Transcranial Photobiomodulation: A Simulation-based Light Dosimetry Study Across Lifespan

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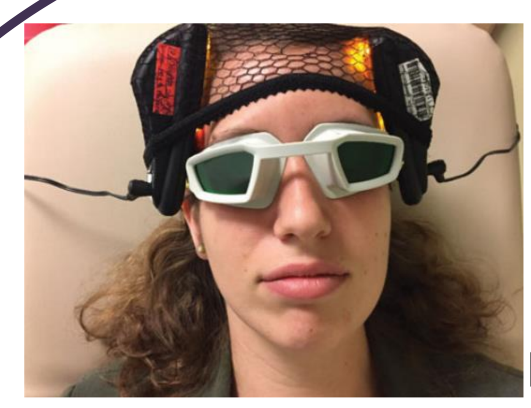
1. Introduction

1. According to National Institute of Health (NIH), 17.3 million US adults suffered from major depressive disorder (MDD) in 2017. However, 35% of the patients did not receive any treatment.
2. Frequent relapses of the cognitive therapy and burdensome side effects of antidepressant are the two major challenges for MDD treatment.
3. Transcranial photobiomodulation (t-PBM) which shines near-infrared (NIR) and red light on head is a promising technique that provides effective and safe MDD treatment.



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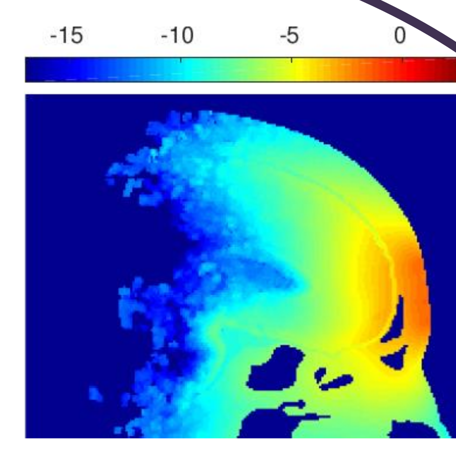


4. Previous studies have performed Monte Carlo simulation on a single head model and quantify the light dosage in different brain regions [2].
5. The increasing needs in personalized therapy require a more precise treatment strategy for each patient. The variation in brain and the extra-cerebral tissues (ECT) across lifespan has significant impact on the light delivery.
6. In this study, a 4-layer head model is employed for 18 selected age groups using data from MRI atlas database in order to quantify the light dosage across lifespan.

2. Materials and methods

Data source and selection

- USC Neurodevelopmental MRI database (https://jerlab.sc.edu/projects/neurodevelopmental-mri-database/).
- Average atlas for age years of 5, 10, 14, 18, 20-24, 30-34, 40-44, 50-54, 55-59, 60-64, 65-69, 70-74, 75-79, 80-84 and 85-89 are selected in the study.

4-layer segmentation

- A whole head model contains 4 layers: white matter (WM), gray matter (GM), cerebrospinal fluid (CSF) and extra-cerebral tissue (ECT).
- An adaptive threshold is applied to the probabilistic segmentations of WM and GM to match the average volume of a certain age population (Fig. 1).
- A uniform threshold 0.5 is used for CSF.
- BETSURF is used to segment the skull and scalp from the T1w MRI image. Skull and scalp are merged to ECT layer.

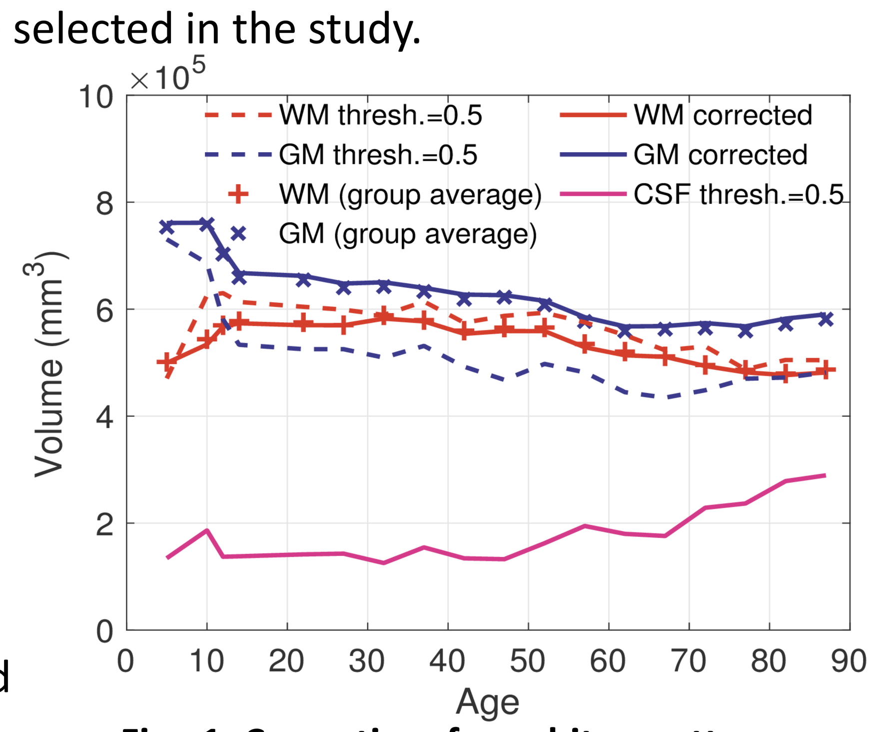


Fig. 1 Correction for white matter, gray matter and cerebrospinal fluid.

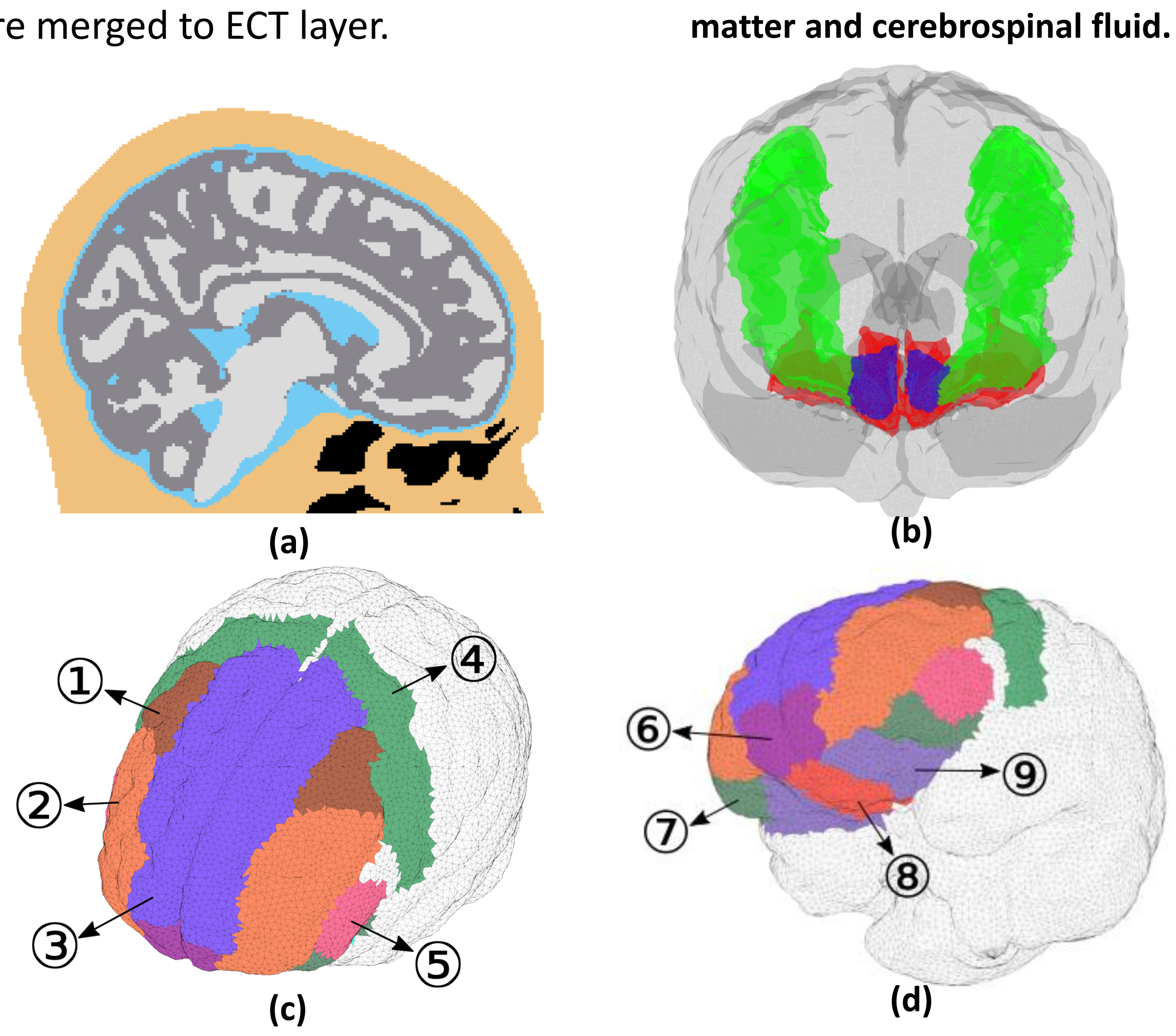


Fig. 2 (a) Representative 18-0 years old 4-layer model, including WM (light gray), GM (gray), CSF (blue), extra-cerebral tissues (ECT, orange). Black regions indicate air cavities. (b) Green regions are dorsolateral prefrontal cortex (dlPFC) and red regions are ventromedial prefrontal cortex (vmPFC). The frontal pole is indicated by blue color. (c) and (d) The parcellations used: 1-caudal middle frontal gyrus, 2-rostral middle frontal gyrus, 3-superior frontal gyrus, 4-precentral gyrus, 5-pars triangularis, 6-frontal pole, 7-pars orbitalis, 8-medial orbitofrontal cortex, 9-lateral orbitofrontal cortex.

Air cavities segmentation

- Frontal and sphenoid sinuses are segmented using ITK-SNAP software (Fig. 2(a)).
- Nasal and pharyngeal cavities are segmented using k-means algorithm.

Brain parcellations and target regions

- Freesurfer "recon-all" command is used to generate Desikan-Killiany parcellations (Fig. 2(c) and (d)).
- Dorsolateral prefrontal cortex (dlPFC): caudal middle frontal gyrus and rostral middle frontal gyrus; ventromedial prefrontal cortex (vmPFC): medial orbital frontal cortex and lateral orbital cortex (Fig. 2(b)).

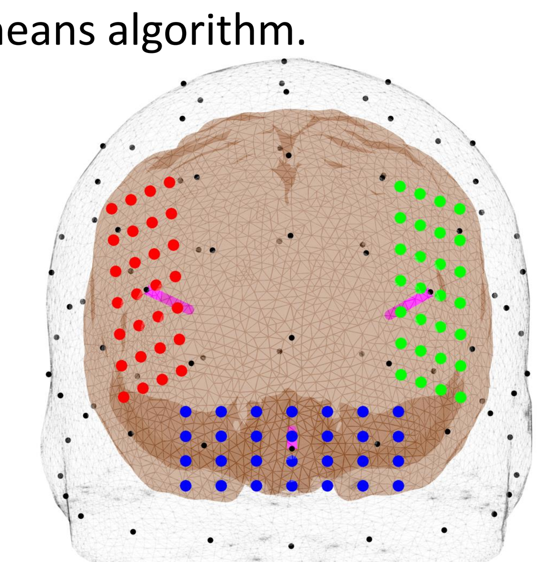


Fig. 3 Source positions: F3-F4 (green and red) and Fpz (blue).

Table 1: Light source descriptions

Manufacturer	Photomedex		
Model identifier	Omnilux New-U		
Emitter	4x7 LED array		
Location (10-20 system)	F3-F4 for dlPFC; Fpz for vmPFC (Fig. 3)	Area irradiated [cm^2]	28.4x2 for F3-F4; 28.4 for Fpz
Wavelength [nm]	670, 810, 850, 980, 1064	Irradiance	30; 300 mW/cm^2
Pulse mode	Continuous wave	Application	t-PBM

Results

Energy deposition at different parcellations over age

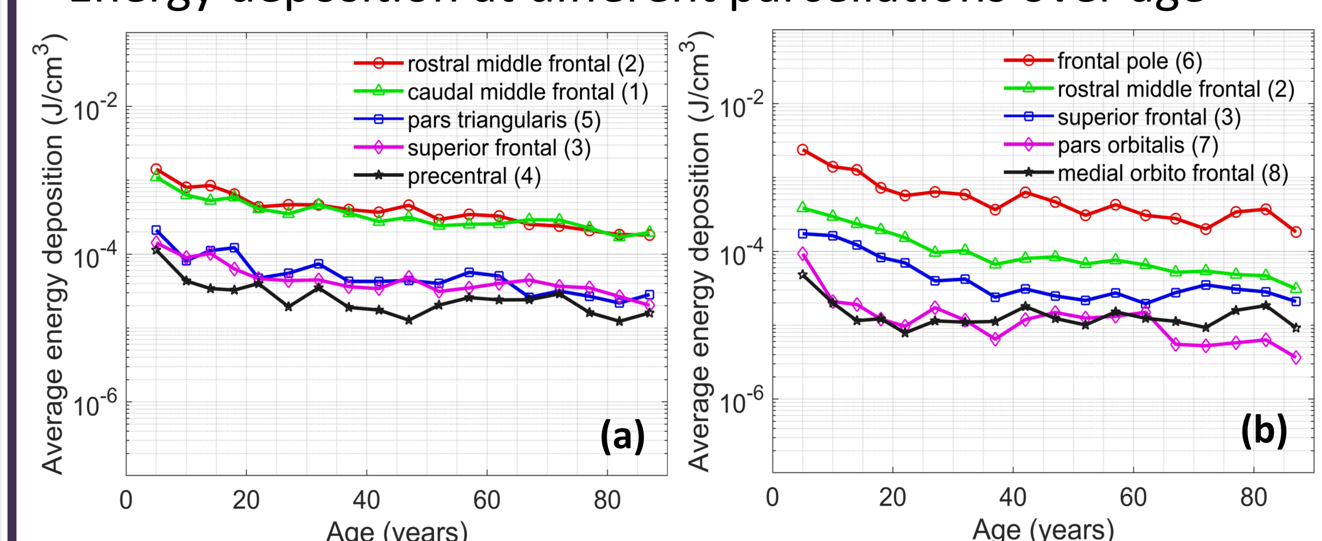


Fig. 4 Energy deposition for parcellations with top 5 energy deposition. (a) F3-F4 position. (b) Fpz position. 810 nm is used. The numbers correspond to the regions in Fig. 2(c)(d).

- From result no shown, 810 nm delivers most energy compared to others over age.
- For F3-F4 position, rostral middle frontal gyrus and caudal middle frontal gyrus that compose dlPFC receive approximately 10-fold more energy than others.
- For Fpz position, the first 4 parcellations are not included in vmPFC.

Energy deposition at dlPFC/vmPFC and treatment exposure time

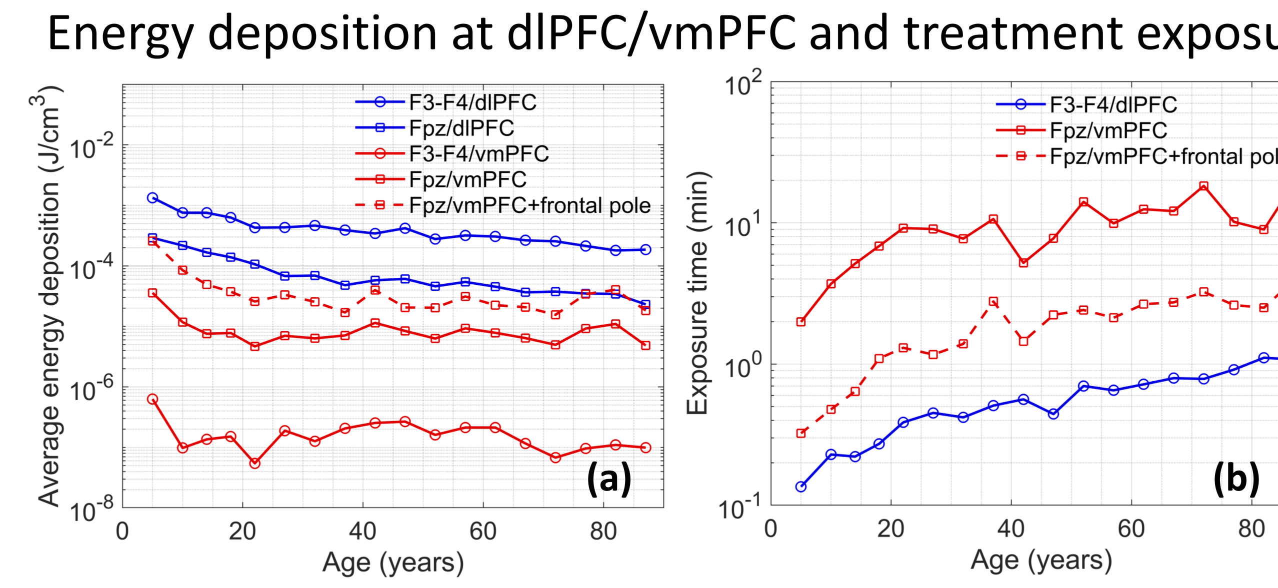


Fig. 5 (a) Average energy deposition using 810 nm and (b) corresponding exposure time to achieve the effective fluence of 3 J/cm^2 at the region of interest. The irradiance is 300 mW/cm^2 (Table 1).

- Decreases in energy deposition can be observed for all source/region pairs as age increases. Stronger decrease can be found in younger age especially at vmPFC.
- Fpz position targeting vmPFC is less efficient than F3-F4 position targeting dlPFC.
- An average 4-fold increase is observed with the addition of frontal pole to vmPFC.
- Exposure time increases with age. The exposure time for Fpz/vmPFC is around 10-20 min after 20 years old while it is less than 2 min for F3-F4/dlPFC.

Relationship between ECT thickness and energy deposition

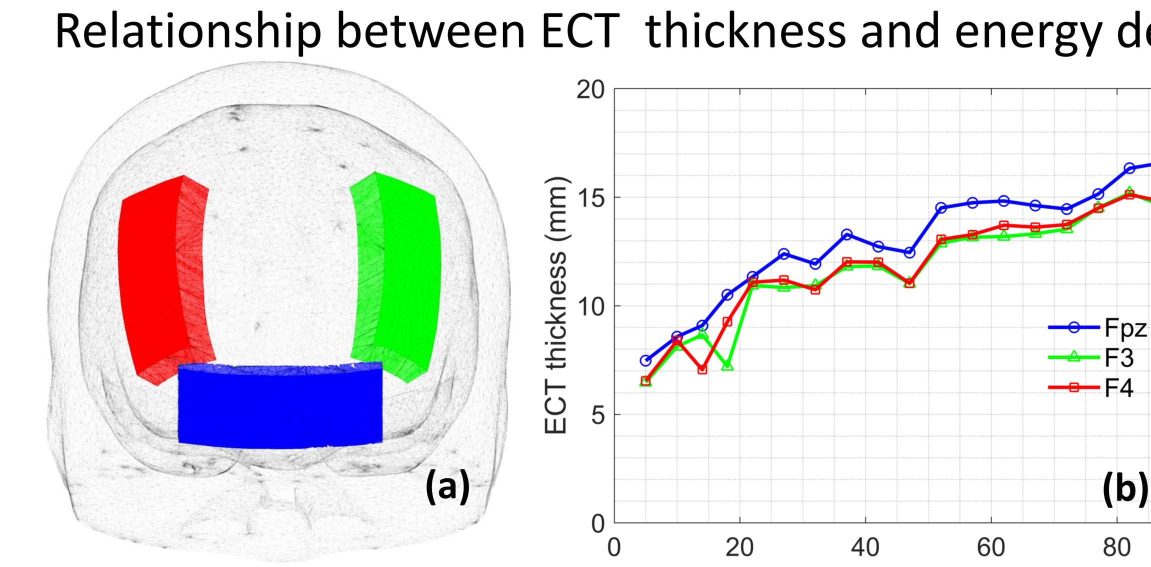
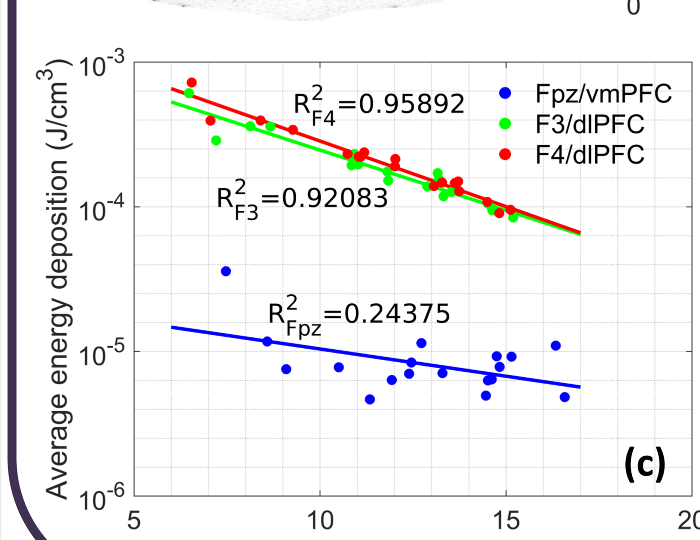


Fig. 6 (a) The ECT region for computing the ECT thickness. (b) ECT thickness across age. (c) Relationship between the ECT thickness and energy deposition at dlPFC and vmPFC. Green, red and blue represent F3, F4 and Fpz position respectively.



- The ECT thickness increases as age increases. ECT thickness under Fpz position is larger than F3 and F4.
- For F3 and F4 positions, strong linearity (R^2>0.9) is found between log-scale energy deposition at dlPFC and ECT thickness, explained by Beer-lambert law.
- For Fpz position, weak linearity is found due to the fact that vmPFC is located under cerebral hemisphere.
- The increased ECT thickness is primarily responsible for the energy decrease for F3-F4 positions.

Conclusions

- 810 nm delivers highest energy over age.
- Energy deposition decreases across lifespan regardless of positions and parcellations.
- Fpz/vmPFC is less efficient than F3-F4/dlPFC.
- Exposure time of Fpz/vmPFC is over 10-fold longer than F3-F4/dlPFC.
- The increased ECT thickness causes the decrease of energy deposition of F3-F4 position.

References

[1] Cassano P, Petrie S R, Mischoulon D, et al. Transcranial photobiomodulation for the treatment of major depressive disorder. The ELATED-2 pilot trial[J]. Photomedicine and laser surgery, 2018, 36(12): 634-646.

[2] Cassano P, Tran A P, Katnani H, et al. Selective photobiomodulation for emotion regulation: model-based dosimetry study[J]. Neurophotonics, 2019, 6(1): 015004.

Acknowledgement

This research is supported by National Institutes of Health (NIH) grants # R01-GM114365, R01-CA204443 and R01-EB026998.