Non-Invasive Neurostimulation Therapies Laboratory

No Evidence Supporting Discontinuation of Hormonal Contraceptives During rTMS for Treatment Resistant Depression

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Background

- Repetitive transcranial magnetic stimulation (rTMS) is an effective and safe treatment for treatment resistant depression (TRD)[1]
- The sex hormones estrogen and progesterone alter cortical excitability[2]
  - Estrogen increases cortical excitability
  - Progesterone decreases cortical excitability
- Progestin-containing medications such as hormonal contraceptives can contribute to negative mood symptoms[3,4] and they might interfere with rTMS treatment through their alterations in cortical excitability

Objective

Interrogate whether progestin-containing medication use affects clinical outcomes of rTMS treatment in females with TRD.

Methods

Data from three previous rTMS clinical trials (CARTBIND[5], THREE-D[6], and TMS-fMRI[7,8]) were pooled for analysis to only include females (*N* = 404) and grouped by progestin-containing medication users (*n* = 52) and nonusers (*n* = 352).

Linear mixed-effects modelling was used to predict 17-Item Hamilton Rating Scale for Depression (HRSD-17) score trajectories across 4 weeks of rTMS treatment in progestin-containing medication users compared to nonusers. Covariates included in the model were timepoint of HRSD-17 score collection, age, benzodiazepine use, and Antidepressant Treatment History Form (ATHF) strength.

Results

Progestin-containing medication use was not a significant predictor of HRSD-17 score trajectory across four weeks of rTMS treatment. Timepoint of recording HRSD-17 score was a significant predictor of HRSD-17 score trajectory.

Figure 1: HRSD-17 Score Trajectories Throughout rTMS in Progestin-Containing Medication Users and Nonusers

X-axis shows timepoints of HRSD-17 score collection (0 = baseline, 1-4 = number of weeks of rTMS. a: Group-level mean HRSD-17 trajectories for progestin-containing medication users compared to nonusers. Error bars indicate standard error b: Smoothed HRSD-17 trajectories using Loess curve. Shaded regions show 95% confidence intervals.

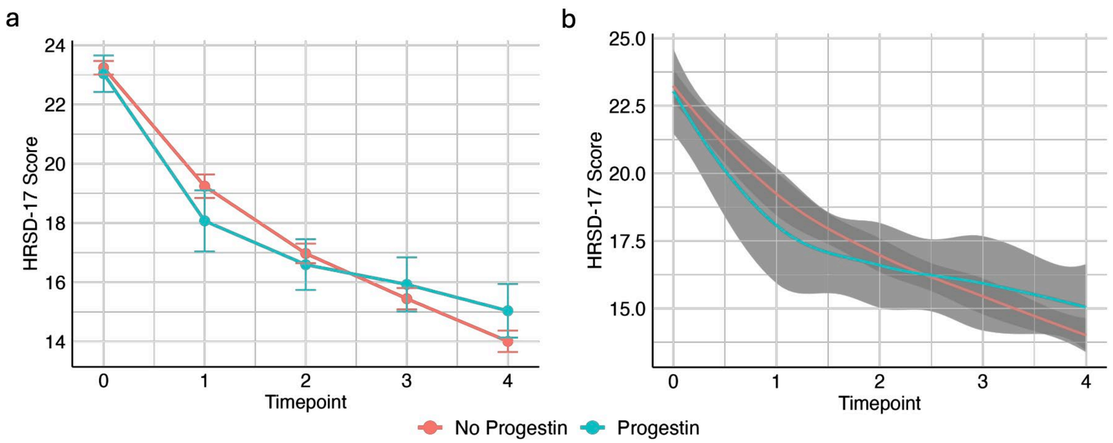

Table 1: Fixed effects of Progestin and Covariates for HRSD-17 Score Trajectories from Baseline to Four Weeks of rTMS Treatment

Parameter	Estimate	SE	df	t-value	p-value	95% CI Lower	95% CI Upper
Intercept	21.77	0.89	419.49	24.42	**<0.001**	20.01	23.53
Progestin	-0.72	0.69	412.51	-1.05	0.295	-2.07	0.63
Timepoint	-2.20	0.09	391.02	-24.66	**<0.001**	-2.37	-2.02
Age	<0.01	0.02	412.45	0.09	0.928	-0.03	0.04
Benzodiazepines	0.82	0.46	404.98	1.80	0.072	-0.08	1.73
ATHF Strength	0.03	0.05	420.55	0.61	0.540	-0.07	0.14
Progestin:Timepoint	0.27	0.25	393.45	1.09	0.276	-0.22	0.76

Note. Bolded p values are significant at α = .05.

Discussion

Use of progestin-containing medications did not interfere with rTMS clinical outcome trajectories in our sample.

Limitations of this study include unbalanced groups between users and nonusers, lack of measurements of blood concentrations of progestin, and lack of information on participants' menstrual cycle phases.

Conclusions & Future Directions

In this first study to assess clinical outcomes of rTMS for treating TRD, progestin-containing medication use does not appear to be associated with rTMS efficacy. We found no evidence to support recommendation for these medications to be discontinued prior to rTMS for TRD.

Future studies should include more balanced groups of users and nonusers, look at other measures of progestin such as blood concentrations, and consider menstrual cycle phase as a potential factor influencing outcomes. Menstrual cycle phase may be particularly influential in accelerated courses of rTMS.

References

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