Gamma Entrainment in of my own Brain

In December of 2016, I came upon an article in "MIT News" [1] that claimed:
Unique visual stimulation may be new treatment for Alzheimer's

The article describes how prof. Tsai at the Picower Institute of Neuroscience first used light to stimulate the Hippocampus, through genetic modification: (direct quotes in blue):

> These initial studies relied on a technique known as optogenetics, co-pioneered by Boyden, which allows scientists to control the activity of genetically modified neurons by shining light on them. Using this approach, the researchers stimulated certain brain cells known as interneurons, which then synchronize the gamma activity of excitatory neurons.
> After an hour of stimulation at 40 hertz, the researchers found a **40 to 50 percent reduction in the levels of beta amyloid proteins in the hippocampus**. Stimulation at other frequencies, ranging from 20 to 80 hertz, did not produce this decline.
> Tsai and colleagues then began to wonder if less-invasive techniques might achieve the same effect. Tsai and Emery Brown, the Edward Hood Taplin Professor of Medical Engineering and Computational Neuroscience, a member of the Picower Institute, and an author of the paper, came up with the idea of using an external stimulus — in this case, light — to drive gamma oscillations in the brain. The researchers built a simple device consisting of a strip of LEDs that can be programmed to flicker at different frequencies.

In short, this **non-invasive** method, without genetic modifications, worked just as well.

Immediately upon reading this, I thought: ***what about audio as non-invasive method to stimulate the brain wave***? (I was thinking of Tibetan monks vocalizing at low frequencies.) Later studies have indeed found that audio entrainment is effective.

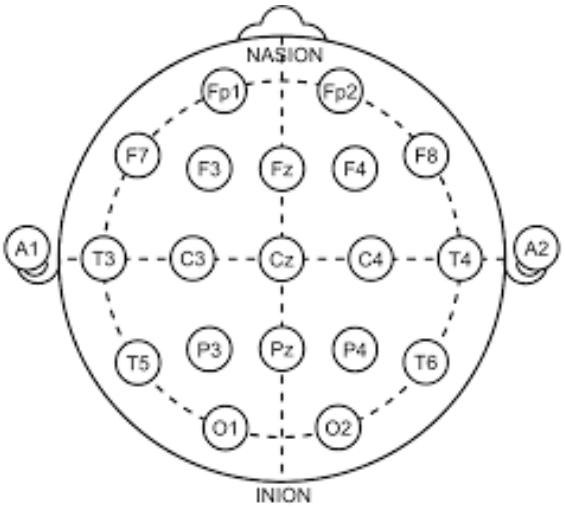
For instance, in [2] Martorell, et. al. summarize:

> We previously reported that inducing gamma oscillations with a non-invasive light flicker (gamma entrainment using sensory stimulus or GENUS) impacted pathology in the visual cortex of Alzheimer's disease mouse models. Here, we designed auditory tone stimulation that drove gamma frequency neural activity in auditory cortex (AC) and hippocampal CA1. Seven days of auditory GENUS improved spatial and recognition memory and reduced amyloid in AC and hippocampus of […] mice. Changes in activation responses were evident in microglia, astrocytes, and vasculature. Auditory GENUS also reduced phosphorylated tau in the P301S tauopathy model. Furthermore, combined auditory and visual GENUS, but not either alone, produced microglial-clustering responses, and decreased amyloid in medial prefrontal cortex. Whole brain analysis using SHIELD revealed widespread reduction of amyloid plaques throughout neocortex after multi-sensory GENUS. **Thus, GENUS can be achieved through multiple sensory modalities with wide-ranging effects across multiple brain areas to improve cognitive function.**

But I didn't know of this result until recently.

Anyhow, for a long time, I have wanted to try to "entrain" my own brain with audio stimuli, which I attempted on a recent weekend. I wired up a few electrodes, ['C3', 'C4', 'P3', 'P4', 'Fz', 'Cz', 'Pz'], on the top of my head (for logistical reasons; see photo).

The sound was generated by a frequency generator APP on my phone (seen in picture), placed some three metres away from the electrodes, to reduce electro-magnetic interference. (But this distance required considerable movement by myself to turn it On/ Off, which had a detrimental effect on my study.)



The Recording

During recording, I:

• sat still for around 7 minutes in relative silence (with only the ambient Lab noise);
• sat still for about 9 minutes with a 40 Hz tone playing, from a sound generator;
• sat still for about six minutes in relative silence again, to see if there was any persistent effect.

(I had intended to sit three periods of nearly seven minutes each, but it was hard to follow the clock while remaining motionless. I also found the 40 Hz sound very relaxing.) At the end-points of these three periods, there was some data noise, as I needed to move and turn the sound on or off.

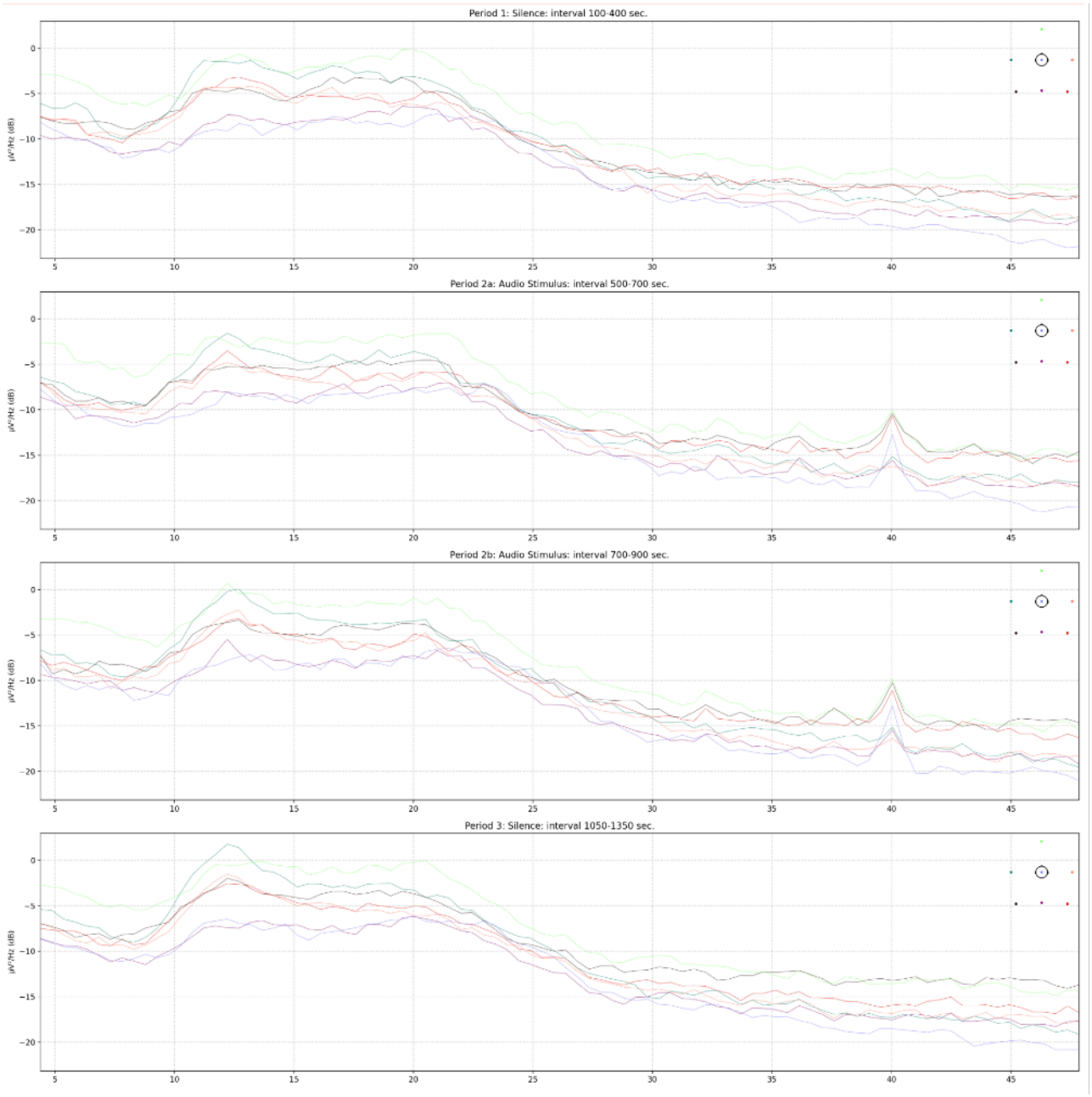
The Results

The plots below show PSD (Power Spectral Density) plots for four time periods during the recording; the first was recorded before the sound was turned on, the next two show the first and second half of the period when sound was played, and the last plot shows a periods after I turned the sound off again.

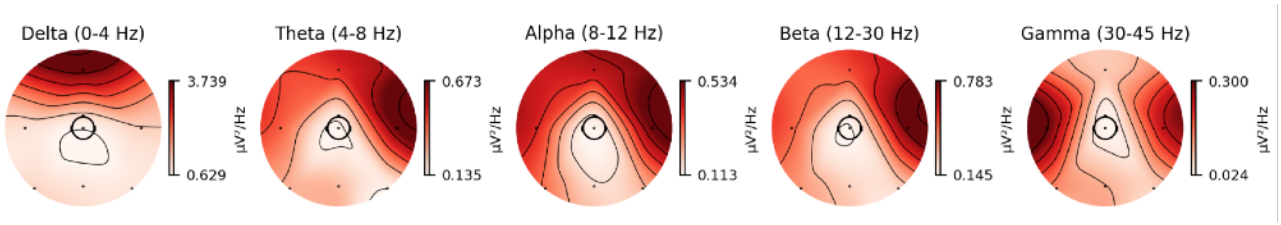
I think the observed peak at 40Hz is indeed appearing in my head. The effect dies away fairly quickly after the sound generator is turned off, but may not be completely absent. It is, however, difficult to separate the “dying out” effect from the noise caused by my own movement and I haven’t seen a clean effect. In any case, the phase-out takes less than 30 seconds, maybe much less.

One should note that this was recorded in the afternoon, when the gamma waves are typically not strong in the brain.

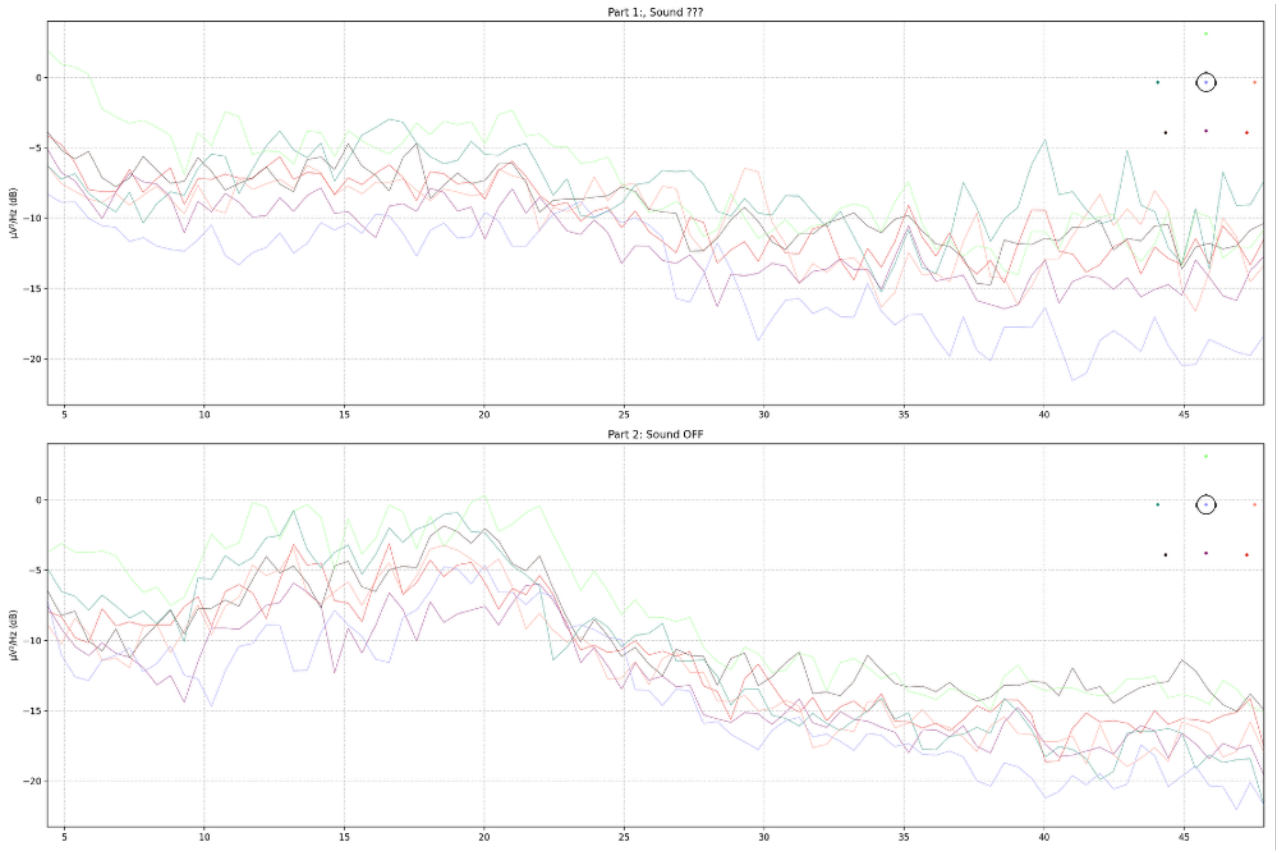
These PSD plots show the signal as recorded at the seven electrodes in standard locations. The x-axis shows the frequencies between 5 and 45 Hz.



Here's where the software places the energies from these recordings (nose pointing up):



In the following two plots, I attempt to isolate where exactly the Gamma wave dies out, but this information is lost in the noise of my own movement. (Plots at 1000-1030 and 1030-1060 seconds, respectively.) Somewhere in the first 30-second recording snippet, the effect dies out.



Why this is interesting (to me)

Now, obviously, one of the aims and benefits of this, if it works and is otherwise harmless, is that amyloid plaque could perhaps be cleared out of the brain more efficiently than what happens in an untreated brain. This would probably be good news for sufferers of Alzheimer's disease, although it may be too late to start clearing plaque from dead brain tissue.

It has more recently been claimed Soula et. al [3] that 40 Hz light stimulation **does not entrain native gamma oscillations** in Alzheimer's disease model mice. (—Or, at least, not deep enough.—)

> There is a demand for noninvasive methods to ameliorate disease. We investigated whether 40-Hz flickering light entrains gamma oscillations and suppresses amyloid-β in the brains of APP/PS1 and 5xFAD mouse models of Alzheimer's disease. We used multisite silicon probe recording in the visual cortex, entorhinal cortex or the hippocampus and found that 40-Hz flickering simulation did not engage native gamma oscillations in these regions. Additionally, spike responses in the hippocampus were weak, suggesting 40-Hz light does not effectively entrain deep structures [….] Thus, visual flicker stimulation may not be a viable mechanism for modulating activity in deep structures.

This negative finding doesn't address the audio-stimulation approach, however.

Furthermore, some research is needed to clarify whether 40 Hz "binaural beats" (generated in the brain, from two sound sources, one to each ear) are effective at all, as effective as straight 40 Hz sound from a single source, and much more.
In short: "further study is required".

References

1. **Unique visual stimulation may be new treatment for Alzheimer's**; https://news.mit.edu/2016/visual-stimulation-treatment-alzheimer-1207

2. **Multi-sensory Gamma Stimulation Ameliorates Alzheimer's-Associated Pathology and Improves Cognition;** Cell 2019 Apr 4;177(2):256-271.e22. doi: 10.1016/j.cell.2019.02.014. Epub 2019 Mar 14.

3. **Forty-hertz light stimulation does not entrain native gamma oscillations in Alzheimer's disease model mice**; Soula, M., Martín-Ávila, A., Zhang, Y. *et al. Nat Neurosci* **26**, 570–578 (2023). https://doi.org/10.1038/s41593-023-01270-2

Dataset

The data was recorded in the EEG Laboratory of the FSG Neuroinformatics. The use of this facility and equipment is gratefully acknowledged. The recorded data is available upon request.