results in a loss of control, and its biological correlates are dysfunctional dopamine cortical – subcortical pathways, particularly of the inhibitory control of the dorsolateral prefrontal cortex (DLPFC).