Transcranial Photobiomodulation Attenuates PTSD-Like Fear Memory and Remodels Hippocampal Monoaminergic Signaling in Rats

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Introduction

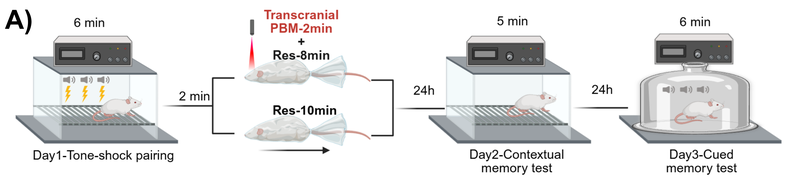
Introduction: Post-traumatic stress disorder (PTSD) involves persistent maladaptive fear memory and limited treatment efficacy. Photobiomodulation (PBM) is a noninvasive neuromodulatory approach with translational potential, but its effects in PTSD remain unclear. This study tested whether transcranial PBM reduces PTSD-like fear in rats and whether effects are linked to hippocampal bioenergetics and monoaminergic signaling.

Methods: Rats underwent tone-shock conditioning and restraint stress. PBM (810 nm, 2 min) was applied post-stress. Fear memory was assessed at early and remote time points. Hippocampal ATP, norepinephrine (NE), corticosterone (CORT), and serum markers were measured. RNA-seq was performed 5 h after PBM.

Results: PBM did not affect early contextual fear but reduced cued freezing at 24 h. PBM increased hippocampal ATP and monoamines (NE), with limited CORT changes. Transcriptomics revealed alterations in monoamine-related genes (Tph1, Htr2c, Rab38, Myo5a).

Conclusions: Transcranial PBM attenuates persistent PTSD-like fear, potentially via enhanced bioenergetics and monoaminergic modulation, supporting its promise as a scalable, noninvasive intervention for trauma-related disorders.

Results



B)

PBM Wavelength	810nm
Power	80 mW/cm^2, scalp 52 mW/cm^2, skull 40 mW/cm^2, cortex
Irradiation time	2 min
Beam area	1.5 cm^2
Pulse parameters	continuous wave

Fig.1. Experimental design and PBM parameters. A) Timeline of tone–shock fear conditioning, restraint stress, PBM treatment, contextual memory test, and cued memory test. **B)** PBM was delivered at 810 nm for 2 min under continuous-wave mode, with tested irradiance at the scalp, skull, and cortex.

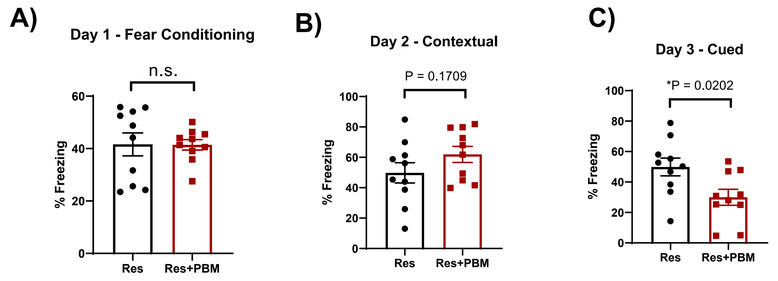
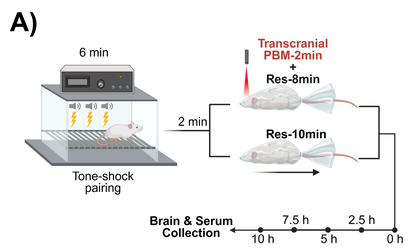
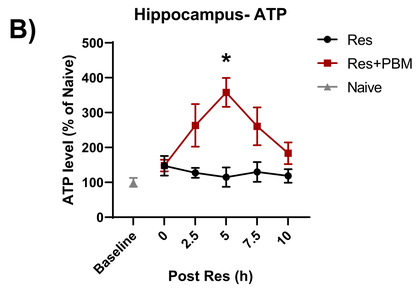
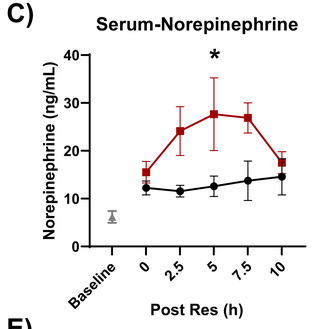
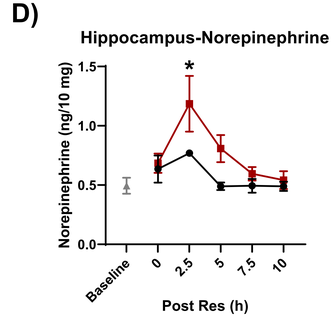


Fig. 2. PBM reduces cued fear memory. A–B) PBM did not change freezing during fear conditioning or contextual memory testing. **C)** PBM significantly reduced cued freezing on Day 3. Data are shown as mean ± SEM.









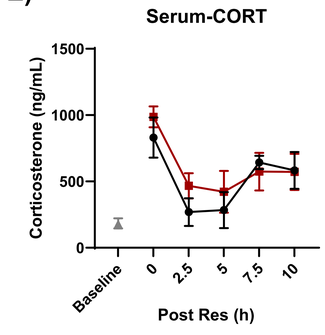
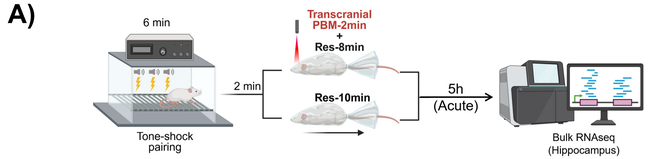
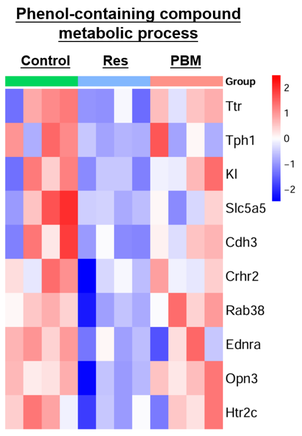


Fig. 3. PBM increases hippocampal ATP and norepinephrine. A) Timeline for biochemical sample collection after restraint stress and PBM treatment. **B)** PBM increased hippocampal ATP levels after stress. **C–D)** PBM increased serum and hippocampal norepinephrine levels. **E)** Serum corticosterone levels were measured across post-stress time points. N=4 each point, Data are shown as mean ± SEM.

Results





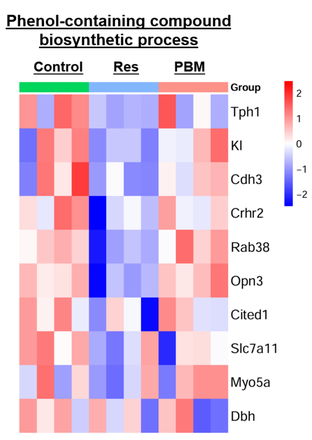


Fig. 4. PBM alters hippocampal monoamine-related gene expression. A) Timeline for hippocampal bulk RNA-seq collection. **B–C)** Heatmaps of genes enriched in phenol-containing compound metabolic and biosynthetic processes (two of the Top 10 changed GO pathways) across Control, Res, and PBM groups.

Conclusion

- **Transcranial PBM attenuated PTSD-like cued fear memory.**
- **PBM enhanced hippocampal ATP and norepinephrine levels.**
- **PBM altered hippocampal monoamine-related transcriptional profiles.**

Acknowledgements

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