A Patient with Treatment-resistant Depression Who Achieved Remission with Heated Yoga: A Case Report

Hitoshi Sakurai, MD, PhD1, Megha V. Nagaswami, BA2, Emily K. Tan, BA2, Ashley K. Meyer, BA2, Chris C. Streeter, MD1,4,5, Felipe Jain, MD2,3, Simmie Foster, MD, PhD2,3, Albert Yeung, MD, ScD2,3, Cristina Cusin, MD2,3, Maurizio Fava, MD2,3, David Mischoulon, MD, PhD2,3, Maren B. Nyer, PhD2,3

1Department of Neuropsychiatry, Kyorin University School of Medicine, Tokyo, Japan
2Depression Clinical and Research Program (DCRP), Department of Psychiatry, Massachusetts General Hospital, Boston, MA, USA
3Department of Psychiatry, Harvard Medical School, Boston, MA, USA
4Department of Psychiatry and Neurology, Boston University School of Medicine, Boston, MA, USA
5Department of Psychiatry, Edith Nourse Rogers Memorial Veterans Hospital, Bedford, MA, USA

ABSTRACT

Novel interventions are needed to manage treatment-resistant depression (TRD), defined as patients who do not respond to two or more antidepressant trials of adequate dose and duration. We report on a 28-year-old female with TRD with nonresponse to several adequate trials of antidepressants who experienced full symptomatic remission after participating in the heated hatha yoga (HY) arm of a randomized controlled trial (RCT) for depression. Patients, including the one of interest, were randomized to 8 weeks of at least twice weekly HY or an 8-week waitlist followed by 8 weeks of HY. HY incorporates yoga plus heat through a series of standardized poses performed in a heated room (105°F). The 30-item Inventory of Depressive Symptoms, Clinician-Rated (IDS-C 30) and 28-item Hamilton Depression Rating Scale (HAM-D 28) were assessed at key time points throughout the study. The patient attended 16 classes over 8 weeks. Her baseline IDS-C 30 score of 42 decreased to 26 following 2 weeks of HY, and continued declining throughout the intervention, with a final score of 6 (remission) after 8 weeks. HAM-D 28 scores decreased from 26 at baseline to 4 (remission) after 8 weeks. At the 1-month follow-up, the patient’s scores remained stable at 4 on IDS-C 30 and 7 on HAM-D 28, respectively. HY may serve as a potential intervention for TRD in patients who have not previously responded to conventional antidepressants. The rigorousness of the intervention must be considered regarding recommendations for use in the general population.

Keywords: case report, depression, heated hatha yoga, remission, treatment-resistant depression

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Introduction

Yoga-based interventions have shown promise as a treatment for depression[1]. A systematic review of seven randomized controlled trials (RCTs) in patients with major depressive disorder (MDD) found equivalence in reduced depressive severity between yoga and antidepressant medications[1]. Whole-body hyperthermia (WBH) also demonstrated a significant antidepressant effect over 6 weeks in an RCT that compared a single WBH session with a lower-temperature sham control in 34 patients with
MDD[2]. Heated hatha yoga (HY, Bikram yoga), the combination of yoga and WBH could therefore have a synergistic effect for the treatment of depression. A standardized form of HY consists of 26 sequenced physical yoga postures and 2 breathing exercises practiced for 90 minutes in a room heated to 40-43°C with 40-60% relative humidity. We report on a patient with treatment-resistant depression (TRD) who failed several trials of antidepressant treatment at adequate dose and duration and finally achieved remission with HY.

### Case report

The patient was a 28-year-old White female with TRD taking bupropion 450 mg/day and escitalopram 15 mg/day, without remission. Other medications were an oral contraceptive (i.e., norgestimate-ethinyl estradiol) and melatonin for insomnia. Past medical/surgical history was unremarkable. In her baseline 30-item Inventory of Depressive Symptomatology, Clinician-Rated (IDS-C30)[3] she endorsed low mood, guilt, lack of energy, decreased appetite, difficulty concentrating, slowed thinking, negative outlook, and fatigue. Additional self-reported clinical symptoms included passive suicidal ideation, and isolation.

The patient participated in an RCT of community-delivered HY for depressive symptoms in which subjects were randomized to 8 weeks of HY or an 8-week waitlist followed by the HY intervention (ClinicalTrials.gov Identifier: NCT02607514). Participants were asked to attend at least two 90-minute HY classes per week for 8 weeks at two local HY studios. The patient was randomized to the HY arm, and received HY right away.

Upon study entry, the patient met criteria for a current major depressive episode with melancholic features on the Mini-International Neuropsychiatric Interview for the Diagnostic and Statistical Manual-Fourth Edition[4]. Her IDS-C30 scores (primary outcome) were 42 at screening and baseline. At baseline, the patient’s 28-item Hamilton Depression Rating Scale (HAM-D28) score was 26 and her HAM-D17 score was 21.

The patient attended sixteen 90-minute yoga classes over 8 weeks (4 classes within weeks 1-2, 4 classes

### Table 1. Changes in Rating Scales

|                     | Screening | Yoga Period | 1-month Follow-up |
|---------------------|-----------|-------------|-------------------|
|                     | Baseline | Week 1      | Week 3            | Week 5 | Week 8 |
| IDS-C30             | 42       | 26          | 15                | 20     | 6      | 4     |
| HAM-D28             | n.a.     | 26          | n.a.              | n.a.   | 4      | 7     |
| *SF-36              |          |             |                   |        |        |       |
| PF                  | 100      | 85          | 95                | 95     | 100    | 100   |
| RP                  | 100      | 100         | 100               | 100    | 100    | 100   |
| RE                  | 0        | 0           | 0                 | 100    | 33     | 100   |
| E/F                 | 20       | 10          | 40                | 55     | 70     | 60    | 70    |
| EW                  | 48       | 44          | 52                | 76     | 76     | 80    | 88    |
| SF                  | 25       | 25          | 38                | 75     | 50     | 88    | 100   |
| BP                  | 80       | 80          | 90                | 90     | 90     | 90    | 100   |
| GH                  | 85       | 75          | 90                | 95     | 75     | 80    | 90    |
| HC                  | 25       | 50          | 50                | 50     | 75     | 50    | 100   |
| *Q-LES-Q            | 44       | 44          | 49                | 59     | 55     | 56    | 55    |
| PSS                 | 14       | 17          | 13                | 12     | 16     | 7     | 4     |
| STAI-S              | 45       | 44          | 44                | 26     | 31     | 32    | 24    |
| STAI-T              | 48       | 49          | 47                | 43     | 43     | 39    | 37    |

*Higher scores indicate improvement.

Abbreviations: BP = bodily pain; E/F = energy/fatigue; EW = emotional well-being; GH = general health; HAM-D28 = 28-item Hamilton Depression Rating Scale; HC = health change; IDS-C30 = 30-item Inventory of Depressive Symptomatology, Clinician-Rated; n.a. = not available; PF = physical functioning; PSS = Perceived Stress Scale; Q-LES-Q = Quality of Life Enjoyment and Satisfaction Questionnaire; RE = role emotional; RP = role physical; SF = social functioning; SF-36 = 36-item Short Form Health Survey; STAI-S = State-Trait Anxiety Inventory, State; STAI-T = State-Trait Anxiety Inventory, Trait
during weeks 3-4, 2 classes during weeks 5-6, and 6 classes during weeks 7-8). Her IDS-C scores decreased from 42 to 26 by the first 2 weeks and continued declining with a slight increase between week 4 (a score of 15) and week 6 (a score of 20), resulting in 6 by 8 weeks. Her HAM-D and HAM-D17 scores decreased to 4 and 3, respectively, by week 8, indicating remission. At the one-month follow-up, remission was sustained, with scores of 4 on IDS-C and 7 on HAM-D. Secondary outcome measures, including quality of life, perceived stress level, and anxiety all improved throughout the HY period (Table 1). All questionnaire scores remained stable at the one-month follow up visit, indicating sustained remission.

Furthermore, at the one-month follow up, her Habits Questionnaire, a measure of exercise, drug/alcohol/tobacco use, and mindfulness practices, indicated positive routine changes. Prior to participating in HY, she lacked interest in physical or cognitive activity; during and post-HY the patient reported walking at least 30 minutes/day and meditating daily for the past two months, along with continued twice weekly yoga practice.

Discussion

This case report presents a patient who, despite non-response to multiple medications, attained symptomatic remission with the addition of HY to her established treatment regimen. Her depressive symptoms began to decline within two weeks of HY treatment and eventually remitted based on the IDS-C and HAM-D. Notably, attendance mapped onto symptomatic change: her IDS-C score declined during the 2-week period in which she took 4 or more classes, but slightly increased between weeks 4 and 6 when she only took 2 classes.

There have been two RCTs reporting effectiveness and feasibility of yoga in patients with MDD and non-response to at least one antidepressant[5, 6]. In one three-armed RCT, 25 patients who were depressed despite at least 8 weeks of antidepressant treatment were randomized to Sudarshan Kriya yoga (SKY; a breathing-based meditation practice) or a waitlist control in addition to an ongoing antidepressant for 8 weeks. After six sessions during the 8 weeks, SKY produced a greater improvement in HAM-D17, Beck Depression Inventory, and Beck Anxiety Inventory compared to the waitlist control. In another RCT, manualized hatha yoga and health education were compared in 122 patients with MDD and non-response to an ongoing antidepressant. Despite no significant difference between interventions in 16-item Quick Inventory of Depression Symptomatology, Clinician-Rating (QIDS-C) at week 10 of the intervention period, yoga demonstrated greater improvement in QIDS-C compared to health education at months 3 and 6 of the follow-up period. Yoga is thought to produce antidepressant effects through various potential biological mechanisms of action: increased parasympathetic nervous system activity, hyperactivity of gamma amino-butyric acid system, and decreased hypothalamic-pituitary-adrenal axis activity[2]. On the other hand, while no RCT has investigated the effectiveness of WBH in the treatment of TRD, WBH’s antidepressant effects may be explained by the recovery of core body temperature and the activation of a response pathway in midbrain serotonergic nuclei[2]. In addition, HY elevates serum interleukin 6 levels[7] as is observed when high-intensity interval training improves depressive symptoms[8]. Since the biological mechanisms of HY are potentially different from those of antidepressant medications, HY could be effective for patients with TRD who did not respond to general antidepressants.

Adverse events of Yoga include musculoskeletal pain, headache, dizziness, and nose bleeds[9], though reports on their frequency are inconsistent, depending on the assessed time period[10]. In a systematic review of 94 yoga RCTs with available safety data, the overall frequency of adverse events was relatively low (2.2%)[11]. On the other hand, a review of nine epidemiological observational studies reported high rates of yoga-related adverse events, with a lifetime prevalence of injuries ranging from 21.3% to 61.8%[9]. In our previous uncontrolled study of HY for depressive symptoms, only 1 out of 28 participants who attended at least one yoga class and a subsequent assessment visit dropped out due to adverse events during the 8-week intervention[12]. Similarly, this report’s patient completed an 8-week yoga intervention without any adverse events. These findings may imply that yoga-related adverse events may differ mechanistically from those induced by antidepressant medications, and treatment-resistant patients who discontinued past antidepressants because of adverse events might find yoga an attractive alternative.
Our patient attended 16 HY classes over 8 weeks, which was the recommended minimum dose. The average number of sessions attended in our previous open-label study of HY was 8.7 or approximately one class per week in a similar population of patients with depression also asked to attend at least two of the same HY classes per week[12]. It is challenging to obtain full patient adherence to the recommended dose of HY, likely due to the intensity of exercise, potentially uncomfortable heat acclimation period, preparation necessary for each class, and time constraints[12]. This patient’s athleticism, as well as the absence of adverse events may have increased her likelihood of enjoying and tolerating the intense exercise. The results of this case suggest that consistent and regular attendance will likely be an important predictor of treatment outcome.

There are several limitations to interpreting this case. First, generalizability is limited because this is just a single patient, and such dramatic improvement may not necessarily occur in other patients with TRD. The patient is especially noteworthy, because she would not have been expected to respond so robustly and rapidly to a complementary therapy with a relatively modest evidence base as mentioned above, in view of her long-standing and severe treatment-resistant depression. Second, placebo effects cannot be ruled out, as it was impossible to blind study participants. Furthermore, we cannot rule out nonspecific effects, including social support (i.e., meeting with study staff), delayed anticipation effects, study assessment measures, and behavioral activation (i.e., getting out of the house)[13] since the patient was not allocated to the waitlist control arm. Third, it is unclear which component of HY, i.e., the yoga postures, the WBH, or both, produced the antidepressant effect. The patient’s athleticism and superior health status may have dampened the inflammatory elevation commonly associated with depression, as well as some of the other physiological processes mentioned above, making it easier to respond to HY. The hypothesized synergy between the postures and the heat has not yet been addressed scientifically and warrants further comparisons of HY vs. non-heated yoga in larger depressed populations.

In conclusion, our patient with MDD who had not responded to several antidepressants achieved full remission through 8 weeks of HY at approximately two classes per week. Our patient was receiving both bupropion 450 mg/day and escitalopram 15 mg/day during the HY intervention, which suggests that the combination of yoga, heat, and antidepressants might have a synergistic relationship. HY may be a potential augmentative strategy for a certain subset of patients (i.e., younger, physically healthy with capability of intensive physical activity) with TRD. More research is necessary to investigate the role of HY for TRD.

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**CONFLICT OF INTEREST**

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