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Transcranial Photobiomodulation Therapy as an Intervention for Opioid Cravings and Depression: A Pilot Cohort Study

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Abstract

Introduction: The opioid crisis, a declared national health emergency, has prompted the exploration of innovative treatments to address the pervasive issues of opioid cravings and associated depression.
Aims: This pilot cohort study investigated the efficacy of transcranial Photobiomodulation (tPBM) therapy using the SunPowerLED helmet to alleviate these symptoms in individuals undergoing treatment for opioid addiction at a rehabilitation center in West Virginia.
Methods: Employing a quasi-experimental design, this study enrolled participants into two groups: one receiving tPBM therapy alongside standard care and a control group receiving standard care alone. The helmet features include the following: total wavelength = 810 nm, total irradiance = 0.06 W/cm^2 (60 m W/cm^2), and total fluence = 172.8J/cm^2.
Results: The results of the Wilcoxon signed-rank tests for within-group analysis and Mann–Whitney U tests for between-group comparisons revealed statistically significant reductions in the intensity (W = 7.36, $p = 0.012$), time (W = 6.50, $p = 0.015$), frequency (W = 6.50, $p = 0.010$), and total scores of opioid cravings (W = 7.50, $p = 0.009$), as well as improvements in depression symptoms (W= 8.00, $p = 0.005$) within the PBM group compared to the non-PBM group.
Discussion: These findings suggest that transcranial PBM therapy could be a promising noninvasive intervention for reducing opioid cravings and depressive symptoms in individuals with opioid use disorder, warranting further investigation through larger randomized controlled trials.

Keywords: transcranial photobiomodulation, opioid use disorder, depression, treatment

Introduction

The opioid crisis escalated into a national health emergency in the United States of America (USA), underscored by the declaration in October 2017. Over 2.702 million people qualify as having opioid use disorders (OUD).[1] It is one of the most devastating public health crises for the USA in the 21st century, with opioids implicated in approximately 75% of drug overdose deaths. In 2022, opioids were responsible for over 68,630 fatalities in the USA, highlighting the urgent need for effective interventions.[2] Particularly affected, the state of West Virginia, reported the highest per capita rate of overdose deaths, emphasizing the crisis's disproportionate impact on specific communities.

Amid this crisis, the quest for effective interventions has led researchers to explore innovative therapeutic modalities beyond conventional pharmacological and psychological treatments. Photobiomodulation (PBM) therapy, employing visible (red) and invisible (near infrared) light wavelengths, has emerged as a promising noninvasive technique aimed at mitigating the physiological and psychological sequelae of OUD. By enhancing cellular and tissue regeneration, reducing inflammation, and promoting wound healing, PBM presents a novel approach to address the underlying neurobiological alterations associated with chronic opioid use, such as changes in the brain's reward system and dopaminergic pathways, reduced dopamine receptor expression, and impaired neuroplasticity.[3,4]

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The complexity of opioid addiction, characterized by intense cravings and the substantial risk of relapse, underscores the necessity for innovative treatment modalities.[5] Transcranial photobiomodulation (tPBM) therapy emerges as a novel approach, with preliminary studies by Schiffer et al.[6,7] suggesting its utility in treating depression and cravings, laying the groundwork for further exploration.[6–8]

Chronic opioid consumption has been linked to structural and functional brain changes, particularly in the reward system and dopaminergic pathways. These alterations contribute to the cycle of addiction, with reduced dopamine receptor expression leading to diminished pleasure from nondrug-related activities and heightened cravings for opioids.[9,10] PBM's potential to increase brain-derived neurotrophic factors, enhance blood flow, and decrease inflammation is a viable intervention to counteract these neurobiological changes and aid in recovery.[6,10,11]

Moreover, the relationship between long-term opioid use and the onset of depression adds another layer of complexity to the OUD treatment. Depression not only exacerbates the difficulty of overcoming opioid dependence but may also drive individuals toward continued drug use as a form of self-medication.[12] The dual capacity of PBM to alleviate both opioid cravings and depressive symptoms offers an integrated approach to OUD treatment, addressing two of the most challenging aspects of recovery.

This study aimed to build upon the existing body of research by examining the effects of transcranial PBM therapy using the SunPowerLED helmet on subjectively reported symptoms of opioid cravings and depression in an outpatient rehabilitation setting in West Virginia. By adding to the nascent evidence for tPBM as a treatment modality for OUD and associated conditions, this research seeks to contribute valuable insights into the potential of PBM therapy as a component of comprehensive addiction treatment programs.

Methods

This prospective pilot cohort study adopted a quasi-experimental design that targeted adults undergoing treatment for opioid addiction at an outpatient rehabilitation center. Participants were recruited and randomly divided into two groups: one receiving tPBM therapy alongside standard care and a control group receiving standard care alone. Standard care for both groups included counseling, medication-assisted therapy, and regular support group meetings.

This study targeted adults 18 years of age and older undergoing treatment for opioid addiction at a facility in West Virginia, which is recognized for its comprehensive outpatient rehabilitation services. The eligibility criteria included a diagnosis of opioid use disorder according to the DSM-5 criteria, the ability to provide informed consent, and a commitment to participate in the entire study duration. The exclusion criterion was the presence of malignancy.

Participants were recruited by the Executive Director of the center, who introduced the study during enrollment in the rehabilitation center. The primary investigators were blinded to the patients enrolled in the study. Participants received comprehensive information about the study's objectives, procedures, risks, and benefits. Interested individuals underwent preliminary screening to confirm their eligibility before enrollment.

To protect participants, the study adhered to strict confidentiality and privacy measures in compliance with Health Insurance Portability and Accountability Act regulations and ethical standards approved by the Institutional Review Board (IRB) of Shepherd University (IRB reference number: 2023042302). Informed consent was obtained from all participants, outlining the study's purpose, procedures, potential risks, and benefits and emphasizing voluntary participation and the right to withdraw at any time without penalty.

The primary risk associated with participation was potential discomfort from discussing subjective experiences of opioid use and depression. This study minimized risks by ensuring a supportive environment during assessments and providing participants with referrals to mental health services if distress was observed. PBM therapy was considered a minimal risk, with no adverse effect reported in similar studies.[13,14] The potential benefits include a reduction in opioid cravings and symptoms of depression, contributing to the participants' overall treatment and recovery process.[6–8]

Assessment scales

Opioid cravings were measured using the Brief Substance Craving Scale (BSCS), a validated instrument for assessing craving intensity, frequency, and duration. Depression symptoms were evaluated using the Patient Health Questionnaire-9 (PHQ-9) Depression Scale, a widely recognized tool for screening, diagnosing, monitoring, and measuring depression severity. Each participant completed a demographic questionnaire.

Data collection

Data were collected at baseline and after completion of the intervention (8 weeks). The participants completed the Substance Craving Scale and PHQ-9 Depression Scale under the supervision of the Executive Director to ensure understanding and accuracy. In addition, demographic information and medication use history, specifically opioid blockers and antidepression medication, were collected at baseline to contextualize the findings and allow subgroup analysis later, if warranted.

Experiment

The PBM group underwent two 180-sec (approximately 3 min) weekly sessions for eight weeks using a light-emitting diode helmet produced by SunPowerLED-Kerber USA, Inc. (Buffalo, NY). The helmet is specified for emitting light at an 810 nm wavelength within the near-infrared spectrum. This wavelength is chosen for its ability to penetrate the scalp and skull to reach brain tissue, based on existing literature that suggests 810 nm is effective for neural tissue photobiomodulation.[3] The helmet operates at an average power density of 0.06 W/cm^2 (60 m W/cm^2) and delivers a cumulative fluence of 10.8 J/cm^2 per session, ensuring adequate dosage for therapeutic effects. Each session duration minimized participant discomfort by limiting the treatment to 180 sec, ensuring a comfortable and tolerable experience, while maximizing the therapeutic potential of PBM for treating opioid cravings and depressive symptoms. The cumulative dose received by the participants was 172.8 J/cm^2. See Table 1 SunPowerLED Helmet and Treatment Specifications for a summary of all helmet specifications.

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Table 1. SunPowerLED Helmet and Treatment Specifications

Component	*Measuring unit*	*Output*
Helmet Irradiance	W/cm^2	.06
Helmet Fluence	J/cm^2	10.8
Helmet # of Diodes	Whole Number	100
Duration of Treatment	Seconds	180
Frequency of Treatment	Days/Week	2
Total Treatments	Days	16
Cumulative Dose Given	J/cm^2	172.8

Results

This study initially recruited 50 participants. However, 11 participants dropped out for assorted reasons: one was incarcerated, two were discharged from the treatment program, one was admitted to an inpatient program, one moved to a different location, three withdrew from all treatments against medical advice, and three opted out. Of the original cohort, 39 participants successfully completed the study, with 22 in the control group and 17 in the tPBM group. Of note, no significant distress was reported by participants during the study. Demographic and baseline characteristics were evenly distributed between the control and treatment groups. The demographic profile of the participants primarily included males (28), individuals who were identified as white (30), those between 30 and 49 years of age (23), married individuals (21), and those employed full time (23). All participants were undergoing treatment for opioid use at a rehabilitation center.

The study employed the Wilcoxon signed-rank test for within-group comparisons and the Mann–Whitney *U* test for between-group comparisons due to the non-normal distribution of the data. Statistical analyses were performed using SPSS version 24.

PBM treatment group

In the treatment group (PBM), the analysis of cravings and PHQ-9 scores revealed significant findings across various measures (Table 2). Craving Intensity, Craving Time, and Craving Frequency showed a significant reduction after treatment. Total BSCS Score, which measures behavioral self-control, also significantly improved. The Total PHQ-9 scores, indicating symptoms of depression, significantly decreased, indicating a reduction in depressive symptoms at the conclusion of the study. Finally, PHQ-9 Difficulty (measuring the degree of impact the depressive symptoms have on daily life) also showed a significant reduction.

Control (Non-PBM) group

In the control group (non-PBM), the examination of cravings and PHQ-9 scores indicated mixed outcomes, as detailed in Table 3. Measures for Craving Intensity, Craving Time, and Craving Frequency for the control group failed to produce a statistically significant difference during the study. The Total BSCS Score, total PHQ-9 score, and PHQ-9 Difficulty score demonstrated minor reductions during the study; however, they failed to meet statistical significance.

Between-group comparisons

In the between-group comparison, significant differences were observed between the treatment (PBM) and control (non-PBM) groups regarding cravings and PHQ-9 scores (Table 4). Craving Intensity scores indicated a statistically significant difference and suggested that treatment notably reduced craving intensity. The Craving Time score, Craving Frequency score, and the Total BSCS score showed a statistically significant difference, indicating the effectiveness of the treatment in reducing craving time and craving frequency as well as a significant difference and improvements in self-control scores due to treatment.

The total PHQ-9 score and the PHQ-9 Difficulty score revealed statistically significant differences between the groups, reflecting the treatment's efficacy in reducing depression symptoms, while indicating the beneficial effects of the treatment on reducing difficulties associated with depression symptoms.

Discussion

This study aimed to evaluate the efficacy of tPBM therapy in reducing opioid cravings and depressive symptoms among individuals with OUD. The results demonstrated significant reductions in craving intensity, time, and frequency, as well as depressive symptoms in the PBM treatment group compared to the control group. The absence of significant changes in the control group strongly suggests that tPBM therapy may effectively reduce both physiological and psychological aspects of OUD. While the exact mechanisms of tPBM therapy influences on brain activity are largely unknown, it potentially addresses neurobiological changes such as altered dopamine pathways, reduced neuroplasticity, and impaired reward system function among individuals undergoing treatment for OUD. These

Table 2. Treatment Group (PBM) Report Cravings and PHQ-9 Scores

	Wilcoxon statistic	p	*z*	*Effect size*
Craving Intensity	7.36	0.012	−2.254	−0.547
Craving Time	6.00	0.015	−2.431	−0.590
Craving Frequency	6.50	0.010	−2.575	−0.625
Total BSCS Score	7.50	0.009	−2.600	−0.630
Total PHQ-9	8.00	0.005	−2.797	−0.678
PHQ-9 Difficulty	4.93	0.016	−2.420	−0.587

BSCS, Brief Substance Craving Scale; PBM, Photobiomodulation.

Table 3. Control Group (non-PBM) Report Cravings and PHQ-9 Scores

	Wilcoxon statistic	p	*z*	*Effect size*
Craving Intensity	6.33	0.668	−0.428	−0.091
Craving Time	6.00	0.856	−0.181	−0.039
Craving Frequency	5.33	0.774	−0.288	−0.061
Total BSCS Score	6.00	0.718	−0.361	−0.077
Total PHQ-9	7.00	0.206	−1.265	−0.270
PHQ-9 Difficulty	5.67	0.272	−1.098	−0.234

BSCS, Brief Substance Craving Scale; PBM, Photobiomodulation.

Table 4. Between-Group Comparison Treatment Group (non-PBM) Report Cravings and PHQ-9 Scores

	Mann–Whitney U *statistic*	p	*z*	*Effect size*
Craving Intensity	92.50	0.005	−2.812	−0.145
Craving Time	98.50	0.008	−2.673	−0.138
Craving Frequency	82.00	0.002	−3.170	−0.164
Total BSCS Score	90.00	0.004	−2.852	−0.147
Total PHQ-9	74.50	0.001	−3.379	−0.175
PHQ-9 Difficulty	97.00	0.011	−2.537	−0.131

PBM, Photobiomodulation.

findings are consistent with previous research highlighting the potential of tPBM therapy in treating various neuropsychiatric conditions, including addiction and depression.[3,6,8,13]

The efficacy of tPBM in reducing cravings within this study aligns with the hypothesis that PBM therapy can influence the brain's reward system, particularly the dopaminergic pathways, which are crucial in the cycle of addiction.[9,10] By potentially increasing brain-derived neurotrophic factors and enhancing blood flow, tPBM therapy may counteract the neurobiological changes induced by chronic opioid consumption, as suggested by Schiffer et al.[6,16] This study also shows promise in supporting other research findings that PBM may help restore normal function by creating an environment that accelerates the brain's ability to heal itself.[15,16] Further, no adverse effect was reported by participants, lending credence to the safety of this therapy.

The significant improvement in depression symptoms supports the dual capacity of tPBM therapy to address both cravings and comorbid depressive symptoms in individuals with OUD. This finding is particularly relevant, given the established link between long-term opioid use and the onset of depression,[12] highlighting the importance of addressing mental health symptoms as part of a comprehensive approach to OUD treatment. Notably, the rehabilitation center where this study was conducted was able to identify those who reported symptoms of depression on the PHQ-9. Incidentally, the PHQ-9 is not a standard form completed by patients undergoing treatment for opioid use at this center. Participants who identified depressive symptoms using the PHQ-9 received appropriate treatment for depression during the study. This concurrent treatment could have influenced the depression outcomes. However, both the PBM treatment group and control groups received the same adjunctive care if depression symptoms were identified. A need for further analysis was not indicated.

When comparing the treatment and control groups, the findings provided compelling evidence for the effectiveness of tPBM therapy in conjunction with standard care over the standard care-only condition, reinforcing the potential of tPBM as a valuable addition to the existing OUD treatment modalities. The lack of significant changes in craving intensity, time, frequency, overall opioid craving, PHQ-9 total, and difficulty scores in the non-PBM group underscores the unique contribution of tPBM therapy beyond standard care practices.

However, these findings must be interpreted within the context of the study's limitations, including its relatively small sample size and dropout rate, which may affect the generalizability of results. The pilot nature of this study and the specific demographic profile of the participants, primarily males, individuals who were identified as white, and those employed full time, suggest that further research is needed to explore the efficacy of tPBM in a broader spectrum of individuals with OUD. It is important to note that, while this study lacked diversity in its sample, opioid use disorder was more prevalent in white males,[15,17] lending to potentially better generalizability. In addition, the potential influence of standard care received by both groups, which included counseling, medication assisted-therapy, and regular support group meetings, is a conceivable confounder in this study.

Future studies should aim to replicate these findings in larger, more diverse cohorts, and employ randomized controlled trial designs to ascertain the long-term efficacy and safety of tPBM therapy. Using a sham device would also be beneficial for ruling out placebo effects. Investigating the mechanisms underlying tPBM's therapeutic effects on OUD is crucial for optimizing treatment protocols. While these findings provide insights into the ability to use tPBM as an intervention to address the complex interplay between opioid cravings and depressive symptoms, future research should investigate the mechanisms by which tPBM influences dopamine-related pathways, as suggested by previous studies on neuropsychiatric conditions.

In conclusion, this study significantly contributes to the growing evidence supporting the efficacy of tPBM therapy in reducing opioid cravings and depression symptoms among individuals undergoing treatment for opioid use disorder. Further research with larger, more diverse cohorts is warranted to validate these findings. Presenting a noninvasive, safe, and potentially effective therapeutic alternative, PBM therapy has emerged as a promising strategy for enhancing the outcomes of OUD treatments.[18] Its capability to address both the physiological cravings and psychological aspects of addiction underscores the critical need for innovative and holistic approaches to combat a crisis that has deeply affected numerous communities worldwide, especially those in the state of West Virginia.

Integrating tPBM therapy as an adjunctive therapy in current OUD treatment practices could provide a complementary approach, potentially amplifying the benefits for those grappling with the dual challenges of addiction and associated mental health issues.[13,14,18] The absence of adverse effects among the study participants underscores tPBM safety, reinforcing its suitability for widespread clinical application.

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Authors' Contributions

J.F..: Conceptualization, investigation, writing—original draft, writing—review and editing, formal analysis, visualization, supervision, and project administration. K.W.H.: Conceptualization, methodology, formal analysis, resources, data curation, writing—original draft, writing—review and editing, and supervision.

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Research data supporting this are not posted for review.

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