

Broad Parietal Repetitive Transcranial Magnetic Stimulation (rTMS): Updated Open-label Results in Alzheimer's Disease

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Early open-label evidence supports the feasibility and tolerability of large-coil rTMS as a scalable neuromodulation intervention for Alzheimer's Disease. It additionally provides preliminary evidence of biological target engagement and clinical efficacy. Further study in our larger planned randomized controlled trial is warranted.

INTRODUCTIONMETHODSRESULTS (n=10)CONCLUSIONSREFERENCES

Plaque and tangle pathology in AD manifests in part as brain network dysfunction, which we can observe on electroencephalography (EEG) in the default mode network (DMN) in the parietal lobe (around precuneus). Repetitive transcranial magnetic stimulation (rTMS) is a safe, FDA-approved (for other conditions), non-invasive tool that modulated brain networks. High-focality rTMS approaches targeting precuneus are promising, but are of limited scalability and not clearly required for positive outcomes.

How can we develop rTMS and other brain stimulation tools in a simple and scalable manner for AD? Can we do this using exclusively off-the-shelf equipment?

Goal: demonstrate the feasibility and tolerability of large-coil parietal rTMS (Figure 1) while exploring its clinical and biological effects.

Design (Figure 2): open-label, n=10, mild-moderate Alzheimer's Clinical Syndrome (2018 criteria), age 50-100. 5 weeks of large-coil parietal rTMS (4 sessions/day x 3 days, then 1 visit/week x 4 weeks). 20Hz stimulation, 1600 pulses per session. RCT upcoming.

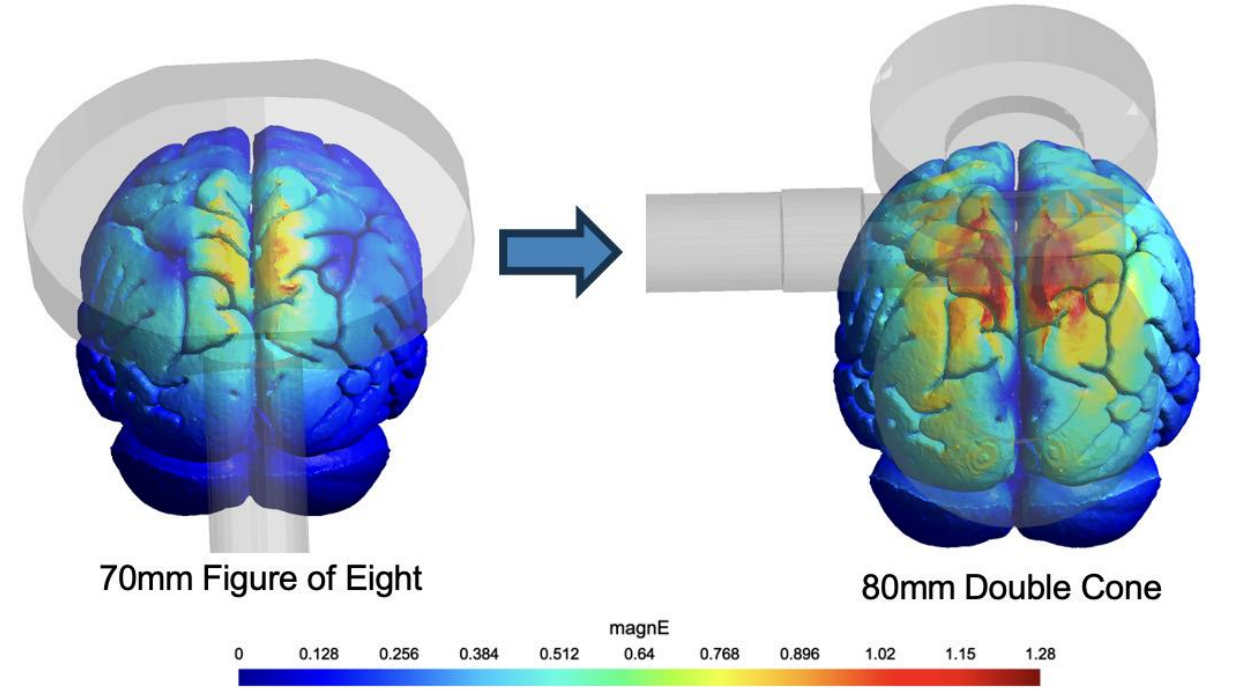


Figure 1: Posterior surface cortical views with coils/casings of induced electric field models of 70mm figure-of-eight and 80mm double cone rTMS coils. MagnE=magnitude of induced electric field (V/m).

- 100% adherence
- No significant AEs
- Subjective improvements in 7/10 participants
- Improvements on CDR, NPI, RBANS (Figure 4)
- EEG gamma increase (Figure 3)

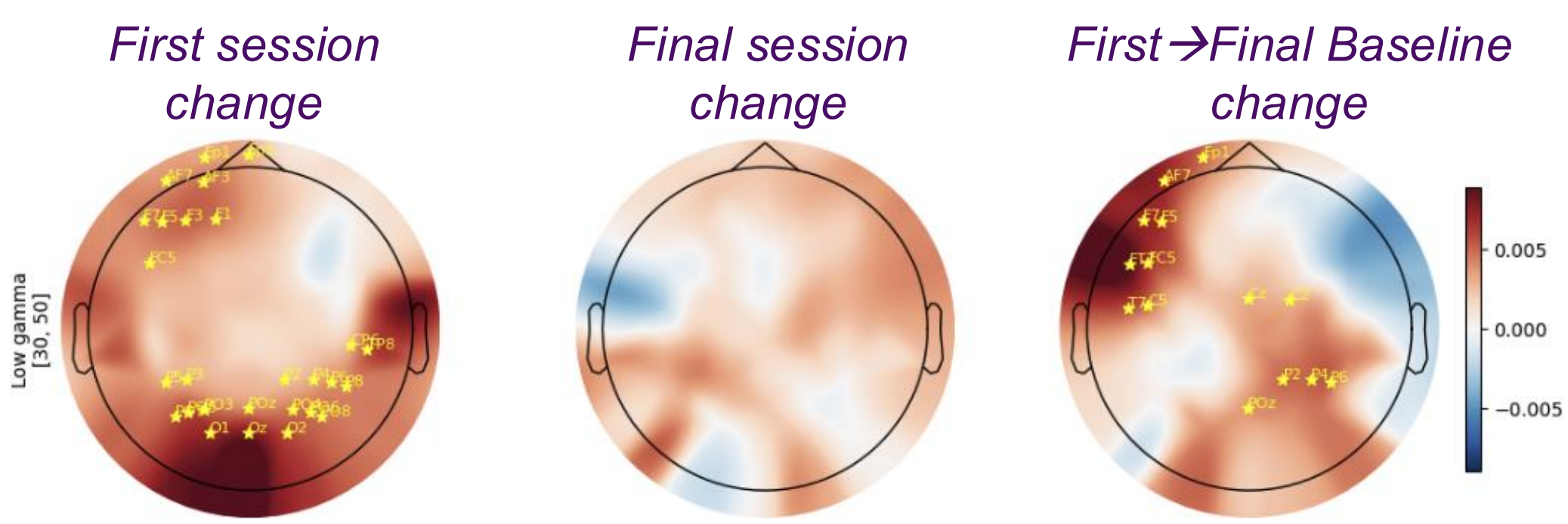


Figure 3: Headplots of relative EEG periodic low-gamma (30-50 Hz) power change in first and last rTMS sessions, as well as from first to final baseline EEGs. * denotes p<0.05

- Encouraging feasibility and tolerability thus far
- Early signs of clinical improvements, biological engagement on EEG
- All the caveats of small open-label studies
- Further study of induction→maintenance rTMS in larger sham-controlled sample over longer time warranted

1) Leuchter MK, Oughli HA, Durbin KA, et al. Broad repetitive transcranial magnetic stimulation (rTMS) of the precuneus in Alzheimer's disease: A rationale and study design. Alzheimer's & Dementia: Translational Research & Clinical Interventions. 2025;11(1). doi:10.1002/trc2.70043

CONTACT & ACKNOWLEDGEMENTS

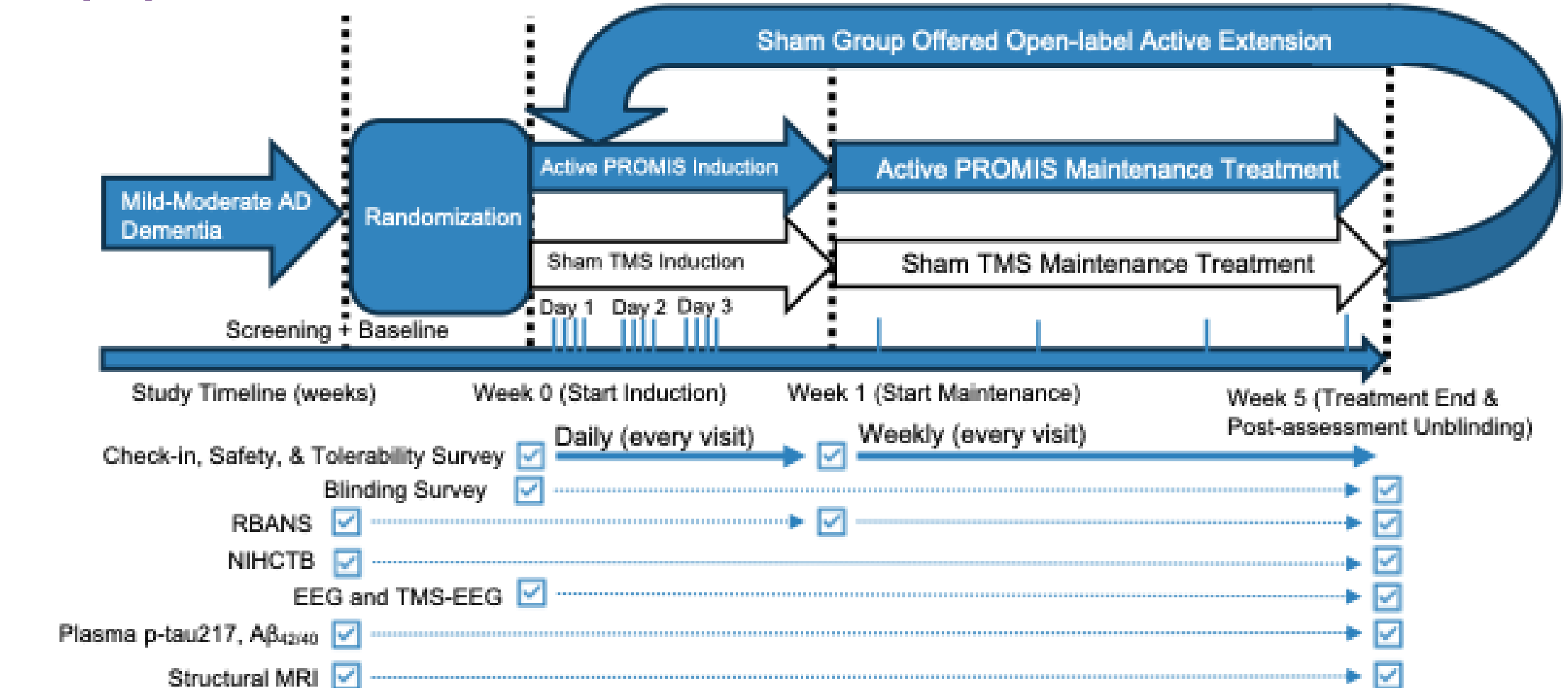


Figure 2: Study Outline. AD, Alzheimer's Disease; EEG, electroencephalography; MRI, magnetic resonance imaging; TMS, transcranial magnetic stimulation; Screening + Baseline, pre-randomization assessment that may impact eligibility; W00, post-randomization baseline assessment before induction treatment; W01, week 1 follow-up visits between induction and maintenance treatment; W05, week 5 end-of-treatment visits. Modified from (1).

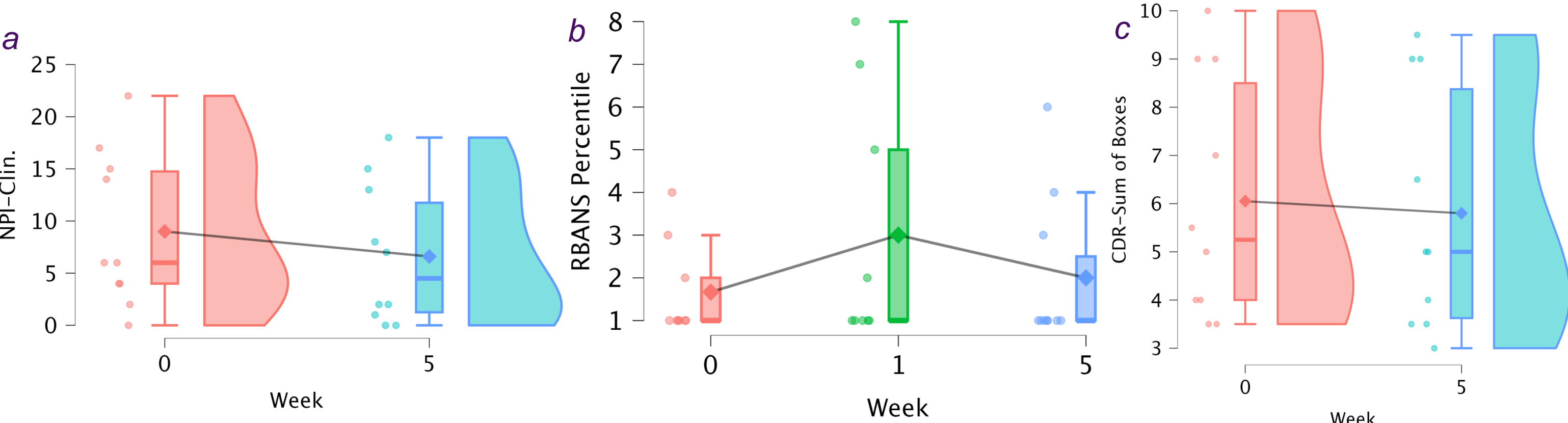


Figure 4: Neuropsychiatric Inventory (NPI; a), Repeatable Battery for the Assessment of Neuropsychological Status--Update (RBANS; b), and Clinical Dementia Rating Scale (CDR; c) Sum of Boxes scores over the course of 5-week study participation. Week 0 is pre-rTMS baseline, 1 is within 72 hours after completing induction phase of rTMS (intensive 4 sessions daily for 3 days), 5 is within 72 hours of completing maintenance rTMS (4 weeks of once weekly rTMS).

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