BSc. Psychology

Gamma wave inducing effects of 40 Hz flickering light in humans

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Foreword

Submitted in partial fulfilment of the requirements of the BSc Psychology degree, Reykjavik University, this thesis is presented in the style of an article for submission to a peer-reviewed journal.

Abstract

Treatment methods for Alzheimer's disease (AD) are limited and can cause unwanted side effects. The amyloid beta cascade hypothesis claims that AD is caused by accumulation of amyloid beta (Aβ) plaques, which results in other symptoms of AD. New findings indicate that by inducing gamma waves in the brain of mice with flickering 40 Hz light, Aβ plaques can be reduced. The effects of 40 Hz light on the human brain in not fully understood. This study explored this inducing effect on a healthy human brain. Subject was a 22-year-old white Icelandic male student. An ABA single-subject design was used to evaluate the effects of 40 Hz flickering light inside prototypic goggles on the power spectral density of gamma waves in brain of the subject measured by 64-channel EEG. Two standard deviation band method showed significant increase compared to baseline of gamma waves, especially in the range of 38 - 42Hz, in the occipital lobe both during and after the experiment. Subject reported no discomfort, dizziness, eyestrain or headache from the goggles. The long-term effects of the flickering light on gamma waves were not measured. Future studies must explore the effects of 40 Hz flickering light on humans with AD.

Keywords: EEG, Gamma, brain wave induction, power spectral density, 40 Hz

Útdráttur

Meðferðarúrræði við Alzheimer sjúkdóm (AD) eru takmörkuð og geta valdið óæskilegum aukaverkunum. Amyloid beta kenningin leggur til að AD stafi af úrfellingum amyloid beta (Aβ) skellum sem valda öðrum einkennum AD. Ný rannsókn sýnir fram á að örvun gamma heilabylgna með 40 Hz flöktandi ljósi geti dregið úr Aβ skellunum í heila músa. Áhrif 40 Hz flöktandi ljóssins á mönnum eru ekki skilið til fulls en þessi rannsókn kannaði áhrif 40 Hz flöktandi ljóss á heilbrigðum mannsheila. Þátttakandi var 22 ára karlkyns Íslenskur námsmaður. ABA-einliðasnið var notað til að meta örvandi áhrif 40 Hz flöktandi ljóssins í gleraugum á power spectral density á gamma bylgjum í heila þátttakandans með 64-rása EEG. Aðferð tveggja staðalfrávikstrengja sýndi marktæka aukningu á gamma bylgjum borið saman við grunnlínu, sérstaklega á milli 38 og 42 Hz, í hnakkablaði bæði á meðan og eftir rannsókn. Þátttakandi greindi frá engum óþægindum, svima, augnþreytu eða höfuðverk af notkun gleraugnanna. Langtímaáhrif 40 Hz ljóssins voru ekki könnuð. Framtíðarrannsóknir þurfa að kanna áhrif 40 Hz flöktandi ljóss á fólk með AD.

Lykilorð: EEG, Gamma, heilabylgjuörvun, power spectral density, 40 Hz

Gamma Wave inducing effects of 40 Hz flickering light in humans

A recent study by Iaccarino et al., (2016) indicated that a non-invasive method of flickering light can induce gamma waves in the brain and reduce pathological symptoms of Alzheimer's disease (AD). They exposed mice with AD to light-emitting diode (LED) bulb that flickered at 40 Hertz (Hz). After an hour-long treatment in the light, the mice showed reduction of amyloid beta (Aβ) plaques levels, which are known to be related to AD (Hardy & Higgins, 1992), by half in the visual cortex. As treatment strategies for AD are limited, the effects reported by Iaccarino et al. (2016) must be explored further. The aim of this study was to explore the gamma inducing effects of 40 Hz light in a human brain using a prototypic LED goggles device.

AD is a chronic neurodegenerative disease which is characterized by dementia, memory loss, language problems, disorientation, mood swings and behavioural issues (Burns & Iliffe, 2009) and affects over 25 million adults in the world (Qiu, Kivipelto, & von Strauss, 2009). After diagnosis the average life expectancy is three to ten years (Zanetti, Solerte, & Cantoni, 2009). There is no cure for AD and all available treatments, which include only four approved medications (Mehta, Jackson, Paul, Shi, & Sabbagh, 2017) and non-pharmacological therapies such as physical exercise and memory training therapy, only temporarily alleviate AD symptoms and can cause undesirable side effects (Alzheimer's Association, 2017). According to the amyloid cascade hypothesis, AD is caused by a deposition of Aβ protein fragments called Aβ plaques around neurons and act as a biological pathogen (Hardy & Higgins, 1992). Other pathological markers of AD such as neurofibrillary tangles inside neurons, decreased microglial activity, cellular death, vascular damage and dementia are all said to be a result of the accumulation of the Aβ plaques. Brain autopsy of people who suffered from AD have shown characteristic presence of abnormal Aβ plaques and neurofibrillary tangles (Arriagada, Growdon, Hedley-Whyte, & Hyman, 1992) and the

magnitude and distribution of the plaques and tangles is highly correlated with severity of dementia in AD (Arriagada, Growdon, Hedley-Whyte, & Hyman, 1992; Hardy & Selkoe, 2002; Tanzi et al., 1987).

An intriguing phenomenon of the neural system are neural waves. Neural waves occur when an ensemble of neurons generate oscillatory activity in harmony to each other which can be characterized by their frequency (Ward, 2009). The harmony forms a wave pattern that can be detected by electroencephalogram (EEG) and is measured in Hz (Ward, 2009). Brain waves are categorized into five main categories: Delta waves (0.3 – 3 Hz), Theta waves (3 – 7 Hz), Alpha waves (7 – 13 Hz), Beta waves (13 – 30 Hz) and Gamma waves (30 – 100 Hz).

Gamma waves are fast waves with a range between 30-100 Hz, though 40 Hz is most typical (Ward, 2009). The functional role of gamma waves have most frequently been studied in animals, and only relatively recently has the functional role of gamma waves in humans been studied (Cheron et al., 2016). Studies on humans have shown links between memory consolidation and gamma waves in the occipital lobe, as the power spectral density (PSD) of spikes of gamma waves was higher for later remembered item compared to forgotten item (Osipova et al., 2006; Düzel, Penny, & Burgess, 2010). Gamma activity has been linked with both working memory (Yamamoto, Suh, Takeuchi, & Tonegawa, 2014), episodic memory in the hippocampus (Nyhus & Curran, 2010), attention (Kim, Ährlund-Richter, Wang, Deisseroth, & Carlén, 2016) and cognitive control in the prefrontal cortex (Cho et al., 2015). An increase in gamma waves has been recorded during cognitive task (Kim et al., 2016). Therefore, gamma waves seem to be an important part of numerous cognitive functions.

From studies that indicate links between many cognitive functions and gamma waves, questions have been raised of relation between gamma waves and AD (Başar, Başar-Eroğlu, Karakaş, & Schürmann, 2000; Düzel et al., 2010; Klimesch, 1996; Nyhus & Curran, 2010;

Stam et al., 2002; Yamamoto et al., 2014). In recent years, studies have reported findings indicating links between gamma waves and AD, where a reduction in gamma waves seem to be correlated with the progression of AD. Changes in brain waves slower than gamma, from 0.3 to 30 Hz, of AD patients compared to healthy control have been established by numerous studies (Besthorn et al., 1994; Elmståhl, Rosén, & Gullberg, 1994; Kowalski, Gawel, Pfeffer, & Barcikowska, 2001; Prichep et al., 1994), but Stam et al (2002) was the first to conduct a study on changes in gamma waves in AD patients. They compared 20 AD patients to 20 healthy with a 151 channel MEG system and showed a reduction in brain of AD patients of upper alpha waves (10 to 14 Hz), upper beta waves (18 to 30 Hz) and in gamma waves (30 to 40 Hz) in occipital and temporal regions. These results are the first evidence of loss of gamma waves in AD. This is supported by the results of a study by Koenig et al., (2005), which showed a reduction of alpha, beta and gamma activity in patients with varying extent of cognitive impairment compared to healthy control. Other studies have shown that gamma activity decreases with age in the frontal cortex of humans (Böttger, Herrmann, & von Cramon, 2002). A study on mice with AD by Goutagny et al., (2013) indicated that reduced gamma and theta oscillations is the earliest biomarker for AD, occurring before other symptoms such as dementia, Aβ plaques and cell death.

Iaccarino et al. (2016) studied genetically engineered mice with AD to investigate if gamma activity is altered in mice's brain with early AD and gamma wave relation to AD. At three-month-old, the mice showed no Aβ plaques nor manifestation of learning or memory deficits but had elevated levels of amyloid precursor protein and lowered gamma activity compared to healthy control. This closely resembles findings which report reduced gamma in human patients with AD (Stam et al., 2002; Verret et al., 2012). Iaccarino et al. (2016) used a technique similar of Galambos, (1992), who used flickering light stimulus to induce a particular wave activity in the brain of cats, to investigate the effects of induced gamma

activity on AD. They used a device with LED bulb to flicker at 40 Hz to induce 40 Hz gamma waves in the visual cortex of the mice for one hour over seven days. The mice which were exposed to the 40 Hz flickering light showed an increase of 40 Hz gamma waves and a reduction of Aβ plaques by 58% in the visual cortex while the control groups, exposed to either random flicker or no light, showed no reduction. The mice also showed an increase in microglial size by 165% and increased microglial processing of Aβ plaques compared to control. However, after 24 hours the levels of Aβ plaques had returned to levels as before the treatment. Thus the study showed that a 40 Hz flickering light was demonstrated as a non-invasive method of reducing Aβ plaques and boost microglia activity both of which are related to AD pathology (Hardy & Selkoe, 2002).

A study by Herrmann, (2001) showed that the visual cortex of humans is receptacle to brain wave induction by flickering light at various frequency. The study showed that brain waves in the visual cortex in humans resonates to flickering light from 1 up to 90 Hz, similar to effects shown in brain of cats (Galambos, 1992; Gray, König, Engel, & Singer, 1989). Beneficial effects of inducing brain waves with flickering light have been questioned, but studies have indicated possible benefits for memory and attention (Huang & Charyton, 2008). This gives a basis for that the effects of Iaccarino et al. (2016) could be replicated in humans.

As the study by Iaccarino et al. (2016) indicates possible therapeutic effects of gamma wave induction, a greater understanding of the effects on human is needed. For this study we hypothesise that 40 Hz flickering light will have an increasing effect on gamma activity, particularly activity in the range of 38 to 42 Hz, in a healthy human brain.

Method

Subject

The subject, recruited by convenience, was a 22-year-old white Icelandic male student from the University of Iceland. The requirements set for this study was to have no personal

history of seizures or epilepsy nor have any relative diagnosed with epilepsy and report no discomforts, disorientation or nausea when watching television, playing video games or looking at flickering or bright lights. The participant was informed that flickering light stimulus can trigger seizures in epileptics. The participant met the study‘s requirements and gave a written, informed consent for his participation. He had prescription glasses he uses daily and practiced physical exercises five to seven times a week. He had consumed two cups of coffee on the day of the experiment, seven and four hours before the experiment. He reported alertness of between eight and nine on a scale where one is falling sleep and ten being fully alert and functional.

Stimuli and equipment

The 40 Hz flickering light stimulation was driven by an astable mode circuit using a 555-timer chip connected to four white LEDs. The current driving the 555-timer flows through two transistors, R1 and R2, and charges a capacitor, C1. While C1 is charging, the output current is high and the LEDs turn on. After C1 has charged to 2/3 of the supply voltage it discharges through R2 and the output current is low and the LEDs turn off. When the voltage reaches 1/3 of the supply voltage C1 resumes charging and the cycle repeats. The rate of this cycle is controlled by resistance of R1 and R2 and capacitance of C1. For the frequency of 40 Hz, two 12 kΩ resistors were used for R1 and R2 and a 1 µF capacitor for C1. The frequency can be calculated with the formula: f = 1.44 / ((R1 + 2 * R2) * C1), which in this case is f = 1.44 / ((12000 Ω + 2 * 12000 Ω) * 0.000001 F) = 40 Hz.

Four white LEDs were placed inside blackened safety goggles, which were made of soft plastic and fit tightly around the eyes with minimal gaps and had an adjustable strap (see Appendix A). The goggles were sprayed with black paint and covered with light obscuring adhesive material. Two of the LEDs were placed on the lateral sides of the goggles and two

on the superior side. This placement assures the light source to be visible in the peripheral field of the vision and did not cause strain on a particular place in the visual field.

A WaveGuard™ original 64-channel EEG wet silver/silver-chloride cap with 10/20 layout (see Appendix B) with left and right mastoid bone reference electrodes from ANT-Neuro was used with EEGO™ Mylab amplifiers. Active shielding was used to limit environmental noise, interference by movement of electrode cables and protect against 50 Hz electrical noise signal as the lab did not have insulation or a Faraday cage.

Procedure and design

An ABA single-subject design was used to estimate the impact of flickering light on gamma wave activity. The flickering light was the independent variable and took three stages (baseline, intervention and post-intervention measure). The PSD in μV^2 of gamma waves as measured with EEG was the dependent variable. A two standard deviation band method was used to compare the intervention stage and the post-intervention measure to baseline. The subject was seated in a comfortable posture in a quiet room with lights on and the 64-channel EEG cap was put on his head. The participant was asked to relax for one minute after the EEG was set up, after which a 24 second baseline brain activity was measured. After baseline measure the stimuli device was placed on the participant's face and adjusted so no external light permeated the goggles. The intervention stage consisted of 30 cycles where the light was turned on for 10 seconds and turned off for 10 seconds. After the intervention phase the stimuli device was removed and a 24 second post-intervention measure was measured.

Data acquisition and analysis

The signal was acquired by EEGO™ Mylab software from the 64-channel cap after amplification from EEGO™ Mylab amplifiers with a sample rate of 4096 Hz with band-pass from 0.3 to 2048 Hz. Resistance of every electrode was below 5 KΩ and EEG data was inspected to make sure no bridging between electrodes had occurred. The data from EEGO

software were imported and pre-processed in Advanced Source Analysis™ (ASA™) software from ANT Neuro. Eye blink artefacts were removed by automatic artefact reject algorithm based on amplitude threshold of upper 75 µV to lower -75 µV. Former studies have validated this artefact rejection procedure (John, 1987), and it was band-pass filtered with a low cut-off from 0.3 and high cut-off from 100 Hz. After which a baseline correction and detrending procedure was applied on the intervention data. Baseline correction is calculated as a 0.2s period which starts 0.1s before and ends 0.1s after the relevant event and is used as reference baseline for each data point.

For Fast Fourier transform (FFT) analysis the 24 second baseline acquisition was split into eight 3 second sections and an average of each section was used as a data point. The intervention stage was split into 30 on-events, consisting of each time the light was turned on, and 30 off-events, consisting of each time the light was turned off. Each event lasted for 10 seconds, but to minimize disruption of blinking artefacts when the light is turned on the first two seconds of each event were excluded. A 3 second period, starting after the two second exclusion, was used as a data point for each event. The 24 second post-intervention measure was processed in the same way as baseline. Each data point of all stages was therefore based on an average of 3 seconds. Using a FFT analysis with ASA™, an average PSD of gamma oscillation (30 – 100 Hz) and 40 Hz gamma oscillations (G40) (38 – 42 Hz) for each data point was gathered from blocks of 0.064 seconds.

Descriptive statistics were analysed with IBM's SPSS Statistics where an average and standard deviation of the PSD of gamma and G40 were computed for baseline, on-events, off-events and for post-intervention measure. Given that the experimental design is a single subject design, a two standard deviation band method was used to evaluate the significance of the results (Nourbakhsh & Ottenbacher, 1994). The two standard deviation band method is based on the assumption that the data is normally distributed. A Shapiro-Wilk

test of normality tested the data from baseline, on-events, off-events and post-intervention measure for normal distribution. According to Shapiro-Wilk test only baseline data was normally distributed, On-Events, Off-Events and post-intervention measure were not normally distributed so therefore the assumption for two standard deviation band method were not met. Regardless the comparison was analysed using the method since the data points were of a sufficient amount.

In two standard deviation band method the standard deviation of the baseline is computed and bands are drawn on a graph representing the mean of the baseline ± 1.96 standard deviations. When scores for the intervention stage and post-intervention measure is added to the graph, they are considered significantly different ($p < 0.05$) from the baseline if two successive data points fall outside the standard deviation bands (Nourbakhsh & Ottenbacher, 1994). For a directional hypothesis, the z score for $\alpha = 0.05$ confidence is 1.654, therefore as the study has a directional hypothesis of increasing gamma waves the computed bands are baseline mean ± 1.654 standard deviation.

Results

The subject reported no discomfort, dizziness, eyestrain or headaches from the 40 Hz light in the prototypic goggle device after the experiment. An inspection from a trained EEG technician indicated that no bridging was between electrodes and no eye-blink artefacts remained after processing.

Average PSD of gamma (30 – 100 Hz) in baseline was 1.294 μV^2 (SD = 0.338), and G40 (38 – 42 Hz) was 1.220 μV^2 (SD = 0.345) and activity localized in the right ventral prefrontal lobe and right ventral occipital lobe. For the intervention phase when the lights were turned on, the average PSD of gamma was 3.129 μV^2 (SD = 1.285) and of G40 was 3.038 μV^2 (SD = 1.282) and was localized primarily in the occipital lobe. The PSD of gamma in the intervention phase when the lights were turned off was 2.880 μV^2 (SD = 1.204) and

G40 was 2.783 μV^2 (SD = 1.195) and localized primarily in the occipital lobe. The average PSD of gamma oscillations in the post-intervention measure was 3.371 μV^2 (SD = 1.943) and G40 was 3.219 μV^2 (SD = 1.975) and was localized primarily in the right medial occipital lobe and right ventral prefrontal cortex. In all stages, PSD of G40 accounted for 94% to 97% of the overall PSD of gamma.

For the two standard deviation band method of gamma waves the upper band was calculated as 1.294 + (0.338 * 1.654) = 1.853 μV^2 and lower band as 1.294 + (0.338 * -1.654) = 0.735 μV^2. As seen on Figure 1, two successive data points of on-event of gamma exceed the upper band of 1.853 several times, which indicates a significant increase of PSD compared to baseline ($p < 0.05$). Only three data points of 30 from on-events fall inside the upper and lower bands, one of which is when the light was first turned on. Each data point of the graph represents a mean PSD of gamma of a three second period. The baseline is relatively stable and does not fall out of the upper or the lower bands at any time. The lowest value of the baseline data is 0.96 μV^2 and highest is 1.83 μV^2. The values from on-events vary greatly between connected data points, with the highest difference of 4.67 μV^2, between data point 28 (1.53 μV^2), and data point 29 (6.2 μV^2). Greater variability is seen in PSD of gamma after data point 18 in the data, where spikes ranging from 4.22 μV^2 to 6.59 μV^2 take appear.

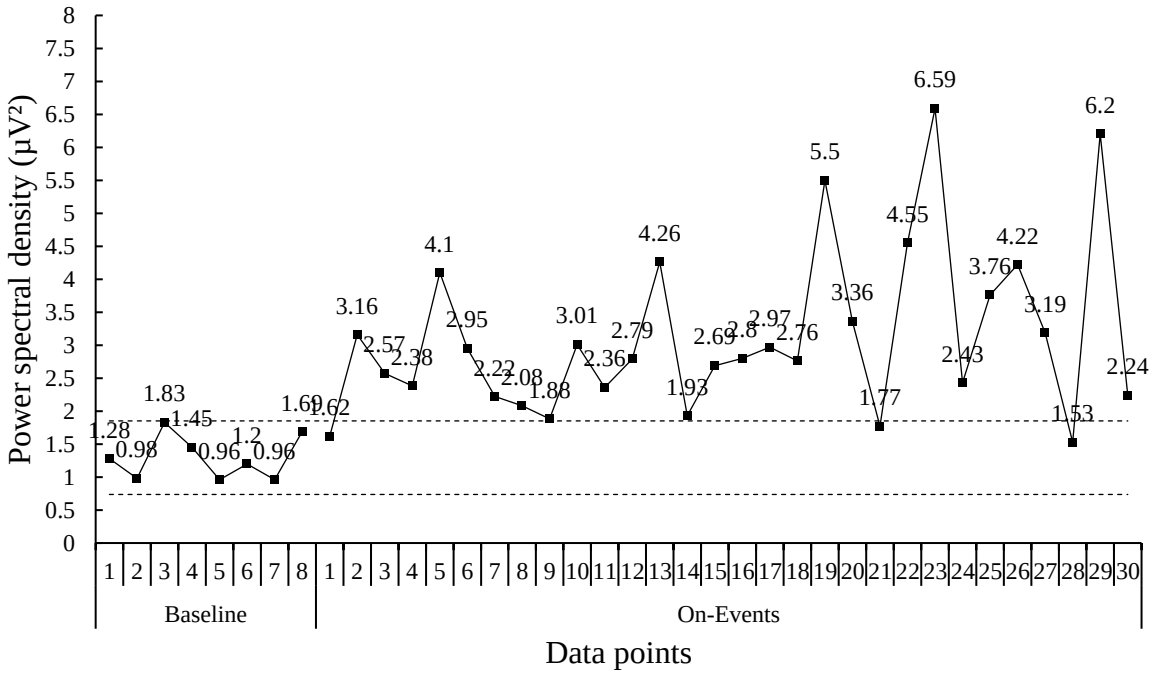

Figure 1. Power spectral density (μV²) of gamma in the subject for baseline and on-events. Shows mean PSD for gamma for each data point in baseline and on-events. The dotted line represents the upper (1.853) and lower (0.735) bands of two standard deviation band method.

Figure 2 shows similar results as Figure 1, where several successive data points of off-events of gamma waves exceed the upper band of 1.853 μV² which indicates that off events also show significant higher PSD of gamma compared to baseline of $p < 0.05$. Of 30 data points of off-events, four out of thirty fell inside the two bands. The highest value is 5.49 μV² which is connected to a value of 1.55 μV², making a difference of 3.5 μV². The lowest value of off-events is 1.45 μV² which is 0.38 μV² lower than the highest value of baseline. Spikes of PSD of gamma begin to appear after data point 9 after a relatively stable data points. The spikes range from 4.24 μV² to 5.49 μV².

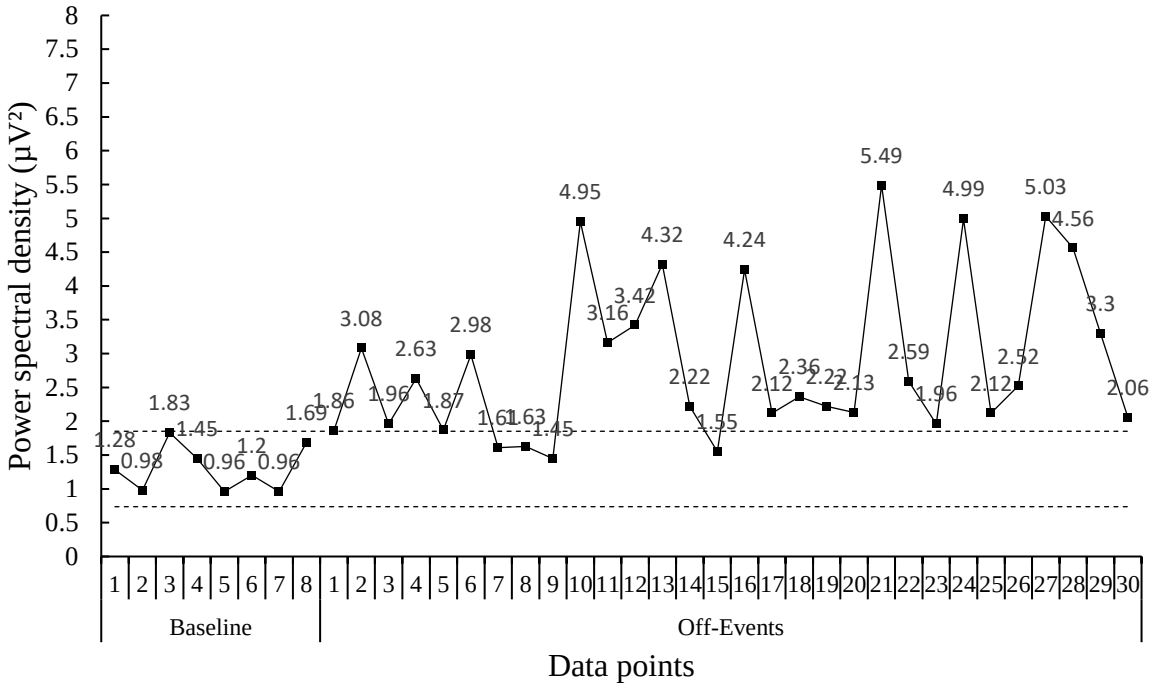

Figure 2. Power spectral density (µV²) of gamma in the subject for baseline and off-events. Shows mean PSD for gamma for each data point in baseline and off-events. The dotted line represents the upper (1.853) and lower (0.735) bands of two standard deviation band method.

As shown in Figure 3, every post-intervention measure data point exceeds the upper band of 1.853 µV². The gamma activity is significantly higher in post-intervention measure compared to baseline ($p < 0.05$). The highest value of all data from the subject is found in the post-intervention measure, a value of 7.79 µV². The highest difference of successive data points is 3.84 µV² between section 7 and 8. The lowest data point is 1.92, and therefore no data point of post-intervention measure falls below the upper band of 1.853 µV². The post-intervention measure does not revert to baseline after the intervention and has a higher mean PSD of gamma (3.371 µV²) than in both intervention phases (on-events = 3.129 µV²; off-events = 2.880 µV²).

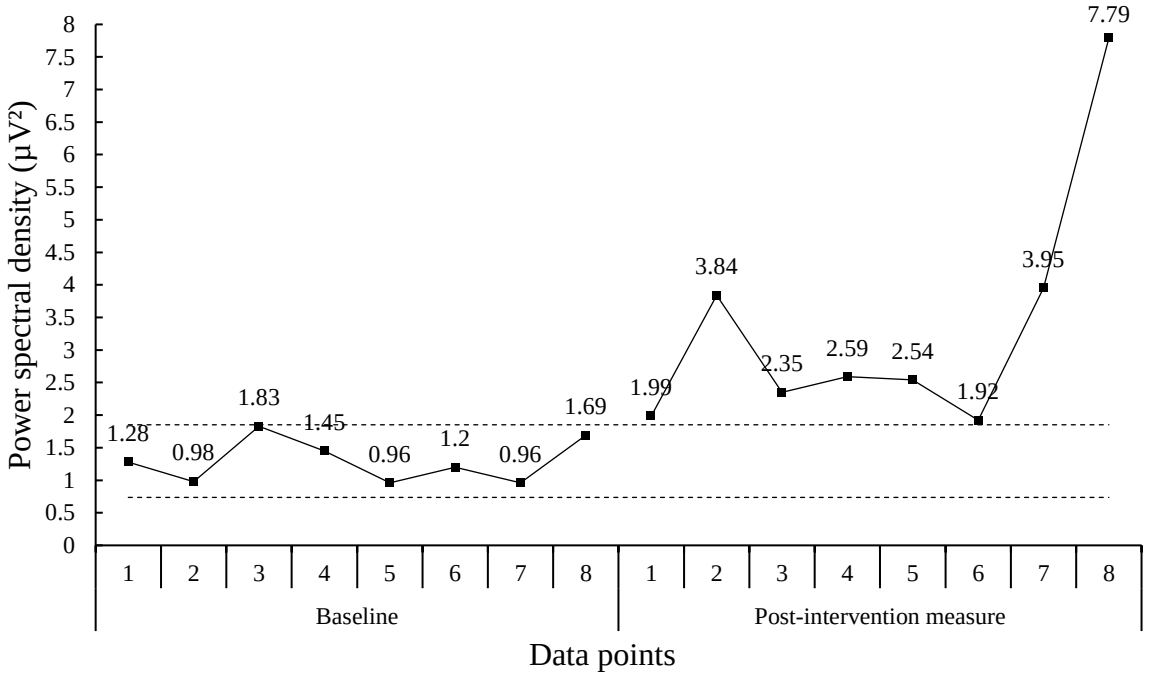

Figure 3. Power spectral density (µV²) of gamma in the subject for baseline and post-intervention measure. Shows mean PSD for gamma for each data point in baseline and post-intervention measure. The dotted line represents the upper (1.853) and lower (0.735) bands of two standard deviation band method.

A two standard deviation band method analysis on PSD of G40 showed similar results as of PSD of gamma. For the two standard deviation band method of G40 waves the upper band was calculated as 1.220 + (0.345 * 1.654) = 1.790 µV² and lower band as 1.220 + (0.345 * - 1.654) = 0.649 µV². According to the analysis, PSD of G40 in on-events, off-events and post-intervention measure were significantly higher than baseline ($p < 0.05$). Three out of thirty data points of on-events, seven out of thirty data points of off-events and two out of eight post-intervention measure data points fell inside upper and lower bands.

As can be seen in Figure 4, localization of PSD of gamma waves show that gamma waves were mostly found in the occipital lobe in on-event, off-event and post-intervention measure. In on-event the occipital lobe had the highest PSD of gamma waves of all other brain areas, whereas in baseline the PSD is much more distributed around the brain. A concentration of PSD of gamma waves is found in the right occipital lobe in post-intervention

measure, and in the prefrontal cortex. A similarity is seen between on-event and off-event, where both show high PSD in the occipital lobe. Off-event seems to be weaker than on-events, whereas off-events was calibrated at maximum of 2.88 μV^2, 0,16 μV^2 lower than on-events at 3.04 μV^2.

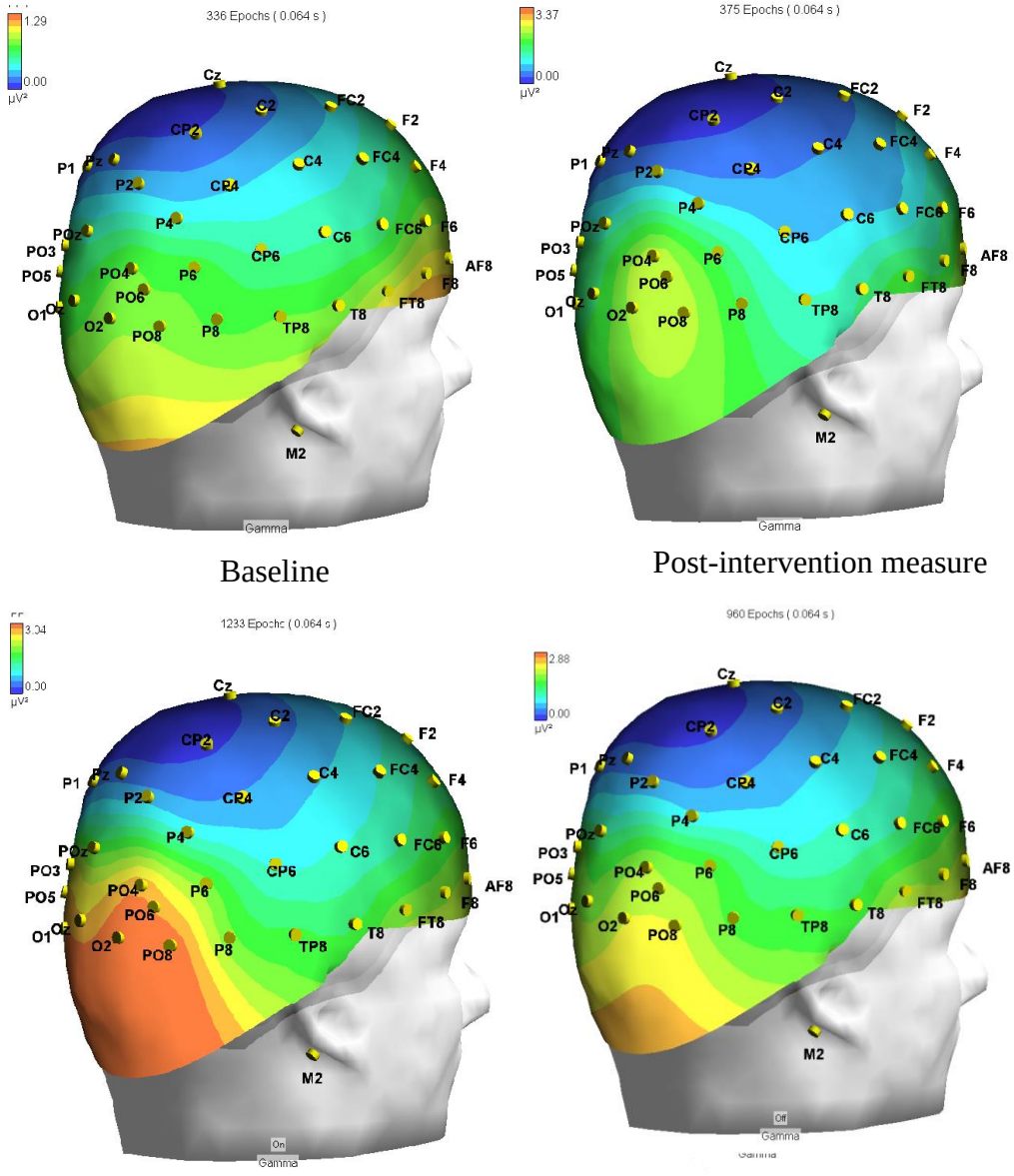

Figure 4. Localization of PSD of gamma activity in each stage of the experiment. Location of PSD of gamma waves in baseline (top left), post-intervention measure (top right), on-event (bottom left) and off-event (bottom right). Each head model is calibrated to the mean PSD of each respective phase.

Discussion

The results showed a significant increase PSD of gamma waves compared to baseline while and after using the 40 Hz flickering light from the prototypic goggle device. The increase was prevalent in on-events, off-events and the post-intervention measure. This is one of the first studies which investigates specifically the inducing effects of 40 Hz flickering light inside goggles on PSD of gamma waves in the human brain. The increase was most prevalent in the occipital lobe and frontal lobe, and most concentrated in the occipital lobe as the flickering light was turned on. The study shows evidence of persistence of the inducing effects as the post-intervention measure did not revert to baseline but was significantly higher compared to baseline. The prototypic goggles did not cause discomfort, dizziness, eyestrain or headaches during or after the experiment indicating that the device was a non-intrusive and non-invasive method of inducing gamma waves. The results supported the hypothesis that the 40 Hz flickering light induced gamma waves, and specifically between 38 and 42 Hz, in a healthy human brain.

AD is a complicated neurodegenerative disease with no cure and treatment options available only temporarily alleviate the symptoms (Alzheimer's Association, 2017). Research of new treatment methods for AD is highly important. One of the supported theories of the cause of AD is the amyloid cascade hypothesis, which states that Aβ protein fragments, called Aβ plaques, accumulate around neurons and act as a biological pathogen (Hardy & Higgins, 1992). As this theory is supported by studies which show presence of these Aβ plaques in the brain of deceased people who suffered from AD (Arriagada et al., 1992), the implication of a non-invasive method of decreasing Aβ plaques as shown by Iaccarino et al. (2016) is great and needs further research. Hardy and Higgins (1992) indicate that other pathological markers of AD such as neurofibrillary tangles inside neurons, decreased microglial activity, cellular death, vascular damage and dementia are all descendant from the

accumulation of Aβ plaques. Based on this theory, the results from the study by Iaccarino et al. (2016) show that 40 Hz light can reduce one of the main factor of AD.

Studies have shown relation between gamma wave activity and many factors related to AD, such as working memory (Yamamoto et al., 2014), episodic memory (Nyhus & Curran, 2010) and cognitive control (Cho et al., 2015). Gamma wave have recently been studied in relation to AD (Başar et al., 2000; Düzel et al., 2010; Nyhus & Curran, 2010; Stam et al., 2002; Yamamoto et al., 2014). Studies have shown reduction in alpha, beta and gamma activity in patients with varying severity of cognitive impairment compared to control (Koenig et al., 2005), and the reduction is mostly located in the temporal and occipital lobes (Stam et al., 2002). Gamma wave reduction additionally has been marked as the earliest biomarker for AD (Goutagny et al., 2013) occurring before other symptoms such as dementia, Aβ plaques and cell death. The findings by Iaccarino et al. (2016) is therefore highly relevant for treatment research for AD. Our study is an important step in understanding the effects if 40 Hz flickering light on gamma waves in the human brain to further explore the effects introduced by Iaccarino et al. (2016). They tested a treatment for the mice with AD exposing them to the 40 Hz light for 1 hour over 7 days, which identified this profound effect on AD pathology. Possible therapeutic effects of the light have not been studied on human AD, but the results from Iaccarino et al. (2016) and this study gives a basis for this effect to be studied on humans in the future.

Earlier studies have shown that the human brain is receptive to brain wave induction by flickering light (Galambos, 1992; Herrmann, 2001) and that brain wave induction by flickering light stimulus could potentially have benefits for attention and memory (Huang & Charyton, 2008). As the stimulus is non-invasive, the study of beneficial effects of flickering light stimulus has great potential. As observed in this study, 40 Hz flickering light does increase gamma waves, and specifically waves between 38 and 42 Hz, in a healthy human

brain. As the gamma waves in post-intervention measure did not revert to baseline, there is evidence of persistence of the effect for some time after the intervention. However, in this study the duration of the effects by the 40 Hz light on gamma waves is unknown, but as shown by Iaccarino et al. (2016) the Aβ plaques reducing effects of the 40 Hz light after the treatment duration lasted for less than 24 hours.

The results of this study showed positive results, however it was based on a single subject and the intervention phase was relatively short. The subject was exposed to the flickering light for five minutes (10s x 30) in total over a period of ten minutes, while Iaccarino et al. (2016) exposed mice to the flickering light for one hour over seven days. The post-intervention measure was recorded for 24 second following the intervention phase and gives evidence that the effect lasts for some time after intervention. However, the effects were not measured an hour or a day after the experiment therefore the duration of the effect is unknown.

Future studies must study the duration of the effects of the 40 Hz light, and estimate how long the effects last compared to duration of intervention. After this would be established, studies could explore the effect on pathological symptoms of AD in humans, and study the effects of inducing gamma waves on cognitive tasks. As our results showed that the prototypic goggle device did not cause discomfort, dizziness, eyestrain or headaches, similar design could be easily implemented in future studies. The gamma waves have been shown to matter a great deal to a normal function of the brain and a deterioration of it has been shown to relate to cognitive impairment. Research is needed to estimate the effects of flickering light on cognitive performance which would have the potential of gamma wave research to exceed therapeutic effects on AD to a field of cognitive enhancement. Most importantly, future research must study if there are therapeutic effects of 40 Hz light for humans with AD.

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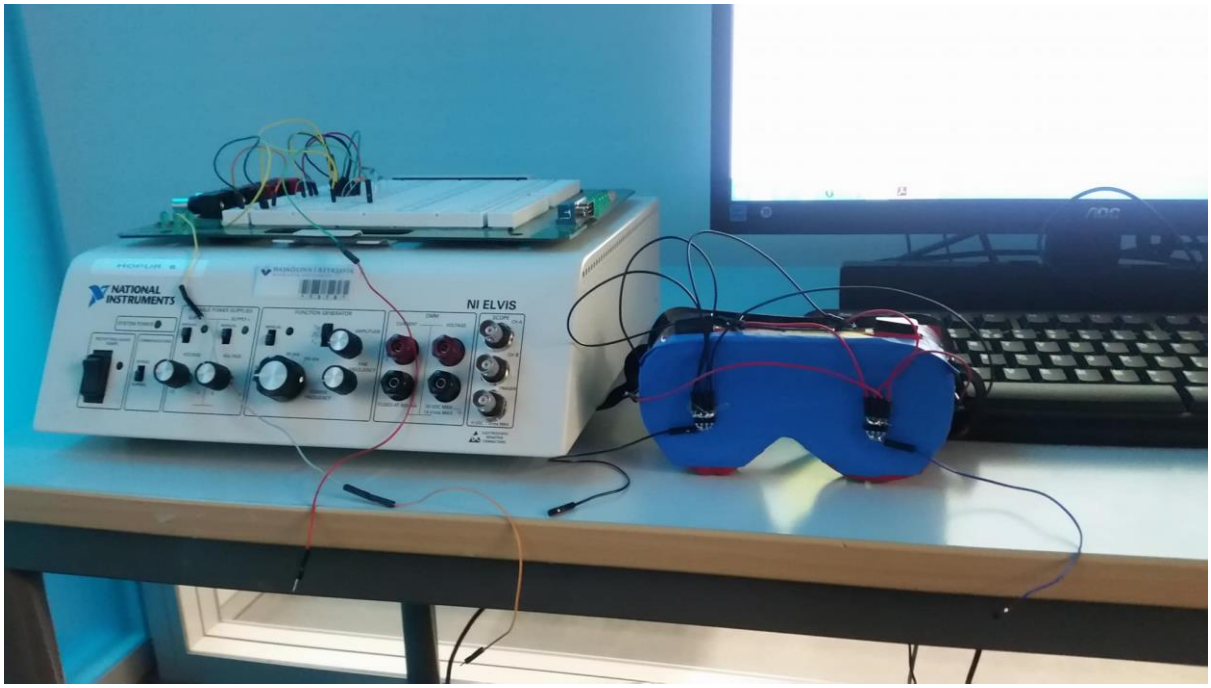
Appendices

Appendix A

The prototypic 40 Hz LED goggles connected to the control board.



Appendix B

The 10/20 layout of a 64-channel cap.