



Commentary: A Breathing-Based Meditation Intervention for Patients with Major Depressive Disorder Following Inadequate Response to Antidepressants: A Randomized Pilot Study

Skye McKennon^{1,2}, Sarah Elizabeth Levitt^{3,4} and Grzegorz Bulaj^{5*}

¹LS Skaggs Patient Wellness Center, Chief Wellness Office, University of Utah, Salt Lake City, UT, USA, ²A Better Way Wellness, Salt Lake City, UT, USA, ³Department of Nutrition and Integrative Physiology, College of Health, University of Utah, Salt Lake City, UT, USA, ⁴Wellness and Integrative Health Center, Huntsman Cancer Institute, University of Utah, Salt Lake City, UT, USA, ⁵Department of Medicinal Chemistry, College of Pharmacy, Skaggs Pharmacy Institute, University of Utah, Salt Lake City, UT, USA

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*Correspondence:

Grzegorz Bulaj
bulaj@pharm.utah.edu

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A commentary on

A breathing-based meditation intervention for patients with major depressive disorder following inadequate response to antidepressants: a randomized pilot study

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Recently, the American College of Physicians published clinical practice guidelines recommending yoga and other non-pharmacological modalities as non-invasive therapies for patients with back pain (1). Whether for back pain, depressive symptoms, or other chronic disorders, can we imagine doctors prescribing “breathing” and “yoga” together with pharmacotherapies? The answer may be forthcoming. An article by Sharma et al. (2) on non-pharmacological treatment of drug-resistant depression is a welcoming addition to growing clinical research on adjunct therapies where pharmaceutical drugs may produce inadequate responses. Developing adjunct therapies that incorporate non-pharmacological and self-management practices offers means not only to improve therapy outcomes but also to maintain health-related quality of life after reaching remission. Since chronically ill patients, caregivers, and health-care providers embrace challenges of refractory medical conditions, medication non-adherence, and increasing treatment costs, clinical findings related to the drug-resistant depression described in Sharma et al. (2) have a broader impact on treatments of chronic diseases.

The Sharma et al. article (2) reports clinical efficacy of the breathing-based practice called the Sudarshan Kriya Yoga (SKY) in patients with major depressive disorder (MDD) who did not respond to antidepressant drugs. SKY is a breathing-based meditative technique of slow, medium, and fast rhythmic breathing cycles, and it does not require meditation experience. The 8-week SKY yoga treatment consisted of intense, 1-week training and 6-session SKY practice (3.5 h/day), followed by 7 weeks of at-home practice (20–25 min/day) and once-a-week 1.5 h sessions. In this controlled study, 25 patients who were taking antidepressants were randomized to either the SKY or waitlist control groups. The primary endpoint was measured using the Hamilton Depression

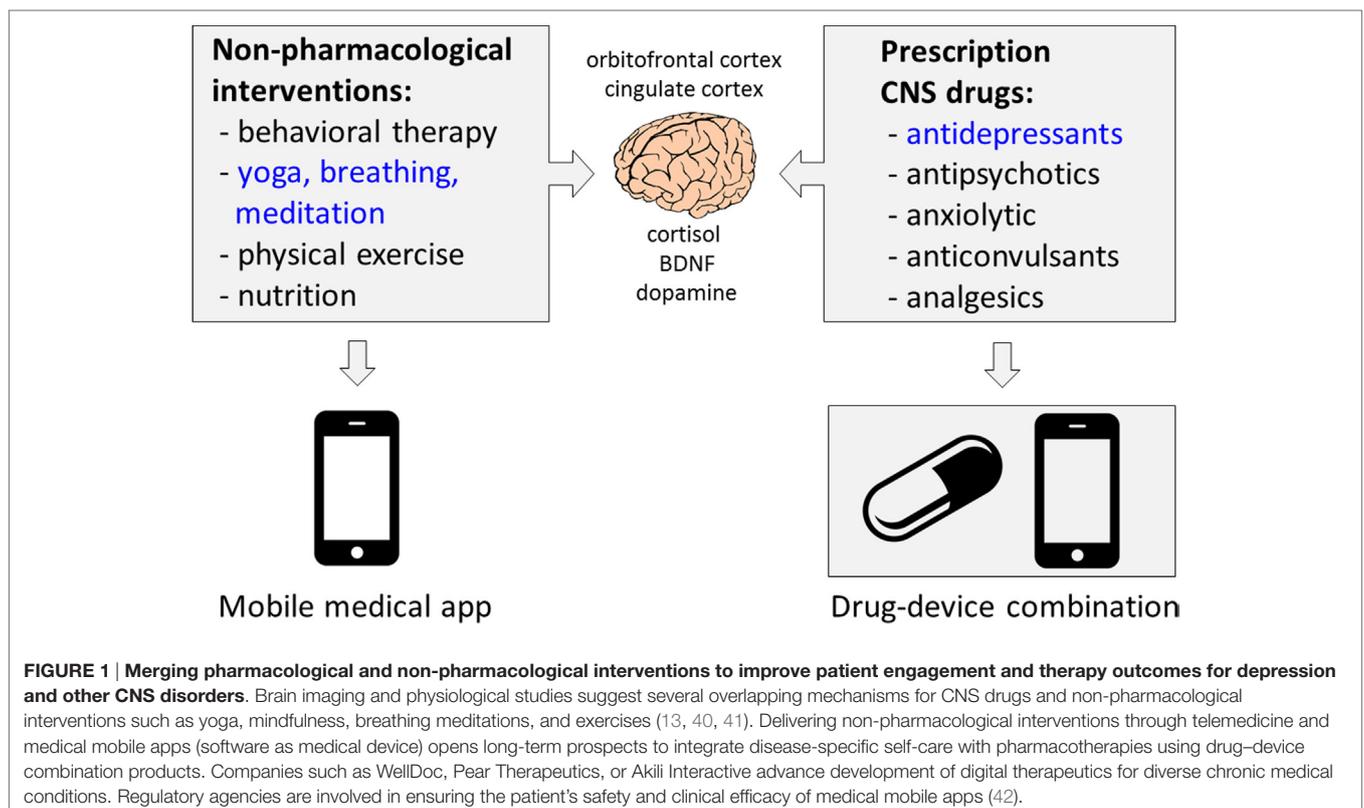
Rating Scale (HDRS), and the secondary points were measured using the Beck Depression Inventory and the Beck Anxiety Inventory scores. Outcome measures were taken at least 1 week prior to the treatment (baseline), and at 1 and 2 months of the study. After 4 and 8 weeks of SKY treatment, significant improvements in depression symptoms were observed, as compared to no changes in the waitlist group. For the intent-to-treat sample, 46% of patients had >50% reduction of HDRS score from baseline.

This is not the first report on clinical efficacy of SKY for the treatment of depressive symptoms (3–5); however, it is the first report on its effectiveness in patients who do not respond to antidepressants. The health-related effects and therapeutic potential of SKY were reviewed (6), and yoga-based interventions for mental health are supported by clinical evidence (7). A recent randomized study showed that mindfulness-based cognitive therapy was effective in patients with drug-resistant depression (8), consistent with previous findings (9). Noteworthy, the 5-week Hatha yoga study did not indicate additional benefits for patients with MDD who were taking antidepressant drugs (10). Yoga is considered as safe if practiced properly, and with few possible adverse effects (11), supporting its potential as adjunctive intervention, which may improve tolerability, compliance, and efficacy of concurrent treatments. While yoga and psychotherapy may appear attractive adjunct therapies for depression, more longitudinal studies are needed to optimize their clinical benefits.

Physiological effects of breathing meditation and yoga indicate their complex pleiotropic nature, while allowing to glean insight

into possible antidepressant mechanisms. Research on neuronal mechanism of meditation techniques, including yoga, shows engagement of specific brain structures (e.g., anterior cingulate cortex) involved in autonomic cognitive and emotional regulation (12–14). Three-month yoga intervention in patients with depression increased serum BDNF levels and decreased cortisol levels (15); this is in accord with yoga supporting stress regulation through the hypothalamic–pituitary–adrenal axis (16). Yoga and breathing exercises can modulate specific brain waves, including increase in the alpha wave activity (17). Effects of yoga correlates with the amount of practice (18), further emphasizing the importance of “dosing” and total duration of yoga treatment for specific chronic medical conditions, for example, for back pain (19–22).

There are two broader aspects of the work of Sharma et al. (2), namely: (1) growing number of clinical studies of diverse non-pharmacological modalities as adjunct treatments of CNS disorders and (2) developing non-pharmacological therapies as digital therapeutics using the “software-as-medical-device” strategy (Figure 1). With respect to the first aspect, nutrition and physical activity are promising adjunct therapies. Dietary and probiotic therapies can decrease depressive symptoms (23, 24), also in patients with MDD (25, 26). Folic acid was shown to be effective in refractory depression (27, 28). Both low- and high-intensity physical activity can improve response to drug therapy for depression (29–31). Lower sertraline doses may be required in patients using physical activity (32). There is also an increasing body of clinical evidence that ketogenic, modified Atkins and low-glycemic diets, or music, are beneficial for seizure control in



patients with drug-resistant epilepsy (33–38). Mindfulness-based interventions are effective for substance use disorders (39).

With respect to the second broader aspect of the Sharma et al., mobile health (mHealth) technologies offer new opportunities for non-pharmacological modalities to be developed as adjunct therapies for the CNS disorders and delivered as drug–device combination products (43). There are several mobile apps and computer-based games that show clinical benefits in patients with depression (44–47). Given availability of mobile apps for deep breathing, yoga, nutrition, or physical exercise, it is feasible to integrate their contents in order to “repurpose” such mobile apps as digital interventions for people living with depression and other chronic disorders. Implementation of mHealth technologies includes pivotal clinical testing in order to receive regulatory approvals and to increase their acceptance among patients, primary care providers, and health-care industry,

including third-party payers. A recent study suggested that mobile app intervention was more effective in people with moderate depression (44), emphasizing research needs for delineating specific clinical indications, in addition to improving clinical efficacy, patient engagement, and long-term effectiveness. This commentary aims to increase awareness of the medical research community and physicians about (1) clinical research on non-pharmacological adjunct therapies for depression and other CNS disorders and (2) opportunities to integrate non-pharmacological interventions with self-care using digital health technologies, including mobile software becoming medical devices.

AUTHOR CONTRIBUTIONS

SM, SL, and GB reviewed the literature and wrote the manuscript.

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