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Psychological benefits 2 and 4 weeks after a single treatment with near infrared light to the forehead: a pilot study of 10 patients with major depression and anxiety

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Abstract

Background: Many studies have reported beneficial effects from the application of near-infrared (NIR) light photobiomodulation (PBM) to the body, and one group has reported beneficial effects applying it to the brain in stroke patients. We have reported that the measurement of a patient's left and right hemispheric emotional valence (HEV) may clarify data and guide lateralized treatments. We sought to test whether a NIR treatment could 1. improve the psychological status of patients, 2. show a relationship between immediate psychological improvements when HEV was taken into account, and 3. show an increase in frontal pole regional cerebral blood flow (rCBF), and 4. be applied without side effects.

Methods: We gave 10 patients, (5 M/5 F) with major depression, including 9 with anxiety, 7 with a past history of substance abuse (6 with an opiate abuse and 1 with an alcohol abuse history), and 3 with post traumatic stress disorder, a baseline standard diagnostic interview, a Hamilton Depression Rating Scale (HAM-D), a Hamilton Anxiety Rating Scale (HAM-A), and a Positive and Negative Affect Scale (PANAS). We then gave four 4-minute treatments in a random order: NIR to left forehead at F3, to right forehead at F4, and placebo treatments (light off) at the same sites. Immediately following each treatment we repeated the PANAS, and at 2-weeks and at 4-weeks post treatment we repeated all 3 rating scales. During all treatments we recorded total hemoglobin (cHb), as a measure of rCBF with a commercial NIR spectroscopy device over the left and the right frontal poles of the brain.

Results: At 2-weeks post treatment 6 of 10 patients had a remission (a score ≤ 10) on the HAM-D and 7 of 10 achieved this on the HAM-A. Patients experienced highly significant reductions in both HAM-D and HAM-A scores following treatment, with the greatest reductions occurring at 2 weeks. Mean rCBF across hemispheres increased from 0.011 units in the off condition to 0.043

units in the on condition, for a difference of 0.032 (95% CI: -0.016, 0.080) units, though this result did not reach statistical significance. Immediately after treatment the PANAS improved to a significantly greater extent with NIR "on" relative to NIR "off" when a hemisphere with more positive HEV was treated than when one with more negative HEV was treated. We observed no side effects.

Conclusion: This small feasibility study suggests that NIR-PBM may have utility for the treatment of depression and other psychiatric disorders and that double blind randomized placebo-controlled trials are indicated.

Trial registration: ClinicalTrials.gov Identifier: NCT00961454

Background

The National Comorbidity Survey [1] reported that 46% of men and 58% of women were found to have suffered in their lifetime at least a two week period in which they experienced a persistent depressed mood. Major depression disorder (MDD) has a lifetime prevalence of about 16% [2], and it is estimated that by 2020, it will be the second greatest contributor to the impairment of global health [3]. A recent Australian survey reported that anxiety disorders were the most common mental disorder with a lifetime prevalence of 26% [4]. We present our findings from an open study of a novel therapy for these prevalent, deleterious conditions.

Photobiomodulation (PBM), also known as low level laser therapy (LLLT), is the application of phototherapy, often from a red or near-infrared laser, or from a non-coherent light source, such as a light emitting diode (LED). It been reported in over a thousand scientific publications to have therapeutic efficacy for a wide range of disorders in humans without any observed harmful effects. PBM has been demonstrated in cell culture to increase mitochondrial respiration [5], increase ATP synthesis [5-7], upregulate expression of reactive oxygen species [8], modulate the expression of 111 genes in a cDNA microarray study [9], and increase nerve cell proliferation and migration [10]. PBM has been tested in animals to facilitate wound healing [11], improve inflammatory arthritis [12], promote the process of skeletal muscle regeneration [13], and reduce infarct size in ischemic heart muscle by 50 to 70% in an induced experimental model in rats and dogs [14]. Transcranial PBM, using near-infrared light which penetrates the scalp and skull, can significantly reduce damage from experimentally induced stroke in rats [10] and rabbits [15], can improve the memory performance of middle aged mice [16], and has been shown to reduce damage from acute stroke in humans [17,18].

Several studies have suggested that depression is associated with abnormalities of frontal activation reflected in abnormalities in frontal regional cerebral blood flow

(rCBF) [19-21]. PBM has induced increases in blood circulation in the hands of patients with Raynaud's phenomenon [22,23], in skin flaps [24], and in healthy skin [25]. We sought to examine whether transcranial PBM might alter pre-frontal rCBF as well as whether it can affect the emotional status of patients with major depression with anxiety. We see this small feasibility study as the first of a series of experiments to explore eventually whether PBM might be useful as a safe and effective treatment for psychological disorders, and whether any observed improvement might have a relationship with alterations in our measurements of rCBF and hemispheric emotional valence (HEV), the tendency for one cerebral hemisphere (either left or right) to have, as a trait, a more positive psychological disposition than the other.

Several treatments for depression, such as transcranial magnetic stimulation [26], deep brain stimulation [27], and electro-convulsive therapy [28], transcranial direct current stimulation [29,30], apply energy to the brain and have been effective in the treatment of major depressive disorder (MDD) even though their mechanisms remain uncertain. We believe this is the first study of transcranial PBM, which also applies energy, as a treatment for any psychological illness.

Methods

The protocol was approved by the Massachusetts General Hospital (MGH) Institutional Review Board and was conducted in accord with the principles of the Helsinki Declaration. We studied 10 right-handed patients, described in Tables 1, 2, and 3, who were recruited through advertisements posted on the internet and at a substance abuse clinic. Among those with a history of substance abuse, 6 had a past history of opiate dependence, and 1 had a past history of alcohol dependence. Enrollment was made without regard to gender or ethnicity. Inclusion criterion allowed for patients receiving mental health care if they had not altered their treatment during the month preceding the study. At enrollment we asked that they try, but not be required, to maintain their usual treatment until the study's conclusion. All patients complied with this

