Data Article

Non-invasive auditory brain stimulation for gamma-band entrainment in dementia patients: An EEG dataset

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A R T I C L E I N F O

A B S T R A C T

Gamma entrainment has been shown to enhance beta amyloid ($A\beta$) uptake in mouse models of Alzheimer's disease (AD) as well as improve cognitive symptoms of dementia in both humans and mice. Similar improvements have been reported for both invasive and non-invasive brain stimulation in the gamma oscillatory band, with 40 Hz auditory and visual sensory stimulants employed in non-invasive approaches. Non-invasive stimulation techniques possess the clear advantage of not requiring surgical procedures and can hence be applicable to a wider set of patients. The dataset introduced here was acquired with the aim of examining the network-level mechanisms governing the production of the brain's oscillatory activity during non-invasive auditory gamma-band stimulation, and thereby helping to explain the reported therapeutic effects of entrainment in AD patients. Thirteen elderly participants with memory complaints whose conditions were diagnosed as normal aging (non-AD) or mild AD based on the standard criteria for the diagnosis of AD including the mini-mental state exam (MMSE) took part in data collection in which EEG signals were recorded during auditory stimulation of the brain. The data collection session consisted of an initial one-minute rest followed by an alternating set of six stimulation trials interleaved with five rest

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trials. During each stimulation trial, an auditory stimulant in the form of a 40 Hz chirp was presented to the participant.

The collected data from all participants were preprocessed following the full pipeline of Makoto with the use of EEGLAB and posted as a dataset named: Auditory Gamma Entrainment at OpenNeuro repository. The data record for each participant includes the EEG signal represented in standard BIDS format for one-minute rest followed by the auditory task data. A copy of the source EEG data is also provided in .txt format.

The dataset can be used to study the characteristics of brain oscillations during entrainment, as well as for studies on auditory perception, analysis of resting state potentials in dementia patients, comparison of auditory evoked potentials with resting state potentials, ERP, ERSP, and SSAVP analysis of auditory response in dementia patients, time series analysis of the stimulation and rest trials, and brain connectivity analysis in dementia patients.

Specifications Table

Subject	Neuroscience: Cognitive
Specific subject area	Analysis of EEG signals recorded during auditory stimulation of the brain can reveal the potential therapeutic benefits of gamma-band entrainment.
Type of data	Pre-processed EEG data
How the data were acquired	The data were acquired using a standard 10–20 EEG recording system (19 monopolar channels) while the participants received non-invasive auditory stimulation with a set of table-top stereo speakers.
Data format	Analyzed
Description of data collection	Participants consisted of 13 volunteer patients (8 males, 57–89 years of age) suffering from memory complaints. General exclusion criteria were a history of stroke, traumatic brain injury, schizophrenia, major depressive disorders and electroconvulsive therapy (ECT), or neurodegenerative diseases other than dementia or Alzheimer's disease.
	EEG data were recorded during the presentation of the auditory stimulant. The session consisted of a set of 6 trials of 40 s stimuli interleaved by 20 s inter-trial rest (silence) intervals. During the session, each participant was seated comfortably in a silent room and was instructed to relax their muscles to minimize the muscle artefacts and keep their eyes open.
	Before the start of the first stimulation trial, a one-minute resting state EEG signal was recorded.
Data source location	• Institution: Ziaeian Hospital • City/Town/Region: Tehran • Country: Iran
Data accessibility	• Repository name: OpenNeuro • Data identification number: 10.18112/openneuro.ds003800.v1.0.0 • Direct URL to data: https://openneuro.org/datasets/ds003800/versions/1.0.0

Value of the Data

- Studying the brain's oscillatory activity recorded in this dataset during non-invasive gamma entrainment could help explain therapeutic effects of the newly proposed entrainment methods for treating Alzheimer's disease.
- Analysis of the brain's oscillatory activity in response to external stimulation can provide further insight about the interplay of different oscillatory bands as well as reveal network-

level deficiencies in these oscillations caused by neurodegenerative diseases such as AD and dementia.

- Researchers working on entrainment-based treatment techniques for dementia and AD can design and tune more effective therapy protocols after gaining a better understanding of the oscillatory mechanisms underlying the therapeutic effects of brain entrainment.
- Researchers and clinicians working on brain's auditory system can employ the dataset to investigate the EEG response to auditory stimulation in dementia patients.
- The dataset comprises responses to both stimulus and rest trials which can be used to compare the brain dynamics in these states. In addition, the presence of a one-minute resting state response before the onset of the main task allows for analysing the participant's brain activities without any entrainment-related effects.
- The dataset contains multi-channel EEG records preprocessed using a well-established method and is essentially ready for applying different analytical methods such as: ERP, ERSP, SSAVP, phase coherence, brain connectivity, source localization and ICA, time series analysis, Granger causality, or other processing methods.

1. Data Description

The "Auditory Gamma Entrainment" dataset contains EEG signals recorded in one session of an auditory entrainment task (see Methods) from 13 participants who had referred to the memory clinic of Ziaeian Hospital in Tehran, Iran, with memory complaints. The participants were diagnosed through neurologic examination either as normal aging (non-AD) or suffering from mild AD (two participants were subsequently excluded from the study as the diagnosis of their status required further examination).

The repository directory in OpenNeuro [1] observes the BIDS standard formating of the data [2]. According to this standard, the metadata of the entire dataset and of the participants are stored as .json and .tsv file formats in the main folder. The EEG data and its metadata for each participant are stored in separate folders named by participant's ID (The 'S' character alongside the participant's number make up the participant's ID). The metadata contain information about channel names and their coordinates, the task description and the events specified during the task for each participant. The events are specified with numbers 1 and 2, representing the beginning of the rest and stimulus trials, respectively. In addition, the main EEG data is stored in .set format, which is compatible with EEGLAB [3] (an interactive MATLAB toolbox). Using this toolbox, the data and the metadata can be easily loaded together. A folder named "sourcedata" in the main folder contains another copy of the main EEG data in .txt format. The .txt files include the data arranged in rows and columns in which each column is the time series of the EEG data corresponding to the channel number specified in metadata, and each row represents the EEG snapshot at a single time sample for the entire set of channels.

The EEG data consist of two tasks performed with open eyes: (1) the Rest data recorded during a one-minute interval before the onset of the main task, and (2) the gamma auditory entrainment task (the main task). Unfortunately, the Rest data for participants with ID numbers 9 and 13 are missing. The EEG data files of the two tasks are stored in separate files with distinct names in each participant's specified folder as described above.

The preprint of a manuscript based on the data has been posted on bioRxiv [4]. The manuscript reports on the evaluation of the enhancements caused by entrainment in the temporal and spatial coherence of oscillatory activity in the brain as well as in the cross-frequency coupling of theta and gamma activities.

2. Experimental Design, Materials and Methods

2.1. Participants

The participants were selected among a group of elderly patients referring to the memory clinic of Ziaeian Hospital in Tehran due to memory problems whose conditions were evaluated

Table 1
Participants' demographics.

Index	Participant ID	MMSE score	Gender	Age	Dementia state	Smoking history	Education level	Superior hand
1	S1	28	Male	65	Non-AD	No	6th grade	Right
2	S2	23	Female	70	Mild AD	No	12th grade	Right
3	S3	27	Male	75	Non-AD	No	5th grade	Right
4	S4	21	Male	82	Mild AD	Yes	6th grade	Right
5	S5	21	Male	75	Mild AD	Yes	5th grade	Right
6	S6	-	Female	69	-	No	–	Right
7	S7	19	Male	89	Mild AD	Yes	6th grade	Right
8	S8	24	Male	70	Non-AD	No	5th grade	Right
9	S9	26	Female	57	Non-AD	No	5th grade	Right
10	S10	28	Male	81	Non-AD	No	3rd grade	Right
11	S11	20	Female	88	Mild AD	No	3rd grade	Right
12	S12	30	Female	63	Non-AD	No	5th grade	Right
13	S13	-	Male	60	-	No	-	Right

by a neurologist. After applying exclusion criteria as follows, the remaining participants entered the study and provided informed written consent. General exclusion criteria were:

- Less than 55 years of age.
- History of stroke, schizophrenia, traumatic brain injury, or major depressive disorders.
- Electroconvulsive therapy (ECT) over the prior six months.
- Other neurodegenerative diseases such as multi-system atrophy, progressive supranuclear palsy, Parkinson's disease, and cortico-basal degeneration.

For two participants (S6 and S13) who were subsequently excluded from the study since the diagnosis of their status required further examination, the EEG records are included in the dataset but some of the other data points are not.

The cognitive status of each participant was assessed using the mini-mental state examination (MMSE). The MMSE scores as well as the demographic information of the participants are presented in Table 1.

2.2. Task execution

For measuring raw rest-state potentials, a one-minute resting state EEG signal with open eyes was recorded from each participant before starting the main task. Then, the auditory task was performed which consisted of 6 trials of stimuli interleaved with 5 trials of rest. Each stimulus trial lasted 40 s during which a pre-designed auditory stimulant was played with two speakers placed in front of the participant at 50 cm distance and 50 cm apart from each other. The rest trials consisted of 20 s of silence. The entire task resulted in 340 s ($6 \times 40 + 5 \times 20$) of EEG signal. Fig. 1 illustrates the task's schematic design. The room was maintained quiet during the task and the participants were instructed to sit comfortably, relaxed, and inactive with their eyes open. The sound volume level was set to about -40 dB and for further tuning each participant was asked whether the sound was too loud to be annoying or was hard to hear.

This protocol for data collection was defined after test protocols were carried out on young healthy volunteers in order to adjust the duration of the session and stimulation intervals as well as determine a suitable number of trials per session, the modality of stimulation (auditory or visual), and the geometric placement and the volume level of the audio signal.
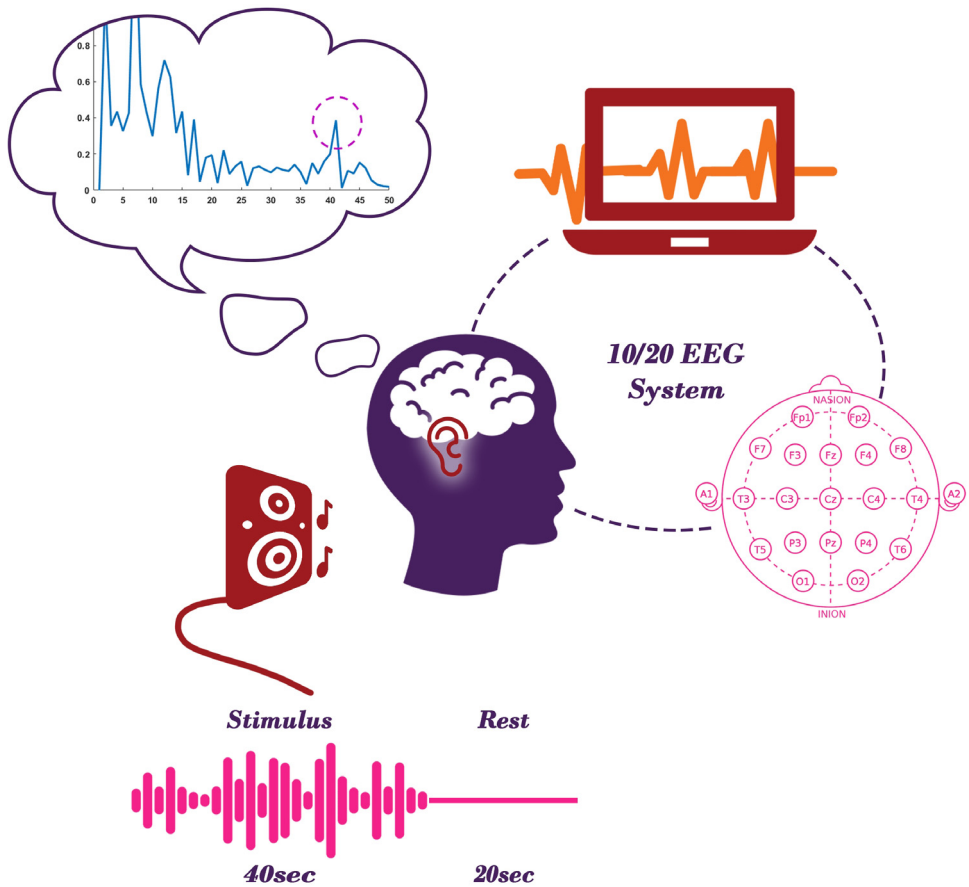
Fig. 1. General schematic of the data collection procedure.

2.3. EEG recording

The EEG data were recorded using 19 monopolar channels in the standard 10/20 system referenced to the earlobes (AA channel), sampled at 250 Hz, and the impedance of the electrodes was kept under 20 kΩ. To avoid muscle artifacts, participants were instructed to relax their body and not move their head.

The EEG cap was not taken off between the recording of the one-minute resting state EEG signal and the main task, and these two data records were collected in one continuous session and were subsequently partitioned apart.

2.4. Data preprocessing

Following Makoto's pipeline [5] and with the help of EEGLAB, the following preprocessing steps were performed on the recorded raw data:

1. Apply 1 Hz high pass filter to remove baseline drifts.
2. Apply (45–55) Hz notch filter to remove the 50 Hz line noise.

3. Reject bad channels as a critical step before average referencing with the use of "clean_rawdata()" EEGLAB plugin.
4. Interpolate the removed channels.
5. Re-reference the data to the average of all channels to obtain a good estimate of reference-independent potentials.
6. Apply "clean_rawdata()" for cleaning the data by running artifact subspace reconstruction (ASR).
7. Re-reference the data to the average again to compensate for any potential changes in the data caused by the previous step.
8. Run independent component analysis (ICA) to identify EEG sources as well as the sources associated with noise and artifacts.
9. Fit single and bilateral (if available) current dipoles.
10. Further clean the data by source (dipole) selection using "IClabel()" plugin in EEGLAB.

All of the above steps were conducted separately for both the raw data of the one-minute rest and of the main task for each participant.

2.5. Auditory stimulant

Each stimulus trial was a single 5 kHz sinusoid carrier with zero phase modulated with a zero phase 40 Hz rectangular wave with 4% duty cycle (1 msec Off and 24 msec On cycles) lasting for 40 s. There were 6 stimulus trials interleaved with 20 s periods of silence (zero values) as rest trials. The entire 340 s auditory record containing all stimulus and rest intervals was stored in .wav format with a 44,100 Hz sampling rate using custom MATLAB scripts.

Ethics Statement

The study was approved by the Review Board of Tehran University of Medical Sciences (Approval ID: IR.TUMS.MEDICINE.REC.1398.524) and the experiments were conducted under the supervision of a neurologist at the Department of Geriatric Medicine of Ziaeian Hospital in Tehran, Iran. The research was carried out in accordance with The Code of Ethics of The World Medical Association (Declaration of Helsinki). Informed written consent was acquired from the participants prior to the experiment and the information regarding the identity of the participants including name and date of birth were not saved in the dataset nor used in any of the analyses. The participants freely chose to take part in the data collection procedure and were free to withdraw at any stage of data collection.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT Author Statement

Mojtaba Lahijanian: Methodology, Software, Formal analysis, Investigation, Data curation, Writing – original draft; **Mohammad Javad Sedghizadeh:** Data curation; **Hamid Aghajan:** Conceptualization, Methodology, Writing – original draft, Writing – review & editing, Supervision, Project administration, Funding acquisition; **Zahra Vahabi:** Data curation, Supervision.

Acknowledgments

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