SAINT® Neuromodulation System to Treat Major Depressive Disorder in Adolescents

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Background

Approximately 20% of adolescents in the U.S. have experienced a major depressive episode (MDE) with 40% being diagnosed with treatment-resistant depression (TRD), increasing suicide risk. This necessitates effective and rapid treatment options for this vulnerable population. SAINT® is a functional connectivity-guided, accelerated form of intermittent theta burst (iTBS) transcranial magnetic stimulation.

SAINT has shown high and rapid remission rates in open-label and controlled trials in adults with TRD;[1-3] however, the effectiveness of SAINT for treating TRD in adolescents is otherwise unknown. We ventured to evaluate the efficacy of SAINT in treating adolescents as part of an ongoing open-label, multicenter trial.

Methods

Seven clinical sites across the US participated in this trial.

Inclusion Criteria:
- Ages 18-21
- Primary MDD diagnosis without psychotic features
- ≥1 failed antidepressant medication trial in current depressive episode
- Not pregnant or planning to become pregnant during acute treatment

Exclusion Criteria:
- Contraindication to TMS
- Contraindication to fMRI
- Participants with an abnormal brain MRI as determined by PI, study physician or designee
- High risk of suicide or suicide attempt in last 6 months

All participants received a 5-day course of SAINT via the ***SAINT Neuromodulation System*** (NMS) which consists of: MagVenture MagPro X100 stimulator (MagVenture A/S, Denmark); MagVenture C-B60 and Cool-B65 coils; Localite neuronavigation system (Localite GmbH Sankt Augustin, Germany); and Magnus Cloud (Magnus Medical Inc., U.S.) for functional target generation. The SAINT protocol was administered according to previously published parameters[1].

The primary outcome was the Clinical Global Impressions Scale of Improvement (CGI-I) score following the final treatment session. Secondary outcome measures included the Montgomery Asberg Depression Rating Scale (MADRS) rated immediately post-treatment and the CGI-S to measure symptom severity. MADRS Item 10 was used for specific assessment of suicidal ideation.

MADRS Item 10: Suicidal Thoughts

Representing the feeling that life is not worth living, that a natural death would be welcome, suicidal thoughts, and preparations for suicide. Suicidal attempts should not in themselves influence the rating.

0 Enjoys life or takes it as it comes.
1
2 Weary of life. Only fleeting suicidal thoughts.
3
4 Probably better off dead. Suicidal thoughts are common, and suicide is considered as a possible solution, but without specific plans or intention.
5
6 Explicit plans for suicide when there is an opportunity. Active preparation for suicide.

Conclusion

These preliminary findings indicate that a 5-day course of SAINT can provide rapid and significant improvements in depression symptoms in an adolescent population, warranting larger clinical trials. Due to the trial being ongoing, data for long-term outcomes is limited. Yet, data from the first participants to complete the 12 month timepoint suggests that response and remission rates carried throughout the 12 months of follow-up. A significant decrease in suicidality was also observed in this cohort immediately following treatment, holding potential for SAINT to be an effective, rapid-acting tool for treating suicidal ideation in this vulnerable population.

Adolescents with moderate treatment-resistant depression treated with SAINT NMS experienced significant antidepressant response and decreased suicidal ideation immediately post-treatment.

Results

13 adolescent participants (4 male, 9 female) were enrolled and completed the 5 day course of SAINT. Participants had a mean MADRS score of 19.2 baseline indicating moderate to severe depression; post-treatment mean MADRS scores dropped to 12.8. 69.2% of participants experienced remission and 92.3% experienced a response at either cessation of stimulation or 5 days post-treatment.

MADRS: baseline vs. 5 days post

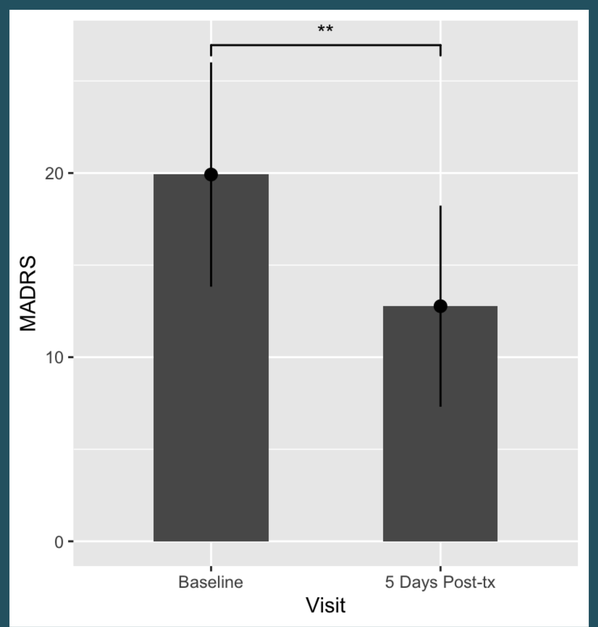

Figure 1: At baseline, participants had a mean MADRS score of 19.9 (SD=6.09). The mean MADRS score 5 days post-treatment was 12.8 (SD=5.46) across all included participants (n=13, paired t-test; p=0.0068, 95% CI [2.38, 11.93]) indicating a mean decrease of 35.9%. Cohen's d=0.905 indicating large effect size.

Suicidality: baseline vs. 5 days post

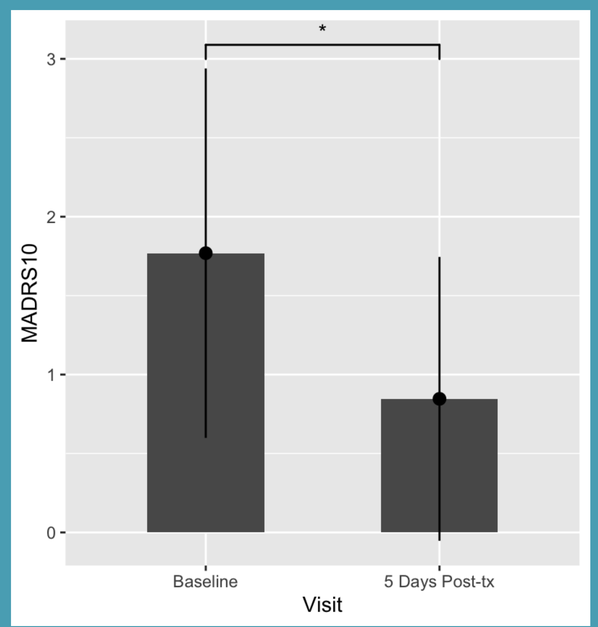

Figure 2: At baseline, participants who endorsed suicidal ideation had a mean MADRS item 10 score of 1.77 (SD=1.17). The mean suicidal ideation metric (MADRS item 10 score) 5 days post-treatment was 0.846 (SD=0.89) across all included participants (n=13, paired t-test; p=0.0268, 95% CI [0.13, 1.72]), a mean decrease of 52.1% from baseline. Cohen's d=0.699 indicating moderate effect size.

Response and remission: immediate post

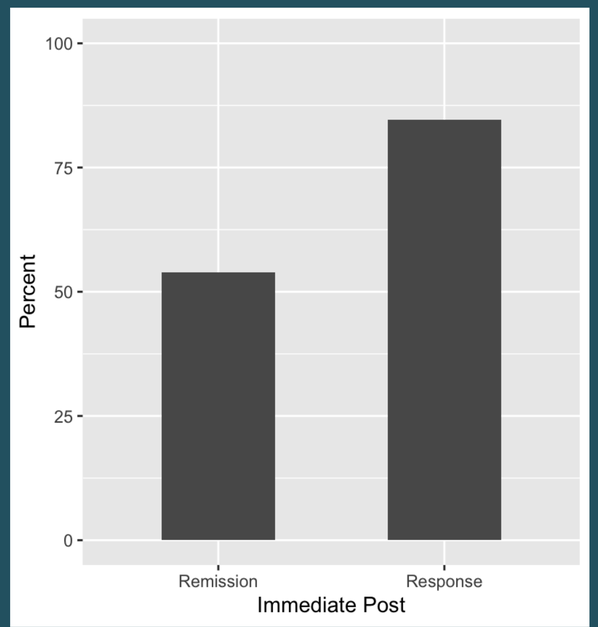

Figure 3: 69.2% of participants were in remission at cessation of stimulation or at 5 days post-treatment. 92.3% of participants were in response at cessation of stimulation or at 5 days post-treatment. Remission was defined as MADRS ≤ 10 or a CGI-I score ≤ 2. Response was defined as a decrease in MADRS by at least 50% or a CGI-I score of ≤ 3.

Response rates over 12 months

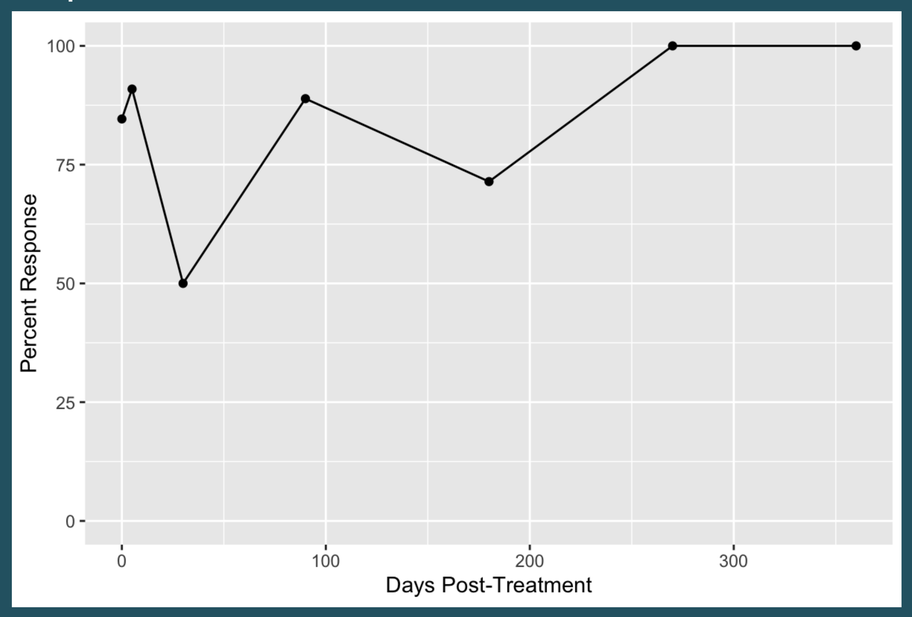

Figure 4: At the end of treatment day 5, the mean CGI-I score was 0.839 (n=13), an 84.6% response rate. Available long-term follow-up data shows sustained response across all timepoints with response rates of 90.9% (n=11) at 5 days post-treatment, 50% (n=6) at 1 month post, 88.9% (n=9) at 3 months post, 71.4% (n=7) at 6 months post,100% (n=5) at 9 months post, and 100% (n=2) at 12 months post.

Remission rates over 12 months

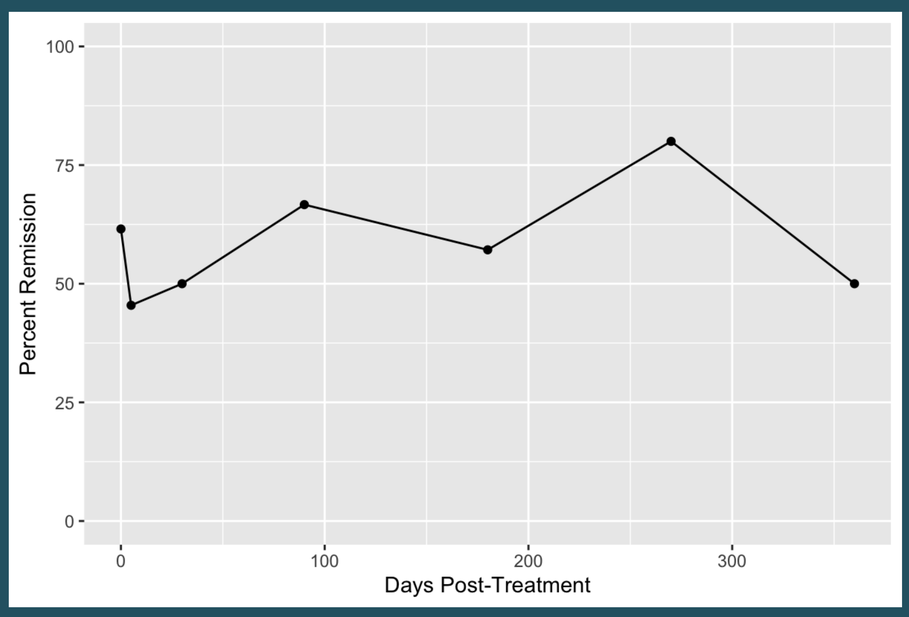

Figure 5: At the end of treatment day 5, the mean CGI-I score was 0.839 (n=13), a 61.5% remission rate. Available long-term follow-up data shows sustained remission across all timepoints with remission rates of 45.45% (n=11) at 5 days post-treatment, 50% (n=6) at 1 month post, 66.7% (n=9) at 3 months post, 57.14% (n=7) at 6 months post, 80% (n=5) at 9 months post, and 50% (n=2) at 12 months post.

References

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2. Williams NR, Sudheimer KD, Bentzley BS, et al. High-dose spaced theta-burst TMS as a rapid-acting antidepressant in highly refractory depression. Brain J Neurol. 2018;141(3):e18. doi:10.1093/brain/awx3792.
3. Cole EJ, Phillips AL, Bentzley BS, et al. Stanford Neuromodulation Therapy (SNT): A Double-Blind Randomized Controlled Trial. Am J Psychiatry. 2022;179(2):132-141. doi:10.1176/appi.ajp.2021.20101429

ClinicalTrials.Gov registration: NCT05819021 This trial was approved by Advarra IRB (IRB#00000971).

Disclosures

This trial was sponsored by Magnus Medical Inc. Dr. Williams and Dr. Bentzley are co-founders of Magnus Medical Inc. and inventors of affiliated intellectual property. Dr. Williams sits on the board of Magnus Medical with both equity and stock options; Dr. Bentzley is a salaried employee with equity and stock options. Katy H. Stimpson, Mike Feyder, TJ Ford, are salaried employees with equity and stock options at Magnus Medical Inc.