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Simultaneous aerobic exercise and rTMS: Feasibility of combining therapeutic modalities to treat depression

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Dear Editors

Aerobic exercise (AEx) is the most commonly studied mode of exercise for the treatment of depression [1]. AEx has been implemented as a standalone approach as well as an adjunctive treatment concomitant with pharmacologic and psychotherapeutic treatments [2–5]. AEx is effective in reducing depressive symptoms whether employed singularly or with other anti-depressant treatments. The safety and efficacy of repetitive transcranial magnetic stimulation (rTMS) for treatment of depression is also well documented [6,7]. Given the benefits of both AEx and rTMS individually, it seems plausible that combining these treatments may augment positive plasticity and therapeutic responsiveness. Prior to determining effectiveness, our goal in the present study was to provide preliminary evidence of feasibility and tolerability for combining AEx (stationary cycling) and rTMS into one simultaneous treatment for individuals with depression (Fig. 1).

This study was approved by the Institutional Review Board at the Medical University of South Carolina and prior to participation written informed consent was obtained from all patients.

Treatment session

Patients currently receiving outpatient rTMS treatment for depression completed a single session of AEx on a recumbent sport tricycle (KMX Recumbent Sports Tricycle, KMX, Hampshire, United Kingdom) with a stationary indoor trainer (Kinetic Magnetic 3.0 Trainer, Minneapolis, MN). No modifications were made to the physician prescribed rTMS treatments (Brainsway H-Coil, 18Hz, 2-Sec on, 18-Sec off, 1980 pulses). Patients were encouraged to cycle for the duration of their rTMS session at a self-select intensity that was between a 12 and 17 on the Borg rate of perceived exertion scale [8]. Heart rate and blood pressure were assessed prior to- and during exercise to ensure safety. Patients were also given the opportunity to ride the stationary cycle for multiple sessions if they chose to do so.

Patient reports

Patients completed a brief questionnaire that assessed alertness, enjoyment, and level of difficulty of cycling using a 5-point Likert Scale (1 = Strongly Disagree; 5 = Strongly Agree). Additionally, patients were asked 1) if they would be willing to cycle again if allowed; 2) if they perceived that the TMS coil moved during the treatment session; and 3) how frequently they currently exercise. Patients were also encouraged to provide written feedback outside of the questions asked. Patients that completed multiple exercise sessions answered an additional questionnaire.

Six patients (4 female; ages 23–67) completed a single session of AEx while receiving rTMS treatment with the Brainsway coil. Mean Patient Health Questionnaire-9 (PHQ-9) score before beginning rTMS treatment was 18 ± 2 with the exception of one patient that was receiving a once-weekly maintenance dose of rTMS (PHQ-9 = 6). Mean PHQ-9 score at the time of study participation was 12 ± 6 . No adverse events were reported and all patients cycled for the duration of their rTMS treatment session (12–18 minutes). Importantly, all patients reported that they enjoyed AEx while receiving rTMS (Rating 4.5/5.0) and would be

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willing to ride the stationary cycle again during future treatments. On average, patients reported that AEx was neither difficult nor easy which would be consistent with having individuals perform moderate intensity aerobic exercise. Half of the patients reported that AEx made them feel more alert while receiving their treatment. All participants reported being physically active with exercise frequencies ranging from 1 to 2 to 5 or more times per week.

Two patients (33%) reported feeling the coil move during their treatment session. One patient described the movement of the coil as a "very tiny bit." For the other patient, rTMS treatment was briefly paused to readjust the coil. Subjective feedback included: (1) "I wish I could do the bike and TMS everyday; " (2) "It took my mind off of depression; " (3) "It took my mind off of TMS; " (4) "It was an adventure that I hope helps me and others." We received constructive feedback from one patient who stated that when pedaling at faster speeds, she needed to focus on keeping her head still. She suggested that the armrests would make cycling more comfortable and stated that pedaling at higher intensities makes one's head sweaty. Neither patient reported that the addition of AEx interfered with their treatment in any way.

Three patients continued to perform AEx for multiple sessions although only two of these patients completed the additional questionnaire. Both patients stated that they would prefer to receive rTMS with AEx rather than rTMS alone and would recommend AEx to other patients receiving rTMS. Specifically one patient stated, "I felt best with the bike ... I see no reason why patients can't do the bike while getting TMS treatment ... Great connection with physical and mental health!"

Patients completed their exercise session anywhere between four and thirty-five treatments into their treatment course, which may explain the difference in PHQ-9 scores at the time of rTMS treatment commencement and time of study participation. We acknowledge that by enrolling patients after completing a portion of their rTMS treatment plan, depressive symptoms could have decreased or resolved, thereby possibly biasing results and the participants' experience. Additionally, one potential study patient declined participation due to her feeling that her current level of physical fitness would not permit her to cycle for an entire treatment session. It is possible that those individuals who opted to participate in this study enjoyed exercising more, had higher levels of physical fitness, had less severe depressive symptoms, or believed that completing simultaneous cycling with their rTMS treatment might benefit them in some way.

Clinician reports

Clinicians responsible for setting-up and supervising the treatment sessions were also asked to complete a brief questionnaire regarding the logistics of adding AEx to rTMS treatment as well as other feedback regarding the combination of these therapeutic approaches. The consensus amongst these clinicians was that: (1) It was not difficult to set-up; (2) Having patients ride a stationary cycle during their treatment did not make administration of rTMS more difficult; and (3) They would encourage and be willing to have other patients receive this combination treatment. Constructive feedback from clinicians was directed towards movement of the coil during the treatment session, which was addressed by tightening the

rTMS cap, and longer appointment times (suggested 3–5 minutes) to allow time for set-up and transitioning on and off the stationary cycle. Otherwise all clinicians were supportive of adding AEx to rTMS and regularly encouraged their patients to exercise.

Future directions

Preliminary evidence suggests that simultaneous rTMS and AEx is feasible and well received by both patients and clinicians. The primary obstacles of combining these modalities include requiring slightly longer appointment times to account for set-up and preventing potential movement of the treatment coil. Note that this study was done with the Brainsway system, which has a coil fixed to the patients head with a chin strap and a gravity assist to keep the weight of the coil away from the subject. It may be more challenging to use this with other TMS systems. However, these obstacles can be readily addressed and future experiments should assess the feasibility of adding AEx to a full treatment course of rTMS as well as the effectiveness of this treatment approach on depressive symptomology. An exciting neurobiological possibility is that AEx and rTMS work synergistically and are more effective when paired rather than when delivered individually. Additionally, patients receiving this combination may also realize the health benefits associated with AEx.

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Dr. George has no equity ownership in any device or pharmaceutical company.

He does occasionally consult with industry, although he has not accepted consulting fees from anyone who manufactures a TMS device, because of his role in NIH and DOD/VA studies evaluating this technology. His total industry related compensation per year is less than 10% of his total university salary.

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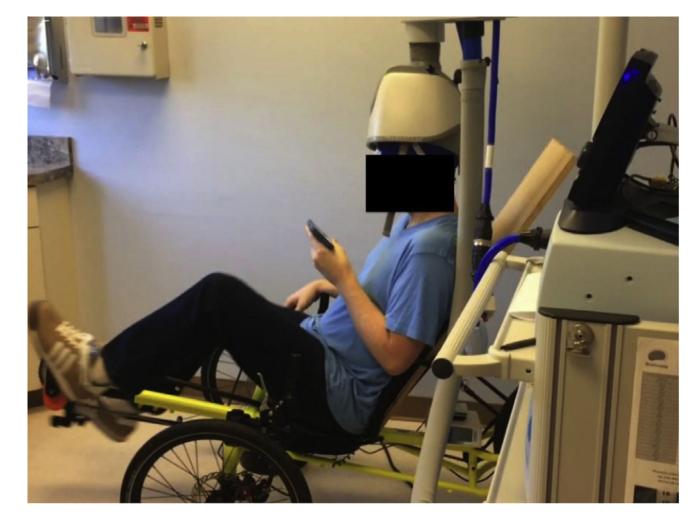


Fig. 1. Simultaneous aerobic exercise and rTMS.