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Electrophysiological Effects of Transcranial Infrared Laser Stimulation

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Electrophysiological Effects of Transcranial Infrared Laser Stimulation

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Abstract

Electrophysiological Effects of Transcranial Infrared Laser Stimulation

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Transcranial Infrared Laser Stimulation (TILS) is a non-invasive intervention that has been found to modulate mitochondrial respiration and cellular functions in brain neurons. In healthy adults, eight minutes of TILS to the right prefrontal cortex has been shown to improve memory and attention. However, little is known about what electrophysiological effect TILS has on the brain. Thus, the objective of this study was to map and image electrophysiological effects in the cerebral cortex during and after TILS to the right prefrontal cortex. A transcranial infrared laser beam at 1064 nm was used on healthy human adult participants. Participants were randomly assigned to one of two conditions, which they were blind to: TILS to the right side of the forehead, or a sham TILS treatment. The participants' electrophysiological oscillations were recorded from the scalp using 64-channel electroencephalograms (EEG) with eyes closed during a 5-minute baseline, 8-minute TILS or sham treatment, and five-minute post-treatment recording. The results show that TILS significantly increased the density of alpha and beta waves as compared to sham, with the largest increases seen in the alpha waves.

Increases in alpha and beta waves were seen bilaterally in anterior and posterior regions of the brain. Changes were dose-dependent but did not continue after the TILS treatment ended. The results from this study help us to further understand the mechanistic link between photobiomodulation and the cognitive enhancing benefits from TILS and can help guide future clinical applications of TILS.

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Chapter 1: Introduction

Transcranial Infrared Laser Stimulation (TILS) is a form of photobiomodulation, a process that uses nonthermal light, including low-power lasers and light emitting diodes (LED), to modulate cellular functions in neurons and other cell types (Rojas and Gonzalez-Lima, 2011). Photobiomodulation is safe and non-invasive and has been shown to be an effective therapy for a number of medical conditions, including certain types of pain (Colter et al., 2015), arthritis (Brosseau et al., 2004), stroke and traumatic brain injury (Naeser et al., 2011). TILS specifically has been found to improve cognitive function in adults (Barrett and Gonzalez-Lima, 2013; Gonzalez-Lima and Barrett, 2016; Blanco, Saucedo, and Gonzalez-Lima, 2017; Blanco Maddox, and Gonzalez-Lima, 2017).

TILS works by increasing mitochondrial energy metabolism and cerebral hemodynamics (Wang et al., 2017). An infrared, nonthermal light is aimed at the forehead, passes through the skin and skull and is received by neurons in the cerebral cortex, around 3 cm below the scalp (Tedford et al., 2015). Mitochondria in the neurons absorb the light, which causes the up-regulation of the enzymatic activity of cytochrome-c-oxidase (CCO). CCO is the rate limiting step in ATP production, so increasing the upregulation of CCO leads to an increase in neuronal metabolic capacity by way of increased production of ATP, as well as increased supply of oxygenated blood (Wong-Riley et al., 2005; Rojas and Gonzalez-Lima, 2013; Wang et al., 2017).

In healthy adults, 8 minutes of TILS using a 1064 nm laser has been shown to improve memory and attention, including prefrontal based working memory (Barrett and Gonzalez-Lima, 2013), rule-based category learning (Blanco, Saucedo, and Gonzalez-

Lima, 2017), and sustained attention (Blanco, Maddox and Gonzalez-Lima, 2017). Though it is understood how TILS affects energy metabolism of neurons and cerebral hemodynamics, very few studies have examined how TILS affects electrical activity in the brain. A first study used 8-channel EEG recording taken with closed and open eyes in 6 participants before, during and after TILS. Participants underwent 10 minutes of TILS at 1064 nm, continuous wave laser with a power density of 250 mW/cm_2 and they found that TILS increased alpha, beta and gamma waves in the brain, though the largest increases were seen in alpha waves (Vargas et al., 2017). However, in this first study, there was no sham control and participants were not blind to treatment. A second study completed analysis of 20 participants that received 11 minutes of TILS from a 1064 nm, continuous wave laser with a power density of 162 mW/cm2. In that study, a 64-channel EEG recording with open eyes was taken before, during and after TILS treatment and found that TILS showed significant increases of alpha and beta frequency bands (Wang et al., 2019). However, participants received both sham and TILS conditions on the same day, with sham taken first, followed by TILS. Without a randomized design, it is not possible to rule out sequence effects on the observed EEG changes. The 162 mW/cm2 power density in this second study was also lower than the 250 mW/cm_2 used in all previous sham-controlled TILS studies that have shown augmented cognitive functions (Barrett & Gonzalez-Lima, 2013; Hwang, Castelli, & Gonzalez-Lima, 2016; Blanco, Maddox, & Gonzalez-Lima, 2017; Blanco, Saucedo, & Gonzalez-Lima, 2017; Holmes et al., 2019). To avoid falling asleep during EEG recordings, the participants in the second study had their eyes open.

However, to investigate TILS effects thoroughly on alpha waves, it is important to record with the eyes closed to permit measurement of stronger alpha waves (Wang et al., 2019).

To overcome the limitations of the previous two studies, the aim of the present study was to map thoroughly EEG effects of 250 mW/cm^2 TILS vs. sham on brain waves under eyes-closed resting conditions. Our main research question was: Does TILS significantly change cortical electrical oscillations in the human brain using a randomized sham-controlled design with eyes closed? Based on the two previous TILS-EEG studies, we hypothesized that TILS would significantly change the electrical waves and that we would specifically see an increase in alpha and beta frequency bands. To investigate this, we took 64-channel EEG recordings before, during and after the administration of a 1064 nm continuous wave laser with a power density of 250mW/cm^2 to the right side of the forehead using a randomized between-subject, sham-controlled design with participants blind to treatment.

Chapter 2: Methods

Participants

A total of 14 healthy participants were recruited from the University of Texas at Austin, including students from the student subject pool and graduate students, staff and faculty volunteers. Participants had an average age of 23.78 years, 11 were female and 3 were male. Eight participants were Hispanic, 2 were Asian, and 12 were Caucasian. Exclusion criteria included: (1) under 18 years old, (2) pregnant, (3) administration of any TILS up to 14 days prior, and (4) wearing wigs, hair extensions or braids that could not be removed for the duration of the experiment. No interested potential participants met any of the exclusion criteria. The study protocol was approved by the Institutional Review Board (IRB) at the University of Texas at Austin and informed consent was obtained from all participants prior to the start of the experiment. Participants from the student subject pool received course credit as compensation for their time.

Study Design

The experiment used a single-blinded, sham-controlled design. Participants were randomized into one of two groups, described in detail below, for their initial visit: TILS or sham. A total of 16 EEGs were collected, thus 2 participants were run through both conditions and there was a minimum of 2 weeks in between each condition for each participant. An a priori statistical power analysis was performed using G*Power3 (Faul et al., 2007) to test the difference between two group means using a two-tailed, independent

T-test, a medium effect size (*d*=0.6) and an alpha level of 0.05. The results showed that a sample size of 45 participants in each group would be required to achieve a power of 0.8.

EEG Equipment

The EEG data were collected using a 64-channel biopotential measurement system (ActiveTwo, Biosemi, The Netherlands). The reference channel used was channel 48, Cz. Each participant wore an EEG head cap with 64 electrodes positioned according to the standard 10-10 electrode placement. Because the laser light cannot penetrate the EEG cap, the cap was pushed back to the participants' hairline, as placed by Wang et al., (2019). The average forehead size of 19 to 21 year olds is 58.3 ± 6.6 mm for women and 61.4 ± 9.7 mm for men (Sirinturk et al., 2017), so although individual forehead sizes vary we can estimate that the cap was pushed back approximately 58.3 to 61.4 mm.

TILS Equipment

A 1064-nm continuous-wave (CW) laser supplied by Cell Gen Therapeutics, LLC (Model CG-500 laser, HD Laser Center; Dallas, Texas, United States) was used in this study. The laser had a uniform, circular beam area that measured 13.6 cm^2 and had a measured power output of 3.4 W. This Food and Drug Administration (FDA) has cleared this device as safe for human use for muscle or joint pain, wound healing, improving circulation and improving muscle aches. The laser was administered to the right side of the forehead which was exposed to a power density of 250 mW/cm^2 (3,400 mW/13.6 cm^2 = 250 mW/cm^2) and energy density of 120 J/cm^2 for 8 minutes. Previous research by Barrett and Gonzalez-Lima (2013) has shown that only 1-2% of laser treatment passes through the frontal bone and reaches the cortical surface of the brain, so approximately 1.2-2.4 J/cm^2 actually reaches the cortical surface. These specific parameters were chosen because of the significant cognitive benefits they showed in our previous studies (Barrett and Gonzalez-Lima, 2013; Blanco, Saucedo, and Gonzalez-Lima, 2017; Blanco, Maddox, and Gonzalez-Lima, 2017). The University of Texas at Austin Laser Safety Program approved the laser and the laser operating procedure, and the Laser Safety Officer approved the room the laser was used in. During both the sham and TILS treatments, both the experimenter and the participant remained inside the locked laser room and a sign was placed on the outer door of the room indicating that the laser was in use. Because the laser could damage eye tissue if shone into the eye, both the experimenter and participant wore protective eyewear (900-1000nm: 5+, 1000-2400 nm: 7+; 2900-10600 nm: 7+) at all times and the participant was instructed to keep their eyes closed for the duration of the experiment.

Intervention Procedures

For those in the sham condition, the laser machine was turned on and participants could hear the fan of the machine whirring. The laser itself was never turned on. The experimenter pointed the turned-off laser at the right side of the participants forehead, like he or she would if the laser was turned on, for a duration of 8 minutes. This would prevent the participants in the sham condition from knowing which condition they were in if they opened their eyes against the experimenter's instructions.

Experiments consisted of a five-minute baseline period, an eight-minute TILS or sham treatment period, and a five-minute post-treatment period, for a total length of 18 minutes. The EEG device recorded all 64 channels continuously throughout the 18 minutes. After the experiment was over, participants were asked if they would be interested in returning for a second, optional session after 2-weeks, but only two participants agreed to this.

Data Analysis Plan

All EEG data were pre-processed using the EEGLAB toolbox (Delorme and Makeig, 2004) on the MATLAB platform (MATLAB, 2019). First, the data were visually examined, and any obvious movement artifacts, like from eye blinks, eye movement and jaw movement, were removed. Next, each of the raw time-series was bandpass filtered between 0.5 and 70 Hz and then notch-filtered to remove any 60 Hz noise. Finally, we ran an independent component analysis (ICA), which identified different components. These components were visually inspected and any components that represented movement artifacts were removed from the data. The common mean among the 64 electrodes was used as the reference for the 64-electrode EEG data.

After pre-processing, the data were analyzed in two ways. We used a power spectral density (PSD) analysis in order to compare our results to the findings in Vargas et al. (2017). We also ran a power density analysis calculated using the root mean square of the time series, which is the analysis used in Wang et al., (2019). For the PSD analysis, the baseline data were analyzed with a native function, ‘pwelch’, in MATLAB (MATLAB, 2019) to calculate the power spectral density estimate for 8 electrodes for both the TILS and sham group. The eight electrodes used in the analysis included fp1, fp2, t7, t8, p3, p4, o1 and o2. Those electrodes were selected in order to represent samples from the right and left side of the frontal, temporal, parietal and occipital lobes. We verified there were no significant baseline differences between sham and TILS groups with the two-sample T-Test, two-tailed $p<0.01$ after a false discovery rate (FDR) correction.

Then a power density analysis using the root mean square of the time series was run on both TILS and sham EEGs to compute the average band power of delta (0-4 Hz), theta (4-7 Hz), alpha (7-12 Hz), beta (12-30 Hz), and gamma (over 30 Hz) for each channel during each minute of the EEG across both the sham group and the TILS group. A hamming window was used to correct any edge effects in the band-pass filtering. From these data, 64-channel, time-dependent power density vectors were created for both the sham and the TILS experiment for 8 minute of laser (P_{TILS}) or sham administration (P_{sham}), and 5-minute post-treatment period (P_{post}). A baseline power density vector (P_{base}) was also created based on the last 4 minutes of baseline data. Power values for each EEG recording were compared to the first 4 minutes of baseline of that specific EEG, in such a way that the power in each minute after the start of the laser or sham administration (i.e. minutes 6-18) was divided over the power of the baseline. This resulted in each EEG being calibrated using its own baseline. We then examined at each spectral band delta through gamma and calculated the mean difference of that band power subtracting the sham from TILS. Mean differences were calculated for each minute during laser or sham administration (minute 6 through minute 13) and during the post-treatment period (minute 14 through minute 18). We then performed a two-sample T-test between mean TILS and sham in temporal sequence, with a statistical significance level of two-tailed $p<0.01$ to reduce the probability of error from chance. Effect sizes were calculated for the group differences using Cohen's *d* (Cohen, 1988) and were displayed on topographical maps.

Topographical, 2-D maps were computed using the topoplot function in EEGLAB to visualize both the results of the mean difference analysis for each spectral band and the two-sample T-Test. For the mean difference analysis, topoplot showed us the percent change from the sham group to the TILS group. For the T-test, topoplot showed us the electrodes that were statistically significant at each minute of TILS treatment and the post-treatment recovery period.

Chapter 3: Results

PSD Analysis of Baseline Data

Results from the PSD analysis for baseline data at each of the eight electrodes (fp1, fp2, t7, t8, p3, p4, o1 and o2) are shown in Figure 1 below. The blue line represents data from the sham group and the orange line represents data from the TILS group. The graphs show that the data have a normal, expected curve across 8 different areas of the brain at resting-state baseline, with no significant group differences at two-tailed $p<0.01$ after an FDR correction.

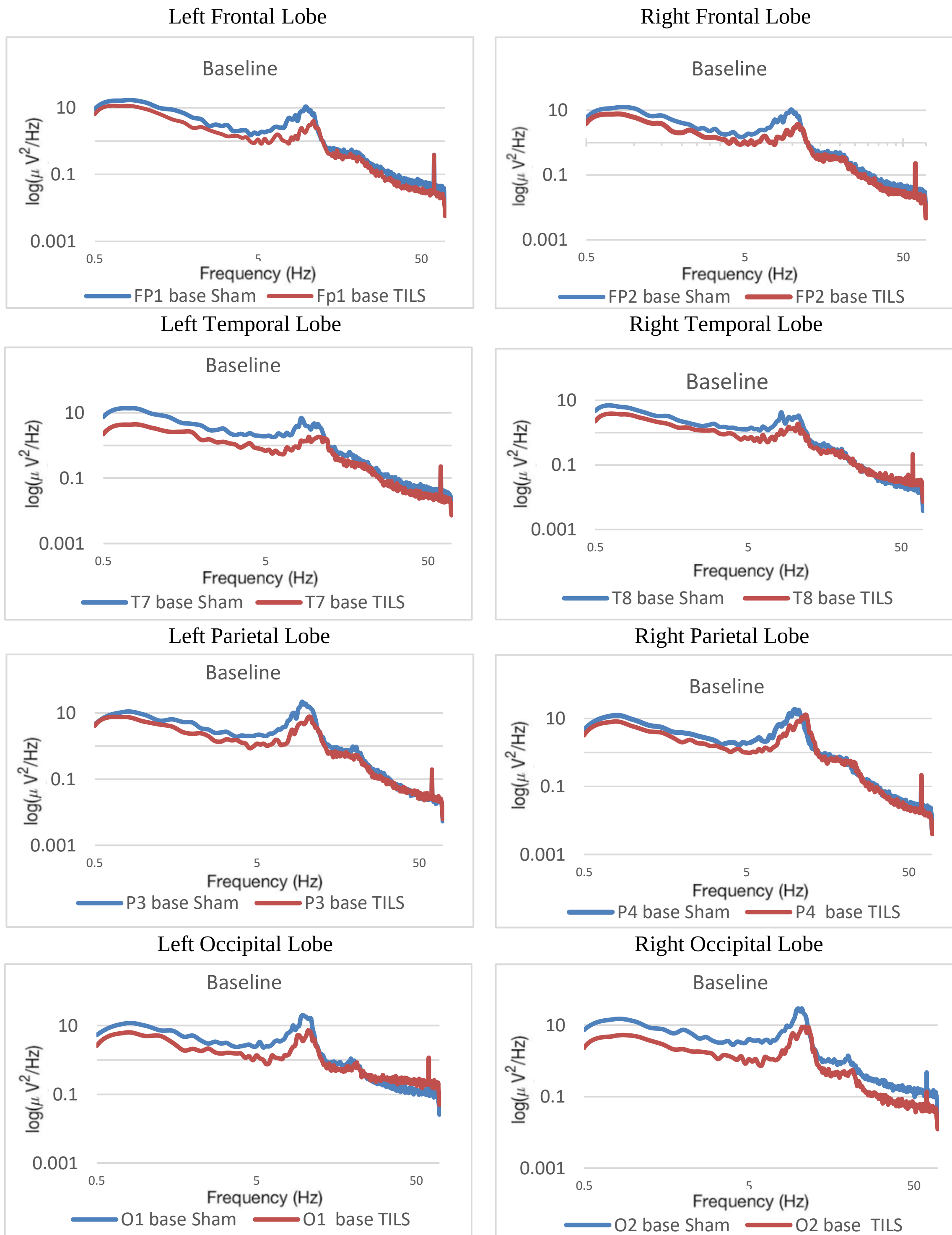


Figure 1: Baseline PSD analysis results.

Delta Waves

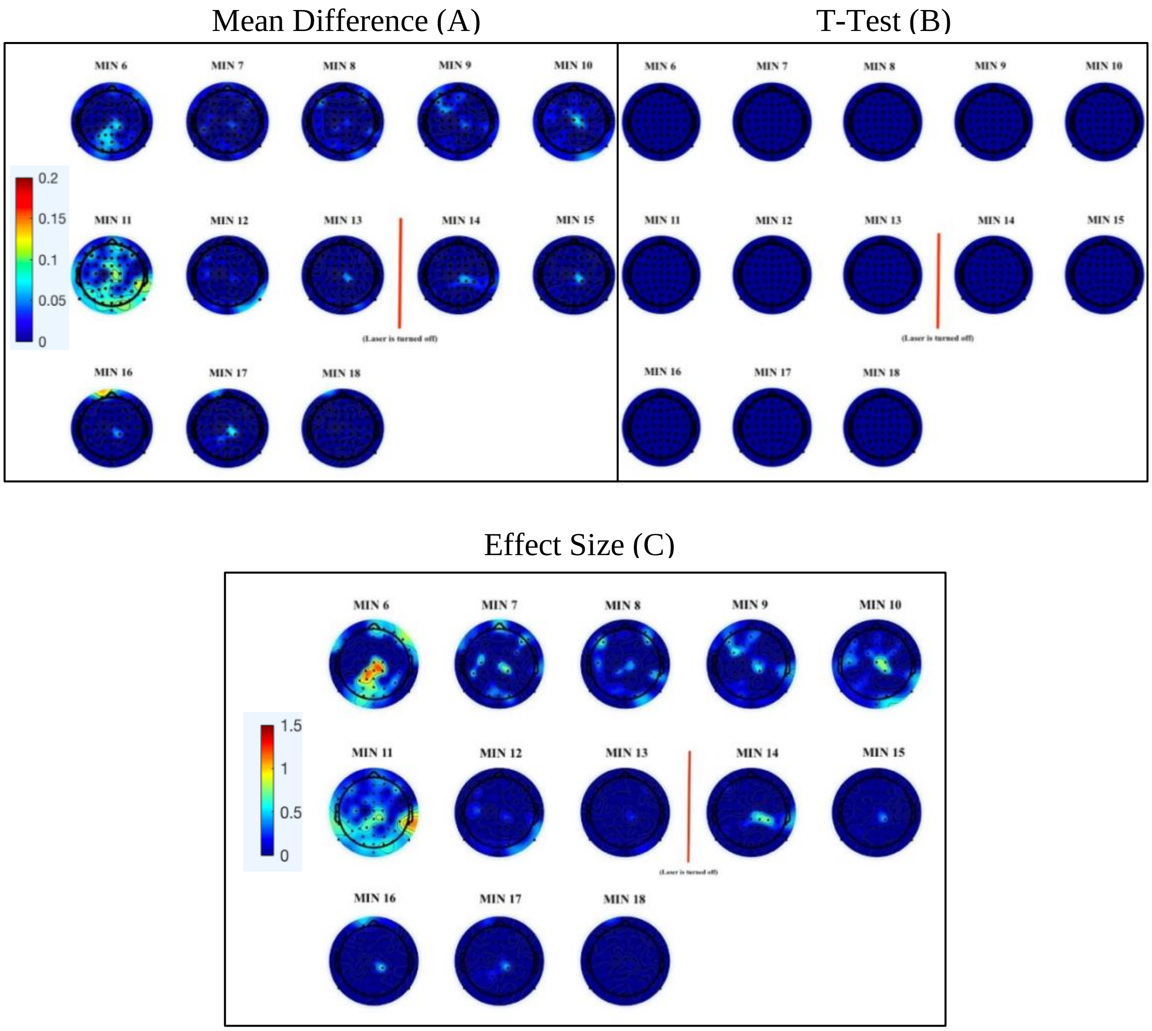
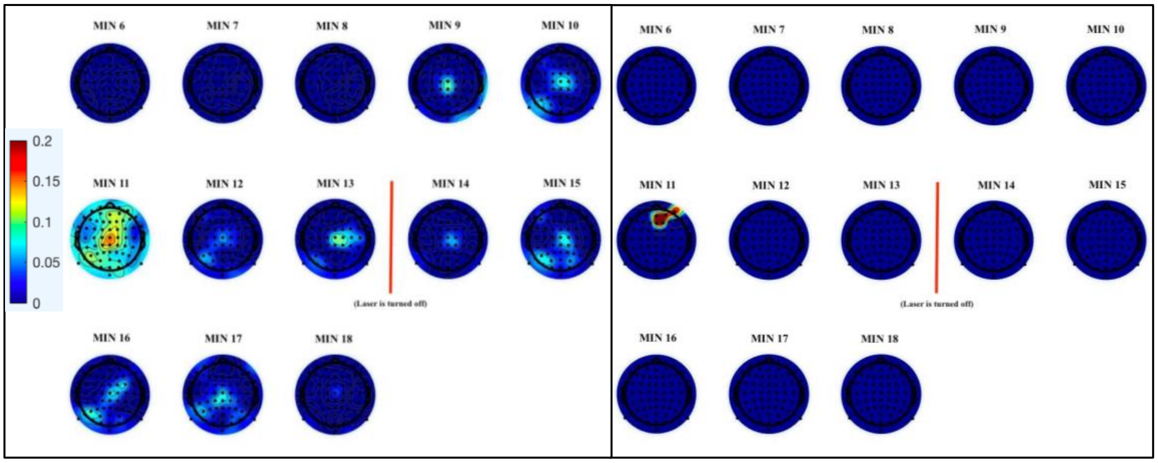


Figure 2: Delta Waves. (A) Results from the mean difference analysis of delta wave activity, subtracting sham group from TILS group. The scale shows the percent change. (B) Corresponding T-test results, where red areas represent electrodes that showed statistical significance. (C) Corresponding effect size maps.

Spatial topographies of group-level mean differences in EEG power density between TILS and sham experiments at the delta frequency band (0.5 to 4 Hz) during the 8 minutes of TILS or sham administration (minute 6 through minute 13) and 5 minutes of post-laser recovery period (minute 14 through 18) are shown in Figure 2(A). Corresponding T-test results are shown in Figure 2(B), where red areas would represent electrodes if they showed any statistical significance at two-tailed $p<0.01$. From these figures there is no statistically significant increase in delta frequency band power across TILS administration or the post-laser recovery period.

Theta Waves

Mean Difference (A) T-Test (B)



Effect Size (C)

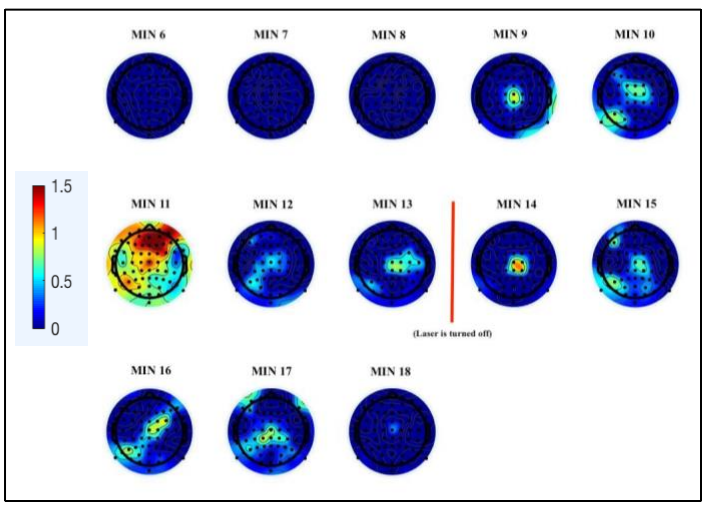


Figure 3: Theta Waves. (A) Results from the mean difference analysis of theta wave activity, subtracting sham group from TILS group. The scale shows the percent change. (B) Corresponding T-test results, where red areas represent electrodes that showed statistical significance. (C) Corresponding effect size maps.

Spatial topographies of group-level mean differences in EEG power density between TILS and sham experiments at the theta frequency band (4 to 8 Hz) during the 8 minutes of TILS or sham administration (minute 6 through minute 13) and 5 minutes of post-laser recovery period (minute 14 through 18) are shown in Figure 3(A). Corresponding T-test results are shown in Figure 3(B), where red areas represent electrodes that showed statistical significance. Like we saw in the delta frequency band, there is no clear pattern of theta wave activation across TILS administration or the post-laser recovery period. The results of the T-test are largely null, with the exception of a statistically significant increase in theta waves during minute 11.

Alpha Waves

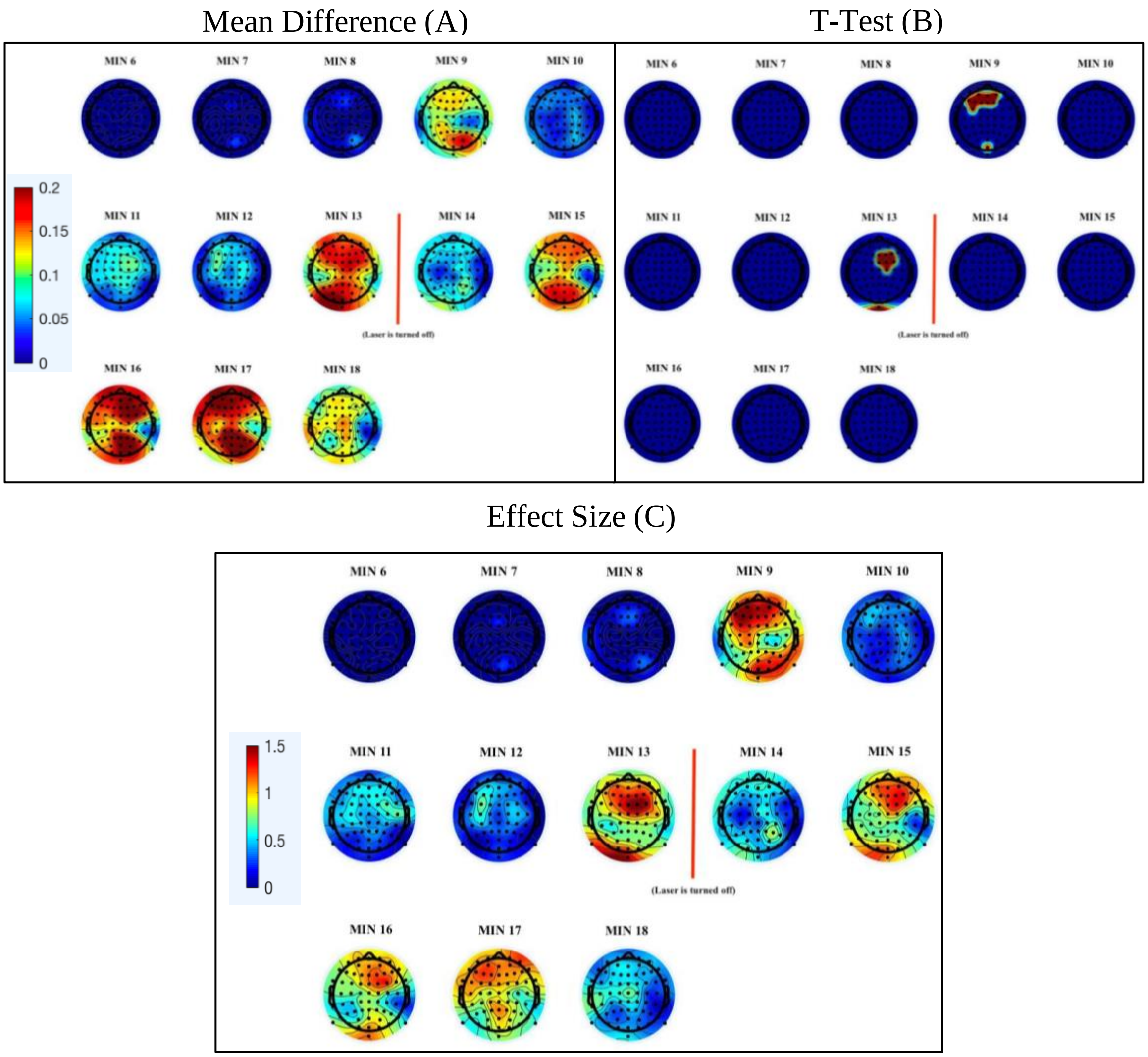


Figure 4: Alpha Waves. (A) Results from the mean difference analysis of alpha wave activity, subtracting sham group from TILS group. The scale shows the percent change. (B) Corresponding T-test results, where red areas represent electrodes that showed statistical significance. (C) Corresponding effect size maps.

Spatial topographies of group-level mean differences in EEG power density between TILS and sham experiments at the alpha frequency band (8 to 13 Hz) during the 8 minutes of TILS or sham administration (minute 6 through minute 13) and 5 minutes of post-laser recovery period (minute 14 through 18) are shown in Figure 4(A). Corresponding T-test results are shown in Figure 4(B), where red areas represent electrodes that showed statistical significance. These figures show a statistically significant increase in mean power density of alpha waves during administration of TILS, particularly in minutes 9 and 13. The increase in alpha power is bilateral and incremental and is present in both anterior and posterior areas. Though the increase in alpha power appears to continue after TILS-treatment ended, it did not reach statistical significance at the two-tailed $p<0.01$ level.

Beta Waves

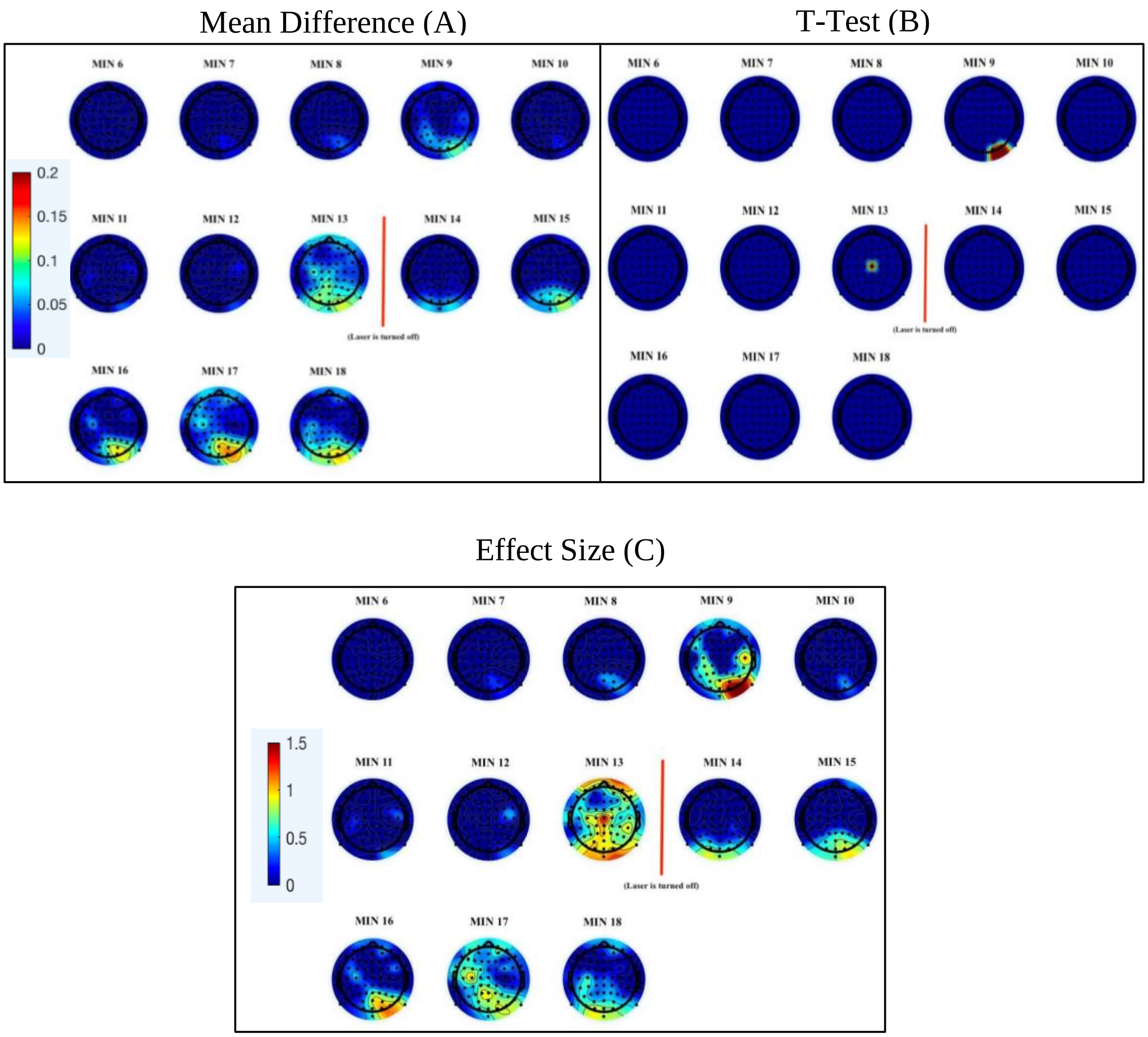


Figure 5: Beta Waves. (A) Results from the mean difference analysis of beta wave activity, subtracting sham group from TILS group. The scale shows the percent change. (B) Corresponding T-test results, where red areas represent electrodes that showed statistical significance. (C) Corresponding effect size maps.

Spatial topographies of group-level mean differences in EEG power density between TILS and sham experiments at the beta frequency band (13 to 30 Hz) during the 8 minutes of TILS or sham administration (minute 6 through minute 13) and 5 minutes of post-laser recovery period (minute 14 through 18) are shown in Figure 5(A) . Corresponding T-test results are shown in Figure 5(B), where red areas represent electrodes that showed statistical significance. These figures show a significant increase in mean beta power during administration of TILS, particularly in minutes 9 and 13. The increase in beta power is primarily localized in the posterior area of the brain. Though the increase in beta power in the posterior areas of brain appears to continue after TILS-treatment ended, it did not reach statistical significance at the two-tailed $p<0.01$ level.

Gamma Waves

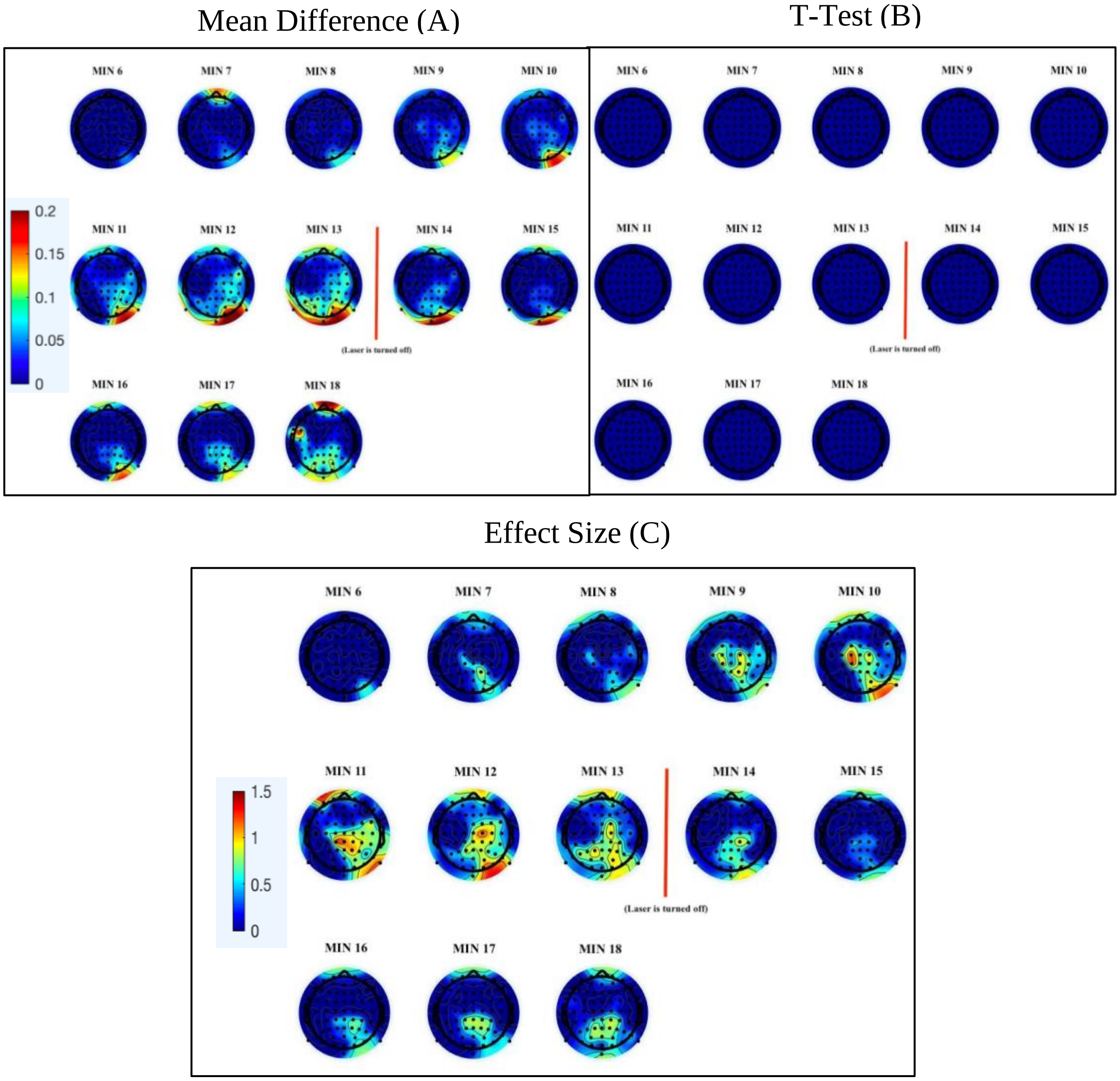


Figure 6: Gamma Waves. (A) Results from the mean difference analysis of gamma wave activity, subtracting sham group from TILS group. The scale shows the percent change. (B) Corresponding T-test results, where red areas represent electrodes that showed statistical significance. (C) Corresponding effect size maps.

Spatial topographies of group-level mean differences in EEG power density between TILS and sham experiments at the gamma frequency band (30 to 70 Hz) during the 8 minutes of TILS or sham administration (minute 6 through minute 13) and 5 minutes of post-laser recovery period (minute 14 through 18) are shown in Figure 6(A). Corresponding T-test results are shown in Figure 6(B), where red areas would represent electrodes if they showed any statistical significance at two-tailed $p<0.01$. These figures show a bilateral increase in mean gamma power, particularly in the right posterior area of the brain in minutes 10 through 12, however this increase did not reach statistical significance.

Chapter 4: Discussion

This study found that 8 minutes of TILS administered to the right forehead increased the power of alpha and beta waves during laser stimulation, particularly at minute 4 and minute 8 of laser stimulation. The findings of this study shed light onto how TILS affects electrophysiological activity in the brain, as well as help us understand the biological underpinnings of how TILS acts to produce cognitive enhancement in humans.

This study found the strongest effects of the TILS treatment to be on the alpha waves, as found by the previous two TILS-EEG studies (Vargas et al., 2017; Wang et al., 2019). Thus, TILS is able to consistently potentiate alpha power whether the eyes are open or closed, whether sham immediately precedes TILS or they are randomized 2-weeks apart, whether lower or higher laser power is applied, and whether 8, 10 or 11 minutes of total simulation are given. The increase in alpha wave power is dose-dependent because as time passes the radiant energy (Energy = Power x Time) increases in a dose-dependent manner over time, becoming statistically significant at minute 4 and minute 8 of the laser. The increase in alpha activity also appears to be bilateral, despite only the right side of the forehead being stimulated. The mean difference analysis of alpha waves shows an increase of alpha wave activity spreading globally throughout the brain surface both during and after TILS treatment, though the T-test analysis reveals that only the anterior and posterior areas of the brain reached statistical significance and the increase in activity was not statistically significant after the laser treatment ended. These findings replicate previous findings by Vargas et al. (2017) and Wang et al. (2019), who also found alpha wave power to increase during TILS administration following the same pattern.

Together, these findings also reveal potential neurobiological mechanisms of the cognitive enhancing effects of TILS. Alpha band frequencies are associated with a wakeful but relaxed state and play a role in attention and the synchronization of brain activity in different frequencies (Ray and Cole, 1985; Klimesch, 2012). In the domain of attention, alpha-band oscillations have been shown to support inhibitory filtering during information processing, a process that suppresses task-irrelevant information and competing processes and neuronal structures, while keeping target information activated (Klimesch et al., 2007; Klimesch, 2011; Vijayan and Kopell, 2012). A person with a highly efficient filter would excel at target detection and discrimination tasks, as task-irrelevant information is inhibited and they are able to better focus on the present task and stimulus. This inhibitory filter would be important in a task like a delayed-match-to sample (DMS) task, which involves holding a given stimulus in short-term memory and then identifying that stimulus from other similar stimuli that were not presented before. TILS has been shown to improve performance on the DMS in healthy college-aged adults (Barrett & Gonzalez-Lima, 2013; Holmes et al., 2019). Alpha-band frequencies are also associated with anticipatory and temporal attention (Klimesch, 2012). These types of attention involve anticipating a stimulus and focusing on the time point of its appearance. Both anticipatory and temporal attention are heavily involved in the psychomotor vigilance task (PVT), which is a task that measures sustained attention and reaction time by having participants respond to a visual stimulus. Performance on the PVT has also been shown to be enhanced by TILS treatment (Barrett & Gonzalez-Lima, 2013). Because our TILS treatment significantly increased the power of alpha waves as compared to sham treatment, we speculate that there may be a mechanistic link between TILS treatment and the cognitive enhancing effects that have been found previously (Barrett & Gonzalez-Lima, 2013; Hwang, Castelli, & Gonzalez-Lima, 2016; Blanco, Maddox, & Gonzalez-Lima, 2017; Blanco, Saucedo, & Gonzalez-Lima, 2017; Vargas et al., 2017; Holmes et al., 2019). Further evidence for this comes from neurofeedback studies that found that when upper alpha amplitude increased from neurofeedback training, improvement in cognitive performance was observed (Escolano et al., 2011; Zoefel et al., 2011; Wan et al., 2014).

The second significant effect of TILS treatment was found on beta waves. Beta wave power increase was smaller than alpha, but also showed statistical significance at minute 4 and 8 of the laser stimulation. Though the mean-difference analysis showed increased activation post-TILS treatment, this increase was not statistically significant. Compared to alpha wave activity, beta waves appear to remain in the posterior region of the brain. Beta wave increase was also found in both the Vargas et al. (2017) and Wang et al (2019) TILS-EEG studies. Beta waves have also been found to be involved in cognitive processes, but to a lesser extent than alpha waves (Ray and Cole, 1985; Güntekin et al., 2013).

An increase in alpha power alone would imply a less aroused, less attentive state in the participants. If this was the case, it could be argued that the increase in alpha power found in the present study was not the result of the TILS treatment, but rather the result of the participants feeling sleepy after sitting in a chair in a quiet room with their eyes closed for a prolonged period of time. However, if this were true, we would not also see an increase in beta wave activity. The statistically significant increase in beta wave power, accompanied by the increase in alpha wave activity, indicates that the effect of TILS is different than just lowering arousal level. Furthermore, the alpha and beta changes during TILS are significant increases relative to the sham-controlled condition, which serves to control that these effects are not simply the result of nonspecific changes during both sham and TILS conditions.

Taken together, the results of this study reveal several key patterns. First, we saw a significant increase in synchronized brain activity across alpha and beta frequency bands. As the TILS treatment goes on longer, alpha and beta power increases in a dose-dependent manner. This effect is time-dependent and the change in power does not become statistically significant for alpha and beta until minute 4 of TILS treatment. Second, despite only stimulating the right side of the forehead, alpha and beta wavelengths showed spectral power increases bilaterally in the brain. Finally, it appears that TILS treatment has little to no effect on delta, theta, and gamma frequency bands. This is consistent with previous literature (Vargas et al., 2017; Wang et al., 2019).

Limitations and Future Directions

The biggest limitation of this study is its small sample size. Due to the COVID-19 pandemic, we were forced to stop collecting data on human participants. Our original recruitment goal was to have collected 40 sham EEGs and 40 TILS EEGs, which would provide us with sufficient statistical power to approximate detection of the true electrophysiological effects of TILS treatment. Another limitation of the study is that the TILS laser used cannot penetrate hair or fabric, so in order for it to reach brain tissue it must be administered to the forehead. In order to accommodate this, we moved the front of the EEG headcap back from above the eyebrows (the standard location) to the participants hair line. This meant that the standard 10-10 system of electrode placement was inconsistent with the placement of our electrodes, rendering us unable to completely accurately identify highly specific scalp regions that showed significant EEG power responses to TILS. From average forehead sizes, we can estimate that the headcap was pushed back approximately 58.3 to 61.4 mm (Sirinturk et al., 2017).

In the future, we would like to continue to recruit more participants. Our goal is to collect a total of 120 EEGs, including 40 sham and 40 TILS. We would also like to collect 40 TILS-Left EEGs, where our protocol would be the same except TILS would be administered to the left side of the participant's forehead. This increase in data collection would allow us to increase our statistical power and find more minute changes in the frequency band power. We are also interested in examining how administration of TILS to the left forehead may yield different electrophysiological changes in the brain than TILS to the right forehead. Finally, we would like to analyze the data using the Loreta software. This software would allow us to estimate the electric activity sources of neurons on the cortex of the brain.

Chapter 4: Conclusion

The present study adds to the nascent literature on the electrophysiological effects of TILS on the human brain. Our single-blind, sham-controlled study found that 8 minutes of 1064 nm laser administered to the right forehead of healthy adults increased the power of alpha and beta frequency bands significantly. The increases were seen bilaterally and appeared to be centered in anterior and posterior regions of the brain. When taken together with results from previous EEG studies on TILS, the results from this study show that photobiomodulation using a 1064 nm laser achieves neuromodulation in part through changes in electrophysiological activity observed in the cerebral cortex.

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