

Transcranial Photobiomodulation to Augment Lithium in Bipolar-I Disorder

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To the Editor:

PHOTOBIO-MODULATION (PBM) WITH NEAR-INFRARED radiation (NIR) can be delivered transcranially (t-PBM).^{1,2} Upon penetration into the brain, light is absorbed by mitochondrial chromophores,³ it boosts brain metabolism⁴ and modulates the cerebral cortex.⁵ Pilot studies have suggested the efficacy of t-PBM for unipolar depression.^{6–8}

Little is known on the effect of t-PBM in patients with bipolar disorder (BPAD).⁹ This report describes how t-PBM with NIR affected residual symptoms and lithium serum levels in BPAD. The institutional review board of the Massachusetts General Hospital approved this chart review.

All four patients had been clinically diagnosed with type-I BPAD and followed by their psychiatrist (P.M.); all were white non-Hispanic and two were women; their average age was 38.5 years [standard deviation (SD): 13]. All had been treated with lithium for at least four years and, despite reaching overall stabilization, they still experienced residuals, such as pervasive anhedonia, anxiety, irritability, impulsivity, sleep disturbances, decreased libido, and sexual dysfunction. Their psychiatrist suggested the use of t-PBM augmentation to address these residuals—especially anhedonia—based on prior reports in patients with unipolar depression.⁸ Patients were informed of the possible benefits and adverse effects of t-PBM and agreed to its off-label use. The protocol was 20 min of bilateral exposure on the electroencephalography points F3 and F4 (aiming at the dorso-lateral prefrontal cortex), twice a week for four weeks. The parameters of exposure were based on previous work⁹: continuous wave, wavelength 830 nm, irradiance 33.2 mW/cm², average fluence 40 J/cm², treatment window 28.7 cm² × 2, and total energy 2.3 kJ per session and 18.4 kJ per four-week cycle [Omnilux New U (28 LED) handheld probe; Photomedex, Inc.]. All patients reported a marked reduction of anhedonia/apathy and increase of libido, together with isolated improvements in anxiety, sleep, irritability, and impulsivity. Noticeably, the magnitude of the clinical improvement was such that little or no changes in concomitant psychotropics were required; only the doses of hypnotics (benzodiazepines) were sporadically adjusted during the

follow-up. Incidentally, after a four-week cycle with t-PBM, patients' lithium levels increased significantly ($p=0.014$) from an average of 0.54 (SD: 0.02) to 0.74 (SD: 0.05) mM, as given in Table 1. The psychiatrist decreased the lithium dose, per clinical guidelines. All patients underwent a lithium dose reduction, with an average 18% (SD: 3) decrease of their initial dosage. The dose adjustment re-established lithium levels comparable with baseline ($p=0.1$), in all patients.

The temporal sequence between the t-PBM cycle and the increase in lithium levels in all four patients—who were otherwise on stable doses and whose lithium levels had been previously stable—is striking and indicative of a possible causal link. The beneficial effects of t-PBM on the residual symptoms persisted after re-establishing lower lithium levels; suggesting that the benefits of t-PBM were unrelated to increased lithium availability in the blood.

Further, given that NIR may induce a superficial separation of water from its electrolytes in living tissues (exclusion zone), the increased lithium serum levels might reflect displacement of lithium from target tissues.¹⁰ If that were the case it might also be hypothesized that t-PBM had beneficial effects notwithstanding the reduction in pharmacological activity of lithium. This is highly speculative and further research on the mechanisms underlying the observed effects is needed.

Authors Disclosure Statement

P.C. has received consultation fees from Janssen Research and Development and from Niraxx Light Therapeutics, Inc. He has received unrestricted funding from Photothera, Inc. and then from Litecure, Inc. to conduct studies on t-PBM for the treatment of major depressive disorder and a study on healthy subjects. He has also received funding from Cerebral Sciences to conduct a study on t-PBM for generalized anxiety disorder. He cofounded a company (Niraxx Light Therapeutics, Inc.) focused on the development of new modalities of treatment based on near-infrared light. He has filed several patents related to the use

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TABLE 1. DOSE AND LITHIUM LEVELS AT BASELINE, AFTER TRANSCRANIAL PHOTOBIO-MODULATION, AND AFTER DOSE ADJUSTMENT

	Age (years)	Baseline		After transcranial photobiomodulation		After dose adjustment	
		Lithium dose (mg)	Lithium levels (mM)	Lithium dose (mg)	Lithium levels (mM)	Lithium dose (mg)	Lithium levels (mM)
Patient 1 ♂	43	1050	0.51	1050	0.71	900	0.55
Patient 2 ♀	36	900	0.55	900	0.67	750	0.57
Patient 3 ♂	22	1050	0.58	1050	0.83	800	0.61
Patient 4 ♀	53	750	0.53	750	0.75	600	0.54
Average	38.5	938	0.54	938	0.74	763	0.57
Standard deviation	13	124	0.02	124	0.05	108	0.02

of near-infrared light in psychiatry. All other authors have no conflict of interest to declare.

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