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Bright Light Therapy and rTMS; novel combination approach for the treatment of depression

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Dear Editor

We introduce proof of concept for novel combination approach, rTMS with Bright Light Therapy (BLT). We discuss why this combination may be superior to rTMS monotherapy.

Major Depressive Disorder (MDD) is severe, disabling and in most cases recurrent condition and standard treatments are often ineffective or not tolerated. Repetitive Transcranial Magnetic Stimulation (rTMS) is safe and effective, non-invasive brain stimulation modality [1]. In a typical protocol treatment is delivered in daily sessions, 20–30 minutes, five days a week, over 4–6 weeks. In naturalistic settings response and remission rates can be up to 58% and 37% respectively [2]. Considering that rTMS is mainly used for Treatment Resistant Depression (TRD), these rates are significant. However, there is lot of room for improvement by optimizing treatment itself. One of the strategies used for this is combining rTMS with other evidence based modalities.

Combination treatment can be done simultaneously with TMS session or sequentially, before or after TMS session. Simultaneous treatment is particularly appealing because average TMS session lasts 20–30 minutes and we have excellent opportunity to deliver chosen combination treatment while patient is in TMS session. Clinicians have successfully combined rTMS with other treatment modalities like psychotherapy for depression [3], exposure therapy for PTSD [4], and more. We utilized Bright Light Therapy (BLT) with rTMS treatment course, and this combination has not been reported yet.

TMS was delivered using H1-coil to the DLPFC according to the FDA-approved protocol [5]. BLT was delivered using North Star 10,000 light box (Alaska Northern lights Inc). It was positioned on the floor, 48 inches from the chair where patient was sitting, facing the light box (Fig. 1). BLT was administered simultaneously with stimulation every session for 20 minutes.

Six adult patients with severe treatment resistant MDD were prescribed treatment with above mentioned protocol. All had advanced treatment resistance and failed 4 or more antidepressant medications from at least two different classes and failed psychotherapy. As long as TMS was safe to administer no exclusion criteria were used in terms of medical or psychiatric co-morbidities. We have followed the most recent Consensus Recommendations [1], in selecting patients, screening for safety and treatment delivery.

All patients completed prescribed course and tolerated treatment well without side effects. On primary efficacy measure, response and remission rates at the end of full treatment course using 17-question Hamilton Depression Rating Scale (HAM-D) were 100% and 50% respectively. On secondary efficacy measure, mean change in HAM-D score was −22.5 (SD = 3.4). Mean baseline HAM-D score was 28.3 (SD = 5.5) and mean endpoint HAM-D score was 5.8 (SD = 3.1).

Use of light for depression dates back to the beginnings of civilization. Since the first description of the syndrome of Seasonal affective disorder (SAD) and light therapy in the seminal paper by Rosenthal [6], BLT has become a widely used treatment method for SAD as well as Non-Seasonal Depressive disorder like MDD, with or without medications [7]. Side effect profile of BLT is very benign and it is easy to use. BLT devices are widely available for purchase without prescription or physician's order.

Benefits of combination treatment could be from the synergism

Fig. 1.

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of adding another evidence based treatment modality to rTMS. It can also be due to the "priming effect", when underlying state of the brain is altered in a way that it improves beneficial effects of stimulation (state dependent effects). In other words, Noninvasive Brain Stimulation (NIBS) effects depend not only on the parameters of external stimulation but also on the underlying state of the stimulated region or network. For instance TMS triggered response is very different during the state of wakefulness versus sleep, anesthesia, and vegetative state [8]. Provocation procedure in the treatment of OCD is one clinically useful example of how pre-activation of the circuit involved in the disorder leads to improved outcomes with treatment [9]. It's possible that if we could activate relevant neural networks implicated in depression we could improve outcomes of TMS therapy in TRD.

Human retina contains photoreceptors – rods and cones – that transform light into electrical signal. They project to retinal ganglion cells (RGCs), which output these signals to brain. About 4–5% of these cells contain photopigment melanopsin and are called intrinsically photosensitive retinal ganglion cells (ipRGCs). The discovery of projections of ipRGCs to brain mood centers has redefined understanding of light-mediated mood regulation.

Involvement of sleep and circadian rhythms in the etiology of mood disorders involves direct and indirect pathways originating from ipRGCs. Indirect pathway has long been studied and is well defined. Signals from the retinal ipRGCs travel along the retinohypothalamic tract to the Suprachiasmatic nucleus (SCN) of the Anterior Hypothalamus. In addition to downstream targets like pineal gland, which is regulating circadian rhythm, SCN drives rhythms in Locus Ceruleus, Amygdala, Lateral Habenula and Ventral Tegmental Area (VTA). Together these structures constitute part of neural circuits implicated in depression.

The direct pathway has been defined more recently and it involves ipRGC projections directly to Medial Amygdala and Lateral Habenula, which are implicated in mood regulation. Amygdala in turn projects to VTA and hippocampus, two brain regions known to have role in depression. Lateral Habenula projects to the VTA and the Raphe Nucleus and forms a node of connection between limbic nuclei, hypothalamic brain regions and brainstem monoamine neurons.

Based on the above BLT can activate neural circuits involved in depression and therefore may have both synergistic and priming effects when combined with TMS, and improve outcomes. Another possible advantage of using BLT with rTMS is the reduction in seizure risk [10].

Overall, patients benefited with significant response and remission rates. We encourage further research into combining BLT with rTMS. This is convenient, simple to set up, safe to use, and could be augmentative to the rTMS course. We recommend that future studies control for the time of day BLT is provided. We propose continuation of BLT at home after termination of TMS course to improve durability.

It is known that there is an interaction between light and a magnetic field in a medium, known as a magneto-optical phenomenon or Faraday's effect. It would be symbolic if these two forces of nature can have synergistic effects within the brain when treating depression.

Declarations of interest

None.

Conflicts of interest

None.

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