Research Paper

The Impact of Brain Auditory Stimulation in the Gamma Band on Cognitive Functions in Early-stage Alzheimer Patients

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ABSTRACT

Introduction: Alzheimer disease (AD), a progressive neurodegenerative disorder marked by deterioration in cognitive abilities, currently affects around 24 to 50 million individuals worldwide. However, effective non-invasive therapeutic options are still unavailable. Disruption of gamma-band neural oscillations (~40 Hz), which underlie higher-order cognitive processes such as working memory and executive function, has been repeatedly documented in both human and animal models of AD. Targeted auditory stimulation at gamma frequencies has recently emerged as a potential neuromodulatory strategy for mitigating these deficits.

Methods: In a controlled experimental framework, 30 individuals clinically diagnosed with early-stage AD, confirmed via functional magnetic resonance imaging (fMRI), and exhibiting mini-mental state examination (MMSE) scores between 10 and 20, were randomly divided into two groups: the intervention (n=15) and control (n=15) groups using a quasi-experimental parallel-group pre–post design. The intervention group received 30 sessions of auditory stimulation using binaural beats centered at 40 Hz over 3 weeks. In contrast, the control group listened to an acoustically comparable audio file lacking gamma-frequency modulation. Cognitive performance was assessed using computerized versions of the Corsi block-tapping test, the Wisconsin card sorting test (WCST), and the digit span test. In addition, resting-state quantitative electroencephalography (QEEG) was conducted to evaluate frontal lobe gamma-band activity under both eyes-open and eyes-closed conditions.

Results: Statistical analysis revealed that gamma-band auditory stimulation resulted in a significant enhancement of visuospatial working memory (P=0.001, Cohen's d=1.42) and cognitive flexibility (P=0.028, Cohen's d=0.78), alongside marked increases in both absolute and relative gamma power in the frontal cortex under eyes-closed conditions (P<0.01).

Conclusion: These findings suggest that auditory stimulation at 40 Hz selectively modulates neural circuits associated with executive and spatial cognitive functions and may serve as a viable non-invasive adjunctive intervention in early-stage AD.

Keywords:
Gamma band, Alzheimer disease (AD), Brain auditory stimulation, Working memory, Cognitive flexibility

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Highlights

- 40 Hz stimulation improved visuospatial working memory (P=0.001, d=1.42).
- Cognitive flexibility significantly increased after intervention (P=0.028).
- Frontal gamma power rose under eyes-closed condition (P<0.01).
- Relative and absolute gamma activity significantly enhanced post-stimulation.

Plain Language Summary

Alzheimer's disease (AD) is a condition that gradually damages memory, thinking, and the ability to carry out everyday tasks. It affects millions of people worldwide, and current treatments can only slow symptoms rather than stop the disease. Because of this, researchers are searching for safe, non-invasive ways to support brain function in people with early-stage Alzheimer's. In this study, we explored whether a specific type of sound stimulation could help improve thinking abilities. The human brain naturally produces rhythmic electrical activity. One pattern, called "gamma" activity (around 40 cycles per second), is linked to memory and attention. Previous research has shown that this type of brain activity is reduced in people with Alzheimer's disease. We recruited 30 individuals with early-stage Alzheimer's and divided them into two groups. One group listened to specially designed audio tones that gently stimulated the brain at 40 Hz over three weeks. The other group listened to similar sounds without this specific pattern. We then measured their memory, problem-solving skills, and brain activity. Participants who received the 40 Hz sound stimulation showed clear improvements in visual working memory and mental flexibility. We also observed increased activity in the frontal areas of the brain, which are important for planning and decision-making. These findings suggest that simple auditory stimulation may help strengthen brain function in early AD. Because this approach is non-invasive and relatively easy to deliver, it may offer a promising additional tool to support patients and their families.

Introduction

Dementia, characterized by cognitive impairment, impacts between 24 and 50 million people globally (Scheltens et al., 2016). Alzheimer's disease (AD) is the most common cause of dementia, constituting approximately 70% to 80% of cases. The primary features of the disease include extracellular beta-amyloid (Aβ) deposits and intracellular neurofibrillary tangles (tau) (Kumar et al., 2015). The affected demographic for AD typically includes individuals over the age of 60, but it can increasingly affect younger individuals. Specifically, the prevalence of dementia in individuals under 50 years old is less than one in 4000 (Scheltens et al., 2016).

AD is a multifactorial disease with a complex pathophysiology. Typically, the disease has an early preclinical stage. Identifying this early stage may serve as a crucial point for successful interventions (McDermott et al., 2018). Lifestyle-related factors such as diabetes, obesity, smoking, and depression have been highlighted as areas that, if modified, can reduce the risk of the disease (Scheltens et al., 2016).

Human electroencephalography (EEG) studies in AD have reported heterogeneous gamma alterations depending on task demands, disease stage, and recording conditions. Therefore, gamma modulation should not be interpreted as uniformly deficient across all contexts. Research has shown that patients with AD experience cognitive dysfunction (Lambon et al., 2003). These individuals demonstrate impaired performance on tasks involving planning, set shifting, inhibition, sustained attention, divided attention, and selective attention (Stopford et al., 2012). Aberrant neural activity can exacerbate the progression of AD pathology, ultimately disrupting neural circuits involved in higher cognitive functions (Cantor et al., 2013). Conversely, neural activity can also be modulated to mitigate AD pathology (Iaccarino et al., 2016). For instance, gamma oscillations (30-90 Hz), associated with multiple higher-level cognitive functions, have been disrupted in various AD animal models (Gillespie et al., 2016; Iaccarino et al., 2016). Altered gamma, including reduced self-synchronization of gamma and diminished gamma power, has been observed in AD patients and in several AD animal models (Verret et al., 2012; Gillespie et al., 2016).

Gamma oscillations can be induced through sensory stimuli, a phenomenon known as gamma synchronization (Iaccarino et al., 2016). The use of auditory sensory stimuli at a specific frequency can lead to synchronization of brain waves. Synchronization refers to the simultaneous rhythmic (or sequential) alignment to external events (Thut et al., 2011). Auditory stimuli at an optimal level for a short duration can activate various brain functions (Chaudhury et al., 2013). It is believed that the positive effects of auditory stimulation result from the activation of monoaminergic brain circuits, including serotonergic and dopaminergic pathways (Moraes et al., 2018). Additionally, auditory stimulation is hypothesized to facilitate neurogenesis in the hippocampus, promote neuronal repair and reconstruction by regulating steroid hormone secretion, ultimately leading to synaptic plasticity (Fukui et al., 2008).

Considering that studies have indicated a connection between neural activity in the gamma band and a wide range of cognitive functions (Herrmann et al., 2004), and concurrently, existing research literature suggests that individuals with AD exhibit disrupted gamma activity and cognitive deficits, the central inquiry of this study is whether brain auditory stimulation in the gamma band influences cognitive functions in individuals in the early stages of AD. The present study builds upon our previously published work, which investigated the cognitive effects of 40 Hz auditory stimulation in patients with early-stage AD (Mehdizadeh Fanid et al., 2025). While the prior study employed a single-group pre–post design focusing exclusively on behavioral outcomes, the current investigation extends this work by incorporating a parallel control group and quantitative EEG (QEEG) measures to examine neurophysiological correlates of the intervention.

Materials and Methods

Data collection

This study employed a quasi-experimental parallel-group pre–post design. Thirty patients diagnosed with early-stage AD residing in Tabriz City, Iran, were allocated into an intervention group (n=15) and a control group (n=15), as shown in Table 1, using convenience sampling followed by group matching based on age, sex, and baseline mini-mental state examination (MMSE) scores. Using targeted sampling, 15 patients were recruited based on a neurologist-confirmed diagnosis consistent with the criteria outlined by the Alzheimer's Association-National Institute on Aging (AANIA). The inclusion required a definitive diagnosis of AD, while exclusion criteria encompassed lack of consent, diagnoses inconsistent with AD, reversible dementias, such as hypothyroidism and substance-related conditions, severe depression, major organ failure, intracranial lesions, history of subdural hematoma or traumatic brain injury, infections, including viral encephalitis, and other non-AD dementias such as frontotemporal and Lewy body dementia. Ethical approval was granted by the University of Tabriz Ethics Committee, with informed consent obtained from all participants or their legal representatives.

Following referral, participants underwent cognitive screening with MMSE, and only those scoring between 10 and 20, indicative of moderate cognitive impairment, were included. Baseline assessments comprised the computerized digit span test for verbal working memory, the computerized Corsi block-tapping task for visuospatial working memory, the computerized Wisconsin card sorting test (WCST) for abstract reasoning and cognitive flexibility, and QEEG recordings targeting gamma-band brain activity. Individuals presenting psychiatric comorbidities, reversible dementia causes, or histories of traumatic brain injury were excluded. The intervention involved auditory gamma-band stimulation administered over 30 sessions across 3 consecutive weeks, delivered daily at a fixed daytime schedule to control for circadian effects. Stimulation took place in a quiet, well-lit environment with participants seated comfortably and monitored throughout. Auditory stimuli were generated using Gnaural (version 2.3.8), producing binaural beats at 40 Hz based on a 440 Hz carrier frequency with a 480 Hz offset, thereby modulating gamma-band activity. Sound was delivered via calibrated Sparkle stereo headphones (Model SPK-X4) at approximately 60 dB. The control condition consisted of an audio stimulus matched to the intervention in duration and sound intensity but lacking structured interaural phase modulation at 40 Hz. While the control stimulus did not include rhythmic gamma-frequency binaural modulation, we acknowledge that broadband acoustic signals may contain energy across a wide frequency spectrum. Therefore, the control condition was designed to control for general auditory exposure rather than to be spectrally silent in the gamma range. Accordingly, the critical distinction between the intervention and control conditions lies in the presence versus absence of structured rhythmic gamma-frequency entrainment rather than absolute gamma-band acoustic energy.

The carrier frequency of 440 Hz was selected because it lies within a comfortable and easily perceivable auditory range for most adults, minimizing listener fatigue and auditory discomfort (Reedijk et al., 2015). A frequency offset of 480 Hz produces a 40 Hz binaural beat (i.e. 480 Hz – 440 Hz=40 Hz), which aligns with the gamma-band frequency range that has been associated with higher-order cognitive processing and sensory integration (Herrmann, 2001; Ross et al., 2014).

Although the optimal carrier and offset frequencies for inducing gamma-band entrainment in AD have not been definitively established, previous auditory entrainment research in humans has reliably employed similar parameters to target gamma-range activity (Chaieb et al., 2015). Furthermore, studies investigating auditory steady-state responses suggest that binaural beat offsets near 40 Hz can elicit measurable gamma-band phase-locking in EEG recordings, supporting the rationale for this parameter choice (Galambos et al., 1981).

These selections represent a compromise between perceptual salience and the goal of engaging neural dynamics in the gamma range while avoiding excessive auditory strain in an elderly clinical population. Supervision ensured compliance, correct headphone placement, and the absence of environmental distractions during all sessions. A subset of participants in the intervention group overlapped with those included in our previously published behavioral study; however, the present manuscript reports novel neurophysiological outcomes (QEEG) and includes an independent control group, allowing for a controlled comparison of intervention effects.

Assessments included the WCST, block-tapping test, digit span test, and QEEG to evaluate gamma wave activity. Steps of the study are shown in Figure 1.

Study instruments

Digit span test

The digit span test assesses verbal working memory or cognitive digit span (MacLeod et al., 2008). In the computerized version of the digit span test, participants encounter numbers presented both auditorily and visually. They are instructed to immediately replicate the presented numbers by inputting them using the keyboard. In the auditory-only rendition of the test, numbers are presented solely auditorily, prompting participants to repeat them immediately. The examiner records the responses into the computer. The sequence of presented numbers begins with two digits and, with each correct response, extends to 9 digits. The test has demonstrated a reported reliability of 0.63 through the test re-test method (Piper et al., 2015).

The block design test

The block-tapping test, an adaptation of the digit span test, assesses visuospatial working memory without reliance on verbal cues. Despite the increasing complexity in sequences and stimuli, functional magnetic resonance imaging (fMRI) studies show consistent overall brain activity during the test, suggesting that encoding challenges do not significantly impact overall brain engagement (Toepper et al., 2010). The direct version of the test requires visuospatial working memory support, excluding the need for cognitive digit span. As the sequence length exceeds 3 or 4, the central executive becomes active (Vandierendonck et al., 2004). In this test, participants observe and memorize sequences of illuminated blocks, then reproduce them by clicking the corresponding blocks. The test starts with two blocks and progressively increases in complexity up to 9 blocks. It concludes that if two consecutive errors occur, it records the longest correctly recalled sequence. On average, individuals recall about 5 blocks, with a reported test retest reliability of 0.73 (Walker et al., 2010).

WCST

The WCST, devised by Grant and Berg (1948), assesses abstract reasoning through a set of 64 cards featuring symbols (triangle, star, cross, circle) in 4 colours (red, green, yellow, and blue). Participants match cards to an initial set, guided by specific characteristics deduced from examiner feedback. Following ten consecutive correct attempts, the principle shifts, indicating a category transition based on Lazak's neuropsychological framework.

QEEG

Resting-state QEEG recordings were obtained from all participants before and after the intervention under two conditions: eyes open and eyes closed. Data acquisition was performed using the eWave EEG system (Pooyandegan Rah Saadat Co., Iran) with a high-pass filter set at 1 Hz, a low-pass filter at 70 Hz, and a sampling rate of 500 Hz. Electrodes were positioned according to the international 10–20 system, with particular emphasis on the frontal sites Fp1, Fp2, F3, F4, Fz, F7, and F8. To minimize contamination of gamma-band activity by muscle artifacts, EEG recordings were visually inspected, and channels with excessive noise were excluded. Independent component analysis (ICA) was applied to remove ocular and muscle-related components, with component rejection based on established spatial and temporal criteria. Subsequent quantitative analysis was conducted

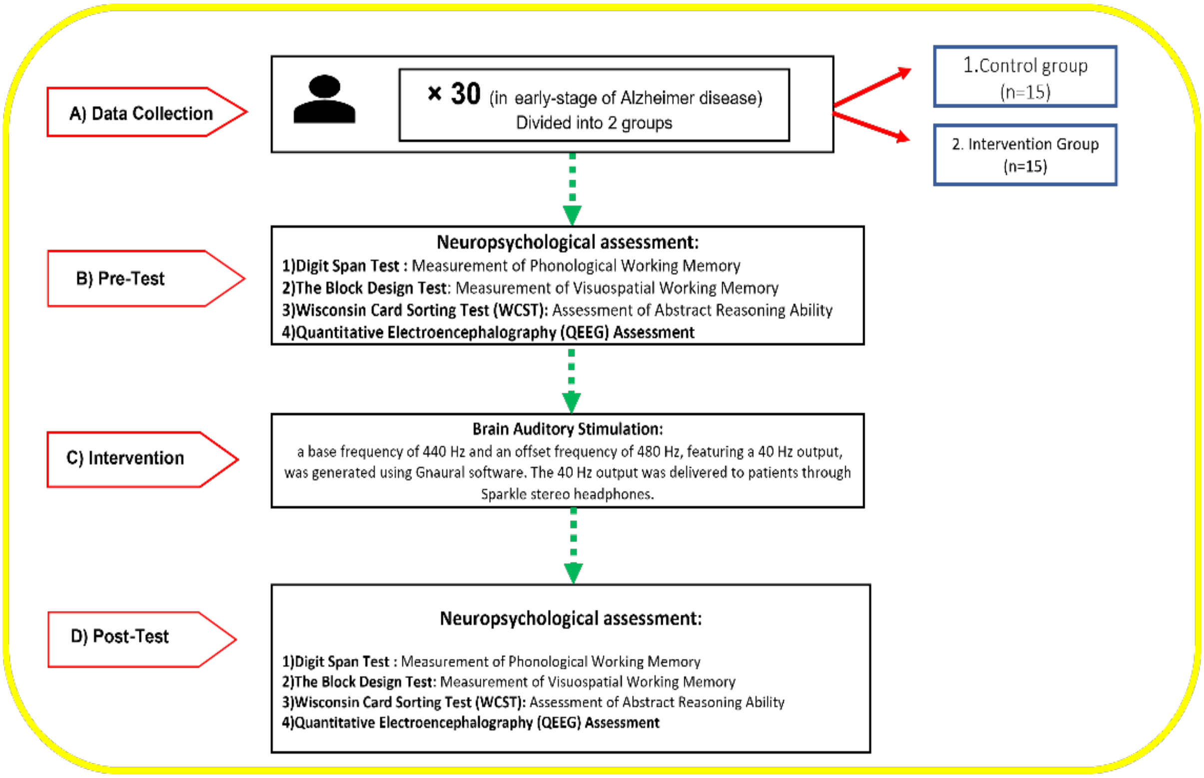

Figure 1. Neuropsychological assessment

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using NeuroGuide software, where absolute and relative gamma power within the 30–45 Hz frequency range were computed for each condition. Spectral analysis employed a fast Fourier transform with a Hamming window and a two-second segment duration. Power values were averaged across the specified frontal electrodes, and relative gamma power was normalized against the total power across all frequency bands to provide standardized measures of cortical activity.

Results

To assess the impact of gamma-band auditory brain stimulation on cognitive functions in AD patients, the initial means of the experimental and control groups were compared before intervention using an independent t-test. The analysis revealed no significant difference between the group means before the intervention (P=0.884), suggesting a baseline homogeneity.

Subsequently, the post-intervention means of both groups were compared using an independent t-test. The Mean±SD for the experimental group after intervention was 48.87±2.72, while the Mean±SD for the control group after intervention was 46.6±3.06. The independent t-test comparison of means showed a significant difference between the two groups (P=0.041). This finding indicates the effectiveness of gamma band brain auditory stimulation on the cognitive functions of AD patients, resulting in an enhancement of cognitive performance in this patient cohort.

To assess the efficacy of gamma-band auditory brain stimulation on working memory for cognitive phonemic tasks in AD patients, the initial means of the experimental and control groups were compared before the intervention using an independent t-test. No significant difference in means between the two groups was observed before intervention (P=0.058).

Subsequently, the post-intervention means of both groups were compared using an independent t-test. The Mean±SD for the experimental group after intervention was 2.5±0.5, and the Mean±SD for the control group after intervention was 1.86±0.44. The comparison of means using an independent t-test revealed a significant difference between the two groups (P=0.001), indicating that the observed mean difference is statistically significant. This finding suggests that auditory gamma-band stimulation enhances working memory for cognitive phonemic tasks in individuals with AD.

In the context of investigating the impact of brain auditory stimulation in the gamma band on the absolute

Table 1. Demographic characteristics of study participants

Variables		No. (%)/Mean±SD
Group	Intervention group	15(50)
	Control group	15(50)
Gender	Man	18(60)
	Woman	12(40)
Age (y)		60.93±17.98

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power of gamma waves in individuals with early-stage AD, brainwave recordings were acquired in both open- and closed-eye conditions, with subsequent comparison of gamma-band absolute power in the frontal region. Initially, mean values of the two experimental and control groups were compared before the intervention using an independent t-test. No statistically significant differences in means between the two groups were observed before the intervention, with P values of 0.933 in the open-eye condition and 0.082 in the closed-eye condition.

Following the intervention, post-intervention means of the two groups were examined using an independent t-test. The Mean±SD for the experimental group after intervention in the open-eye condition was 3.84±2.08, while the Mean±SD for the control group after intervention in the open-eye condition was 3.15±2.39. This difference was not statistically significant (P=0.408), suggesting that brain auditory stimulation in the gamma band did not significantly affect gamma wave power in individuals with Alzheimer's in the open-eye condition.

In the closed-eye condition, the Mean±SD for the experimental group after intervention was 3.02±1.33, whereas in the control group, it was 1.47±0.69. The comparison of means using an independent t-test showed a significant difference (P<0.001), indicating that the application of brain auditory stimulation in the gamma band increased the absolute gamma power in individuals with AD during the closed-eye condition.

To explore the impact of auditory brain stimulation in the gamma band on gamma wave power in individuals with early-stage AD, brainwave recordings were collected under open- and closed-eye conditions, focusing on the frontal region. Initially, the mean values of the experimental and control groups were compared before the intervention using an independent t-test. No noteworthy difference in means was found before the intervention, with P values of 0.170 in the open-eye condition and 0.053 in the closed-eye condition.

Following this, the post-intervention means of the two groups were compared using an independent t-test. The Mean±SD for the experimental group after intervention in the open-eye condition was 2.15±1.45, and for the control group, it was 2.75±1.11. This disparity was not statistically significant (P=0.21), indicating that brain auditory stimulation in the gamma band did not significantly alter the relative gamma power in individuals with AD in the open-eye condition.

In contrast, for the closed-eye condition, the Mean±SD for the experimental group after intervention was 2.6±1.5, while for the control group, it was 4.29±1.44. The comparison of means using an independent t-test revealed a significant difference (P=0.004), indicating that applying brain auditory stimulation in the gamma band effectively increased the relative gamma power in individuals with AD during the closed-eye condition. Further details are provided in Tables 2 and 3 in the subsequent section.

Discussion

This study investigated the effects of auditory gamma-band stimulation on cognitive function and frontal gamma oscillatory activity in patients with early-stage AD. The results demonstrated significant improvements in visuospatial working memory (measured by the Corsi block-tapping task), cognitive flexibility (assessed by the WCST), and frontal gamma power during the eyes-closed condition.

These cognitive enhancements align with previous animal studies showing that 40 Hz auditory or visual stimulation can boost microglial activity and reduce amyloid plaque burden, particularly in the prefrontal cortex and hippocampus (Martorell et al., 2019; Iaccarino et al.,

Table 2. Mean of investigated variables in the intervention and control groups before the intervention

Variables	Mean±SD		P
	Control Group	Intervention Group	
Cognitive functions (WCST)	45.8±2.542	47.45±2.615	0.726
Block-tapping	1.96±0.39	1.63±0.51	0.058
Digit span	2.13±0.228	2±0.387	0.252
Absolute gamma (closed eyes) before	3.029±2.353	1.82±1.04	0.119
Absolute gamma (open eyes) before	2.72±2.41	2.65±2.118	0.933
Relative gamma (closed eyes) before	16.57±7.13	12.44±6.766	0.11
Relative gamma (open eyes) before	6.01±5.07	8.87±6.07	0.17

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2016). Gamma-band oscillations are critically involved in working memory, attention, and sensory integration, and their disruption has been widely documented in both AD patients and transgenic animal models (Verret et al., 2012; Colgin & Moser, 2010). In our study, gamma stimulation sessions were administered in a controlled environment using binaural beats, with strict monitoring of participant adherence and session quality. Notably, the increase in gamma power was observed only in the eyes-closed state, suggesting that frontal resting-state networks may be more responsive to frequency-based entrainment when sensory input is minimized. Importantly, no significant improvements were observed in phonological working memory (digit span task), suggesting differential involvement of neural circuits less sensitive to auditory entrainment. This selective effect highlights the importance of task modality and frequency-specific targeting in cognitive rehabilitation strategies for AD. The selective enhancement of gamma power observed only in the eyes-closed condition may reflect reduced sensory interference and greater engagement of intrinsic neural networks such as the default mode network.

AD is a complex neurodegenerative disorder with limited treatment options. Gamma-band stimulation, particularly at 40 Hz, has emerged as a promising non-pharmacological approach due to its association with cognitive functions and its ability to modulate disrupted neural oscillations characteristic of AD (Palop et al., 2016). External stimulation in this frequency range elicits predictable neural responses (such as event-related potentials and steady-state responses), which can be harnessed therapeutically. Previous human studies have demonstrated the role of gamma oscillations in visual

Table 3. Mean of investigated variables in the intervention and control groups after the intervention

Variables	Mean±SD		P
	Control Group	Intervention Group	
Cognitive functions (WCST)	46.6±3.06	48.87±2.72	0.028
Block-tapping	1.86±0.44	2.5±0.5	0.001
Digit span	1.93±0.37	2.1±0.33	0.209
Absolute gamma (closed eyes) after	1.47±0.69	3.02±1.33	0.001
Absolute gamma (open eyes) after	3.15±2.39	3.84±2.08	0.408
Relative gamma (open eyes) after	2.75±1.11	2.15±1.45	0.21
Relative gamma (closed eyes) after	4.29±1.44	2.6±1.5	0.004

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feature binding, memory, and higher cognitive functions (Tallon-Baudry et al., 1999; Van Wijk et al., 2010; Miller et al., 2018; Griffiths et al., 2019; Benussi et al., 2021; Traikapi & Konstantinou, 2021). Gamma rhythms are notably prominent in the hippocampus, where they contribute to memory processing (Colgin & Moser, 2010; Carr et al., 2012; Buzsáki, 2015). Disruptions in gamma activity have been linked to memory impairments typical of AD, and restoring gamma oscillations via auditory stimulation may enhance cognitive function.

Moreover, Goutagny et al. (2013) demonstrated that reductions in slow gamma activity (25–50 Hz) in the hippocampal CA1 region contribute to memory deficits. Thus, synchronization at 40 Hz could modulate neural oscillations, thereby improving gamma power and cognitive outcomes. Clinical and preclinical studies support the therapeutic potential of 40 Hz stimulation in reducing amyloid pathology and improving cognition (Iaccarino et al., 2016; Clements-Cortes et al., 2016). While limitations remain, gamma-based auditory stimulation offers a promising, non-invasive approach for AD treatment, potentially serving as an adjunct to pharmacological therapies. Additionally, caregivers reported improvements in mood, motivation, emotional regulation, and reduced depressive symptoms in participants receiving auditory stimulation, warranting further exploration of mood-related benefits.

The apparent discrepancy between increased absolute gamma power and reduced relative gamma power likely reflects normalization effects, whereby increases in total broadband power influence relative spectral proportions. This finding underscores the importance of cautious interpretation of relative power metrics.

Given the limited existing data on gamma-band auditory stimulation in AD, further research with larger samples and diverse populations is necessary. Interdisciplinary collaboration across neurology, cognitive rehabilitation, and related fields will be essential to optimize this therapeutic approach and potentially slow AD progression while improving quality of life. Moreover, it should be acknowledged that part of the intervention group has been described in a previous behavioral study. However, the current manuscript addresses distinct research questions by integrating electrophysiological outcomes and a controlled design, thereby providing novel mechanistic insights into gamma-band auditory stimulation in AD.

An important methodological limitation of the present study concerns the control stimulus. Although the control condition lacked structured gamma-frequency binaural modulation, broadband auditory stimuli may still contain energy across multiple frequency bands, including the gamma band. Because detailed spectral analyses (e.g. power spectral density or spectrograms) were not performed, the findings should be interpreted as reflecting rhythmic gamma entrainment rather than strictly gamma-specific acoustic exposure. Future studies should incorporate spectrally verified control stimuli and detailed acoustic analyses.

Another limitation of the present study is that EEG recordings were obtained only before and after the intervention and not during auditory stimulation sessions. Therefore, direct measures of neural entrainment, such as steady-state auditory evoked responses or phase-locking indices, could not be assessed. In addition, the spectral analysis focused primarily on the gamma band, and potential effects on other frequency bands (delta, theta, alpha, and beta) cannot be excluded.

A methodological limitation of the present study is that the control stimulus may have contained broadband acoustic energy, including gamma-range frequencies. Consequently, the observed effects should be interpreted as reflecting the impact of rhythmic gamma-band entrainment rather than exclusive exposure to gamma-band acoustic energy.

Because EEG was not recorded during auditory stimulation, direct indices of neural entrainment, such as auditory steady-state responses or phase-locking measures, could not be assessed. Additionally, spectral analysis was restricted to the gamma band, and potential effects in other frequency bands (delta, theta, alpha, beta) were not evaluated. The electrode montage focused primarily on frontal sites, which may have limited the detection of stimulation-related effects in other cortical regions.

Correlational analyses between changes in gamma power and cognitive improvements were not conducted due to limited statistical power, given the small sample size.

The relatively small sample size limits statistical power and increases the risk of both type I and type II errors. Accordingly, the findings should be interpreted as preliminary and hypothesis-generating rather than confirmatory.

Conclusion

These findings suggest that auditory stimulation at 40 Hz selectively modulates neural circuits associated with executive and spatial cognitive functions and may serve as a viable non-invasive adjunctive intervention in early-stage AD.

Ethical Considerations

Compliance with ethical guidelines

This study was approved By the Research Ethics Committee of the University of Tabriz, Tabriz, Iran (Code: IR.TABRIZU.REC.1400.024). Informed consent obtained from all participants or their legal representatives.

Data availability

The datasets used and analyzed during the current study are available from the corresponding author upon reasonable request.

Declaration of generative AI and AI-assisted technologies in the writing process

No AI tool influenced the scientific content, data analysis, or conclusions of this work.

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Authors' contributions

All authors contributed equally to the conception and design of the study, data collection and analysis, interception of the results and drafting of the manuscript. Each author approved the final version of the manuscript for submission.

Conflict of interest

The authors declared no conflict of interest.

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