Women. Health. Bull. 2026; 13(3)

Published online 2026 July.

Original Article

The Effectiveness of Cognitive Behavioral Hypnotherapy on Executive Functions, Emotion Regulation, Self-Blame and Stigma in Alzheimer's Disease

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Received: June 26, 2025; **Revised:** August 16, 2025; **Accepted:** October 16, 2025

Abstract

Background: Alzheimer's disease is a progressive neurodegenerative disorder that disrupts executive functions and emotional regulation, often leading to self-blame and perceived stigma in elderly patients. Therefore, the present study was conducted to evaluate the effectiveness of Cognitive Behavioral Hypnotherapy (CBH) in enhancing executive functions, improving cognitive emotion regulation, and reducing self-blame and stigma in elderly women with mild-to-moderate Alzheimer's disease.

Methods: This was a quasi-exprimental study with two-group pretest–posttest design. It was conducted from August 2024 to March 2025 on 90 women diagnosed with Alzheimer's disease, recruited through convenience sampling technique from specialized Alzheimer's centers in Tehran, Tabriz, and Ardabil (Iran). The study participants were assigned to either an experimental group receiving Cognitive Behavioral Hypnotherapy (CBH) or a control group receiving standard care. The intervention consisted of 12 individual CBH sessions held once a week, focusing on cognitive restructuring, guided imagery, emotional reframing, and post-hypnotic suggestions aimed at enhancing cognitive and emotional regulation. Outcome measures included Wisconsin Card Sorting Test (WCST), Cognitive Emotion Regulation Questionnaire (CERQ), Self-Blame Questionnaire (SBQ), and Affiliate Stigma Scale (ASS), administered before and after the intervention. Data were analyzed using IBM SPSS version 27 through independent and paired sample t-tests, ANCOVA, and repeated measures analysis.

Results: The experimental group showed significant improvements in executive functions and cognitive emotion regulation compared with the control group. Specifically, participants completed more categories on the WCST (mean difference=1.770, P<0.001) and made fewer perseverative errors (mean difference=–9.232, P<0.001). They also showed better cognitive emotion regulation (CERQ: mean difference=20.367, P<0.001). In addition, self-blame (SBQ: mean difference=–8.127, P<0.001) and stigma (ASS: mean difference=–18.068, P<0.001) were significantly reduced compared with the control group.

Conclusions: Cognitive Behavioral Hypnotherapy significantly enhanced executive functions, improved cognitive emotion regulation, and reduced self-blame and perceived stigma in elderly women with mild-to-moderate Alzheimer's disease. It is recommended that the CBH protocol from this study be implemented as a standard non-pharmacological intervention in Iranian memory clinics, with weekly sessions conducted in quiet settings to enhance executive functions and reduce self-blame and perceived stigma in mild-to-moderate Alzheimer's patients.

Keywords: Cognitive Behavioral Hypnotherapy, Executive Function, Cognitive Emotion Regulation, Self-Blame, Stigma, Alzheimer's Disease

How to Cite: Noroozi Homayoon MR, Saei M, Borjalizadeh Z, Eyvazzadeh Gharajeh H, Sadri Damirchi E, Nasiri. The Effectiveness of Cognitive Behavioral Hypnotherapy on Executive Functions, Emotion Regulation, Self-Blame and Stigma in Alzheimer's Disease. Women. Health. Bull. 2026;13(3):1-12. doi: 10.30476/whb.2026.107590.1360.

1. Introduction

Alzheimer's disease (AD) is one of the most prevalent neurodegenerative disorders associated with aging, significantly affecting the elderly population (1). Characterized by the progressive degeneration of brain cells, particularly in the hippocampus and regions responsible for memory and cognition, Alzheimer's disease leads to symptoms such as forgetfulness, impaired decision-making, reduced attention, and deficits in executive functions (2). In Iran, the prevalence of Alzheimer's disease is rising due to the growing elderly population (3). This disease imposes a heavy burden on caregivers and healthcare systems, highlighting the urgent need for effective psychological and

non-pharmacological interventions that can mitigate cognitive and emotional decline. Implementing such interventions can enhance cognitive and emotional functioning, improve daily activities, and alleviate the societal burden of AD.

Alzheimer's disease significantly affects executive functions, including working memory, attention, and cognitive flexibility, all of which play a crucial role in daily life (4). These functions, essential for planning, problem-solving, and behavioral control, are governed by neural networks primarily located in the prefrontal cortex (5). In patients with Alzheimer, beta-amyloid and tau protein buildup causes synaptic dysfunction and neuron death, impairing working memory, attention, and cognitive flexibility due to damage in hippocampal, prefrontal, and parietal regions. These deficits severely impact daily life, highlighting the need for targeted treatments (6).

Another frequently observed issue in patients with Alzheimer's disease is impaired cognitive emotion regulation. Cognitive emotion regulation refers to the ability to manage and control emotions through cognitive processes, playing a fundamental role in mental health (7). This process is disrupted in AD due to neurocognitive deficits. Emotional regulation is primarily influenced by the prefrontal cortex, amygdala, and cingulate cortex (8). AD impairs prefrontal cortex function, reducing emotion regulation while increasing amygdala-driven emotional reactivity. This imbalance disrupts adaptive strategies (e.g., cognitive reappraisal) while promoting maladaptive ones (e.g., self-blame), worsening emotional control and stress coping. Targeted psychological interventions are needed to improve regulation (9).

Self-blame is another prevalent psychological response in patients with Alzheimer's disease. It often emerges as a reaction to cognitive impairments and memory-related challenges. Self-blame may arise from a sense of incompetence and misplaced responsibility for cognitive decline, potentially leading to an identity crisis in these patients (10). Psychological theories suggest that self-blame fosters guilt and lowers self-esteem, contributing to increased depression and anxiety (11). Additionally, self-blame in patients with Alzheimer's disease reduces coping abilities and treatment motivation, worsening disease progression and social isolation. This negatively impacts mental health, social interactions, and daily functioning (12).

Another critical issue in patients with Alzheimer's disease is stigma. Stigma refers to the negative labeling and marginalization of individuals due to specific characteristics or conditions, exerting profound psychological and social effects on patients with Alzheimer's disease (13). This phenomenon is particularly pronounced in the elderly, as AD progressively impairs cognitive abilities and memory, leading to feelings of shame, social isolation, and reduced self-esteem (14). Social psychology theories, such as stigma theory, indicate that patients with Alzheimer's disease may internalize negative perceptions and self-stigmatize, exacerbating the psychological burden of the disease (15). Social stigma results in limited treatment opportunities, as individuals may hesitate to seek help or participate in social activities (16). Research suggested that interventions like Cognitive Behavioral Hypnotherapy can effectively reduce executive dysfunction, cognitive emotion dysregulation, self-blame, and stigma (17-19). Moreover, critical psychosocial factors including stigma, self-blame, and cognitive and emotional impairments present significant challenges in AD management. These factors can accelerate disease progression, severely diminish patients' quality of life, and reduce adherence to treatment regimens. Within the cultural context of Iran, where negative attitudes toward illness and limited social support may prevail, addressing these issues becomes particularly crucial. Therefore, implementing comprehensive interventions targeting these psychological and social dimensions can enhance cognitive and emotional functioning, improve daily living activities, and alleviate the societal burden of AD. Also, given the growing elderly population and the rising prevalence of Alzheimer's disease in the Iranian society, there is an increasing need for effective therapeutic interventions that address both cognitive functioning and psychological challenges in these patients. Complementary approaches, such as Cognitive Behavioral Hypnotherapy (CBH), may offer promising strategies to enhance executive functioning, improve cognitive emotion regulation, and reduce maladaptive psychological outcomes such as self-blame and stigma. Therefore, the present study aimed to investigate the effects of CBH on executive functions, cognitive emotion regulation, self-blame, and perceived stigma in elderly women with mild-to-moderate Alzheimer's disease. Specifically, we sought to

determine whether CBH could provide measurable improvements in cognitive and psychosocial outcomes, thereby offering an evidence-based complementary intervention to support patients' quality of life and reduce the broader psychological and economic impact of the disease.

2. Method

2.1. Design

This was a quasi-exprimental study with two-group pretest–posttest design to evaluate the effectiveness of Cognitive Behavioral Hypnotherapy (CBH) in elderly women with mild to moderate Alzheimer's disease.

2.2. Selection and Description of Participants

A total of 119 participants were recruited consecutively from specialized Alzheimer's centers in Tehran, Tabriz, and Ardabil, Iran, and assessed for eligibility. Ninety participants who met the inclusion criteria were assigned to either the intervention group (n=45) or the control group (n=45), using a non-random allocation procedure in accordance with the quasi-experimental study design. Participants were not randomly assigned to the study groups; group allocation was conducted according to the predefined allocation procedure of the study. This study involved 90 elderly participants diagnosed with mild to moderate Alzheimer's disease, aged 65 to 85 years (mean age=75, SD=6.5). To ensure accurate staging of Alzheimer's disease, collaboration occurred with neurologists, geriatric psychologists, and clinical staff. These professionals assisted in identifying eligible participants based on established clinical criteria and cognitive assessments. The participants were included if they met all of the following criteria: female sex; a diagnosis of Alzheimer's disease confirmed by a neurologist or geriatric psychiatrist based on DSM-5 diagnostic criteria; mild-to-moderate Alzheimer's disease, defined by a Mini-Mental State Examination (MMSE) score of 18–26 or a Montreal Cognitive Assessment (MoCA) score of 12–22; stable medication use, with no changes in cholinesterase inhibitors (e.g., donepezil or rivastigmine) or other cognitive medications during the three months preceding study enrollment; and the ability to understand basic verbal instructions and participate in structured therapy sessions, as confirmed by a clinical psychologist or occupational therapist. The participants were excluded from the study if they met any of the following criteria: Severe Alzheimer's disease (MMSE<18, MoCA<12), comorbid severe psychiatric disorders (e.g., schizophrenia, major depressive disorder with psychotic features), other neurodegenerative disorders (e.g., Parkinson's disease, frontotemporal dementia), or participation in another cognitive intervention study within the past six months.

2.3. Sample Size Determination

The sample size calculation was based on executive function as the primary outcome, using data reported in a previous study (20). Considering a two-tailed significance level of 0.05, a statistical power of 80%, and an effect size of approximately 0.5, a minimum of 15 participants per group was estimated. To increase reliability and compensate for potential dropouts, 45 participants were enrolled in each group.

2.4. Data Collection and Measurements

Wisconsin Card Sorting Test (WCST): The Wisconsin Card Sorting Test (WCST) was used to evaluate executive functioning, particularly cognitive flexibility and working memory. The test has demonstrated high sensitivity in distinguishing cognitive impairments in Alzheimer's and Parkinson's disease (21). Given the study's focus, WCST was administered with a specific emphasis on assessing cognitive flexibility and attention-related components, while the inhibition (impulse control) subtest was excluded due to its limited relevance in Alzheimer's populations.

2.4.1. Affiliate Stigma Scale (ASS): The Affiliate Stigma Scale (ASS) used to measure cognitive, affective, and behavioral aspects of affiliate stigma among individuals who care for those with mental illness. The scale has been validated across diverse populations and languages, demonstrating strong internal consistency (Cronbach's α=0.82–0.94) and robust associations with caregiver burden, depression, and anxiety (22).

2.4.2. Cognitive Emotion Regulation Questionnaire (CERQ): The Cognitive Emotion Regulation Questionnaire (CERQ) was administered to assess adaptive and maladaptive emotion regulation strategies. CERQ consists of nine subscales and

has demonstrated strong psychometric properties, with reliability coefficients ranging from 0.75 to 0.87 (23). The tool is widely used in clinical and non-clinical settings to examine how individuals regulate emotional distress, particularly in relation to depression and anxiety (24).

2.4.3. Self-Blame Questionnaire (SBQ): The Self-Blame Questionnaire (SBQ), developed by Eways and co-workers, was included to assess self-criticism and self-reassurance tendencies. This instrument evaluates two distinct forms of self-blame—behavioral and characterological—and has been linked to higher levels of psychological distress, particularly in individuals with chronic illnesses (20).

2.5. Procedure

Following recruitment and eligibility assessment, participants underwent baseline (pre-test) assessments of executive functions, cognitive emotion regulation, self-blame, and stigma before the intervention. Participants in the intervention group received 12 weekly individual sessions of Cognitive Behavioral Hypnotherapy (CBH) in addition to their routine medical care, whereas participants in the control group continued to receive routine medical care without any additional psychological intervention. The content and sequence of the 12 CBH sessions are presented in Table 1. Participant flow and dropouts are shown in Figure 1. Following completion of the 12-week intervention, participants who completed the study underwent post-test assessments using the same outcome measures administered at baseline.

The CBH intervention protocol was specifically developed and tailored for elderly individuals with mild-to-moderate Alzheimer's disease. The protocol was informed by established principles of Cognitive Behavioral Hypnotherapy, particularly those outlined by Robertson (25), and was adapted to the cognitive and emotional characteristics of the target population. Prior to implementation, the protocol was reviewed by a panel of five experienced professors in clinical psychology and hypnotherapy. The experts assessed the protocol with regard to its therapeutic appropriateness, clarity, and consistency with established evidence-based principles. Based on their feedback, minor modifications were made to the content and structure of the sessions.

Following expert review, the revised protocol was piloted with 10 participants who met the study's eligibility criteria but were not included in the main study. The pilot was conducted to assess the feasibility, clarity, and practical applicability of the intervention procedures for the target population.

Table 1: Intervention Protocol of Cognitive Behavioral Hypnotherapy (CBH)

Session 1: Introduction and Assessment	The therapist introduced the concept of CBH and built rapport with the participants. Initial assessments were conducted to evaluate baseline executive function, emotional regulation, self-blame, and stigma. The therapist explained the goals of treatment and the connection between thoughts, emotions, and behaviors.
Sessions 2-4: Cognitive Restructuring and Relaxation Techniques	The therapist focused on teaching basic relaxation techniques to reduce anxiety. The therapist guided participants in identifying and challenging negative thought patterns related to self-blame and stigma. Hypnosis was used to reinforce new cognitive patterns and deepen relaxation.
Session 5: Self-Regulation Strategies	The therapist introduced advanced emotional regulation strategies, including mindfulness and grounding techniques. Participants practiced these strategies under hypnosis, reinforcing their ability to manage emotional responses to daily challenges.
Sessions 6-7: Enhancing Cognitive Functioning	The therapist focused on improving cognitive functioning through exercises designed to stimulate memory, decision-making, and problem-solving. Hypnotherapy was used to enhance focus and concentration during these exercises.
Sessions 8-9: Addressing Self-Blame and Stigma	The therapist worked on reducing feelings of self-blame and stigma. Hypnotherapy was used to guide participants in reframing negative internal narratives, promoting healthier self-perceptions and reducing societal stigma.
Session 10: Building Resilience and Coping Mechanisms	The therapist taught participants how to identify and apply resilience-building coping mechanisms. Hypnosis deepened the integration of these strategies, helping participants strengthen their ability to handle stress and adversity.
Session 11: Reinforcing Positive Change	The therapist focused on reinforcing the positive changes made so far. Participants were encouraged to continue practicing cognitive and emotional strategies. Hypnotherapy was used to strengthen commitment to these changes.
Session 12: Review and Conclusion	The therapist reviewed the progress made, reflecting on improvements in executive functioning, emotional regulation, self-blame, and stigma. A final assessment was conducted to measure change, and the therapist provided suggestions for maintaining progress and continuing self-directed practice.

CBH: Cognitive Behavioral Hypnotherapy

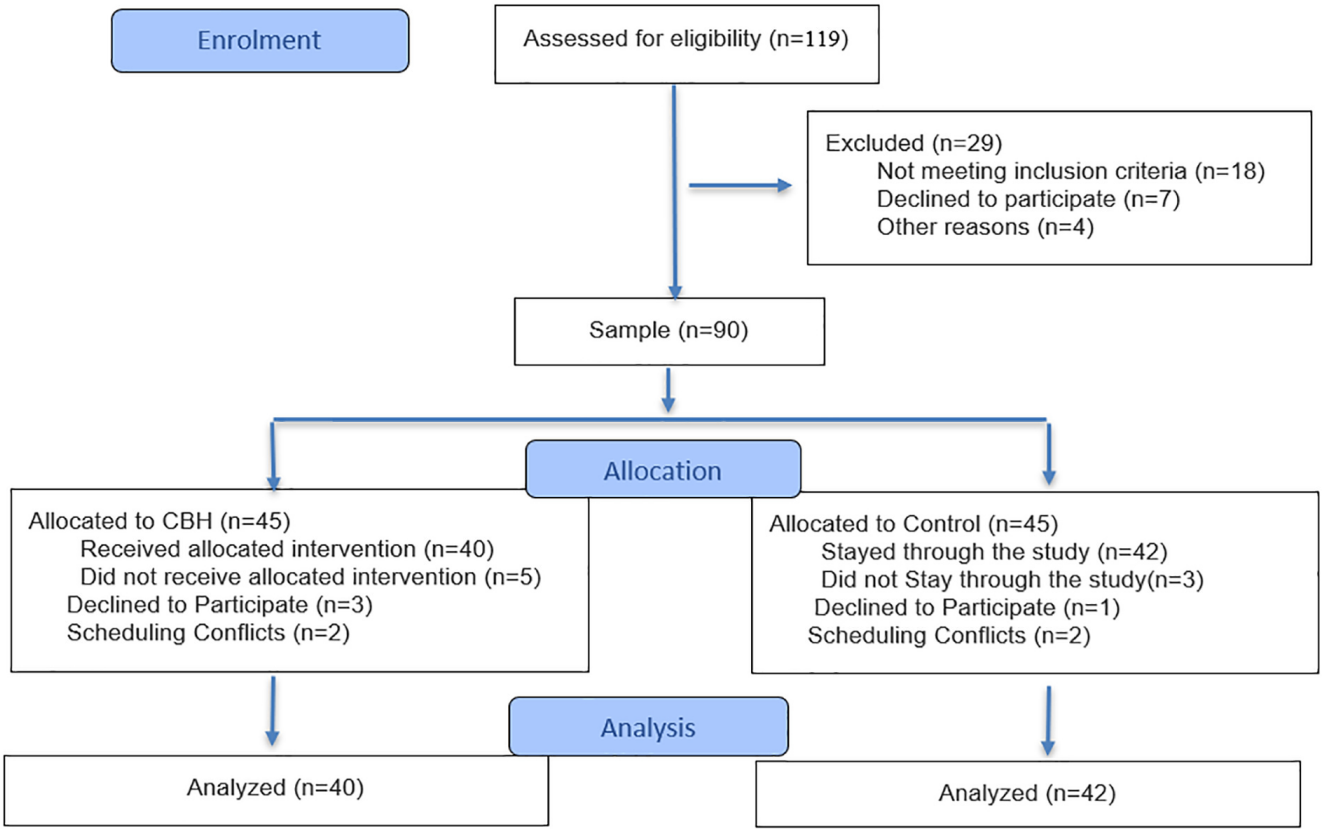

Figure 1: The figure shows the CONSORT flow diagram of the study.

Participant feedback was considered in making minor refinements to the intervention protocol before commencement of the main study. The pilot participants were not included in the final study sample. The detailed session plan, including the objectives and therapeutic techniques used in each session, is presented in Table 1.

2.6. Data Analysis

Data analysis was performed using IBM SPSS Statistics version 27. Descriptive statistics, including mean and standard deviation, were calculated. Baseline differences between the experimental and control groups were assessed with independent t-tests for continuous variables and chi-square (χ^2) tests for categorical variables. T-tests, ANCOVA, and repeated measures analyses were conducted to examine the effects of cognitive-behavioral hypnotherapy on executive functioning, cognitive emotion regulation, self-blame, and stigma. Baseline scores were controlled in the ANCOVA analyses. Assumptions for each analysis, including normality, homogeneity of variances, and sphericity, were checked using appropriate tests such as the Shapiro-Wilk test, Levene's test, and Mauchly's test. A P value<0.05 was considered statistically significant.

3. Results

A total of 82 elderly participants who met the inclusion criteria were enrolled in the study, with 40 participants assigned to the experimental group and 42 to the control group using a non-random allocation procedure. All participants completed both the pre-test and post-test assessments. Participants were classified by age into four groups (65–70, 70–75, 75–80, and 80–85 years) and by educational attainment into four levels: no formal education, basic, secondary, and higher education. The demographic characteristics of the participants are summarized in Table 2.

Regarding education, in the CBH group, 16 participants (35.6%) had no formal education, 12 (26.7%) had basic education, 9 (20%) had secondary education, and 8 (17.7%) had higher education. In the control group, 19 participants (42.2%) had no formal education, 8 (17.8%) had basic education, 11 (24.4%) had secondary education, and 7 (15.6%) had higher education. No statistically significant difference was observed between groups in terms of education (χ^2=0.152, P=0.815).

Table 2: Demographic characteristics of the participants

Demographic Variables		Hypnotherapy		Control		χ^2	P value
		Abundance	Percentage	Abundance	Percentage		
Education	No Formal Education	16	35.6	19	42.2	0.152	0.815
	Basic Education	12	26.7	8	17.8		
	Secondary Education	9	20	11	24.4		
	Higher Education	8	17.7	7	15.6		
Age	65 to 70	14	31.1	10	22.2	14.569	0.691
	70 to 75	10	22.2	11	24.5		
	75 to 80	9	20	15	33.3		
	80 to 85	12	26.7	9	20		

Table 3: Mean and Standard Deviation of pre-test and post-test for deoendent vriables

Variables	Phases	Cognitive Behavioral Hypnotherapy	Control	P value (between group)
		Mean±SD	Mean±SD	
Categories Completed	Pre-test	2.73±0.751	2.69±0.841	0.409
	Post-test	4.68±0.997	2.09±1.055	0.001
P value (within group)		0.001	0.283	
Perseverative Errors	Pre-test	24.10±7.056	23.21±5.953	0.094
	Post-test	13.13±4.513	24.36±6.457	0.019
P value (within group)		0.001	0.552	
Stigma	Pre-test	48.38±5.821	51.93±6.002	0.755
	Post-test	34.08±6.821	52.14±7.049	0.023
P value (within group)		0.001	0.765	
Cognitive Emotion Regulation	Pre-test	90.95±7.435	89.88±7.919	0.916
	Post-test	110.20±8.459	89.83±7.830	0.004
P value (within group)		0.001	0.946	
Self-blame	Pre-test	45.53±10.488	39.83±10.502	0.355
	Post-test	18.60±11.779	41.95±12.173	0.001
P value (within group)		0.001	0.307	

CBH: Cognitive Behavioral Hypnotherapy; SD: Standard Deviation

Regarding age, in the hypnotherapy group, 14 participants (31.1%) were 65–70 years old, 10 (22.2%) were 70–75, 9 (20%) were 75–80, and 12 (26.7%) were 80–85. In the control group, 10 participants (22.2%) were 65–70 years old, 11 (24.5%) were 70–75, 15 (33.3%) were 75–80, and 9 (20%) were 80–85. No significant difference was observed between groups for age (χ^2=14.569, P=0.691). Descriptive statistics showed that the two groups were similar in terms of age and educational level, with no statistically significant differences between them. The pre-test and post-test mean scores for all outcome measures are presented in Table 3. No significant (P<0.05) intergroup differences were found at pre-test.

A T-tests, ANCOVA, and repeated measures analyses were conducted to assess the effect of CBH on dependent variables (Table 3). Compared with the control group, the experimental group showed significant improvements in Categories Completed and significant reductions in Perseverative Errors on the WCST, indicating improved executive functioning. Cognitive emotion regulation also improved significantly in the experimental group (P=0.001). The mean ± SD values for the outcome variables at pre-test and post-test are presented in Table 3. For Categories Completed, the CBH group showed a significant increase from 2.73±0.751 at pre-test to 4.68±0.997 at post-test, compared with the change in the control group from 2.69±0.841 to 2.09±1.055 (P=0.001 between groups). Perseverative Errors decreased in the CBH group from 24.10±7.056 to 13.13±4.513, while the control group remained stable at 23.21±5.953 to 24.36±6.457 (P=0.019). Stigma scores in the CBH group reduced from 48.38±5.821 to 34.08 ± 6.821, compared with 51.93±6.002 to 52.14±7.049 in the control group (P=0.023). Cognitive Emotion Regulation improved in the CBH group from 90.95±7.435 to 110.20±8.459, while the control group showed minimal change from 89.88±7.919 to 89.83±7.830

(P=0.004). Self-blame decreased significantly in the CBH group from 45.53±10.488 to 18.60±11.779, compared with 39.83±10.502 to 41.95±12.173 in the control group (P=0.001). These results highlighted the significant positive impact of CBH across all measured outcomes. Additionally, the experimental group showed significantly lower levels of self-blame and stigma than the control group following the intervention (P=0.001), suggesting significant positive impact of CBH.

Following the intervention, qualitative feedback from participants in the experimental group (n=40) indicated several perceived benefits. Specifically, 53% of participants reported increased mental clarity, 68% reported emotional relief, and 40% reported improved self-perception.

4. Discussion

The present study aimed to investigate the effectiveness of Cognitive Behavioral Hypnotherapy on improving executive function, cognitive emotion regulation, self-blame, and stigma in older adults with mild Alzheimer's disease. The findings of this study revealed that CBH had a positive and significant impact on enhancing cognitive flexibility and working memory/attention, which is consistent with the previous studies (26, 27). However, the present study extended beyond prior work (26, 27), by providing a comprehensive neurobiological explanation for these effects. The improvements seen in executive functions and emotional regulation after CBH may be explained by its effects on two brain pathways. First, hypnosis reduces excessive activity in the default mode network, which helps decrease rumination and self-blame. Second, cognitive restructuring strengthens the prefrontal cortex's control over emotional responses, which leads to better emotion regulation and less perceived stigma (28). Furthermore, unlike previous studies (25, 26) that focused solely on cognitive aspects, our results uniquely indicated that CBH simultaneously improves cognitive emotion regulation, reduces self-blame through modulation of orbitofrontal-accumbens pathways and serotonergic inhibition, and decreases stigma via reorganization of social cognition networks in the temporoparietal junction and medial prefrontal cortex (29). This multidimensional approach, addressing both cognitive and emotional-social domains through specific neurobiological pathways, distinguishes our findings from earlier research that typically examined these outcomes in isolation (30).

Another findings of this study showed that Cognitive Behavioral Hypnotherapy (CBH) had a positive and significant effect on cognitive emotion regulation in elderly women with mild-to-moderate Alzheimer's disease, which is consistent with previous studies (17-19). However, the present study extended beyond prior research (17-19) by providing a comprehensive neurobiological explanation for these effects. Our findings suggest that CBH may enhance cognitive emotion regulation through a dual mechanism. CBH may strengthen top-down prefrontal control over emotional responses, potentially enabling patients to reappraise negative situations more effectively. At the same time, it may modulate bottom-up neurotransmitter activity by increasing serotonergic signaling and reducing excessive noradrenergic input. This combined action seems to restore the balance between cognitive and emotional brain networks, which could lead to more adaptive emotion regulation and reduced maladaptive responses such as self-blame and rumination. These neural changes might underpin the improvements observed in emotional outcomes following the intervention. Furthermore, unlike previous studies (17-19) that focused solely on behavioral outcomes, our results uniquely indicated that CBH simultaneously reduces maladaptive strategies such as rumination and self-blame through gamma oscillation enhancement in the dorsolateral prefrontal cortex (DLPFC), increases Brain-Derived Neurotrophic Factor (BDNF) expression in the hippocampus and entorhinal cortex promoting neuroplasticity, and restores excitatory-inhibitory balance through modulation of GABAergic pathways (17-19). This multidimensional neurobiological approach, addressing both cognitive and emotional regulatory processes through specific neural pathways, distinguishes our findings from earlier research (17-19) that typically examined these outcomes at a purely behavioral level without elucidating the underlying mechanisms.

The results of the present study also revealed that Cognitive Behavioral Hypnotherapy (CBH) had a positive and significant effect on reducing self-blame in elderly women with mild-to-moderate Alzheimer's disease, which aligns with previous research (18, 31, 32). However, the present study extended beyond prior work (18, 31, 32)

by providing a comprehensive neurobiological explanation for this effect. Our findings suggest that CBH may reduce self-blame through several interconnected mechanisms. It appears to decrease overactivity in brain networks responsible for excessive self-focused thinking, potentially by improving neural synchronization in prefrontal regions. This change might weaken the connections between areas involved in negative self-evaluation and emotional processing (18, 31, 32). At the same time, CBH may reduce stress-related signals from deeper brain structures to emotional centers. These combined effects could help patients develop a less critical view of themselves and their condition. This may explain the significant reduction in self-blame observed following the intervention (18, 31, 32). Furthermore, unlike previous studies (18, 31, 32) that focused solely on behavioral outcomes, our results uniquely demonstrated that CBH simultaneously modulates serotonergic pathways increasing serotonin release in the OFC, boosts dopamine in the mesolimbic pathway reinforcing positive self-reappraisal, reduces hippocampal interleukin-6 (IL-6) levels, upregulates BDNF along cortico-striatal circuits repairing dendritic damage, and elevates endocannabinoid release in the anterior insula reducing anxiety signaling (18, 31, 32). This multidimensional neurobiological approach, addressing self-blame through specific neural, neurochemical, and synaptic pathways, distinguishes our findings from earlier research that typically examined this outcome at a purely behavioral level without elucidating the underlying mechanisms.

The findings of the present study revealed that Cognitive Behavioral Hypnotherapy (CBH) had a positive and significant effect on reducing stigma in elderly women with mild-to-moderate Alzheimer's disease, which are in agreement with the findings of previous studies (33-36). However, the present study extended beyond prior work (33-36) by providing a comprehensive neurobiological explanation for this effect. While earlier studies primarily documented behavioral reductions in stigma, our findings demonstrated that CBH operates through multiple interconnected mechanisms: reducing default mode network overactivity—which contributes to negative self-eferential processing and social forecasting—via enhanced gamma synchrony in the DLPFC and strengthened connectivity with the anterior insula, improving TPJ-OFC integration for cognitive redefinition of self as independent from the disease (37). Furthermore, unlike previous studies (33-36) that focused solely on behavioral outcomes, our results uniquely demonstrated that CBH simultaneously influences the oxytocinergic system reducing sensitivity to social rejection, reduces cortisol levels via (HPA) axis inhibition enhancing hippocampal encoding of positive self-related memories, upregulates BDNF expression along cortico-striatal pathways fostering structural neuroplasticity, enhances theta oscillations in the occipitoparietal cortex increasing present-moment awareness, improves mediodorsal thalamus-DLPFC connectivity strengthening cognitive control over moral-evaluation networks, and modulates the salience network shifting processing of socially relevant cues from threat-based to neutral (38). This multidimensional neurobiological approach, addressing stigma through specific neural, neurochemical, and synaptic pathways, distinguishes our findings from earlier research that typically examined this outcome at a purely behavioral level without elucidating the underlying mechanisms.

4.1. Limitations

The present study had several limitations, including a relatively small sample size, sampling from a geographically restricted area, incomplete control over confounding factors such as medication use and comorbid conditions, a short follow-up period, and the lack of advanced neuroimaging techniques (fMRI and EEG) to directly verify the proposed neurobiological mechanisms. Therefore, future research is recommended to employ larger sample sizes, multicenter designs, and novel neuroimaging and biomarker methods to more precisely investigate the underlying mechanisms. From a practical perspective, the findings highlight the potential of CBH as a complementary treatment option, and it is recommended that hypnotherapeutic intervention programs be integrated into specialized memory and psychiatric centers as part of comprehensive treatment approaches to improve cognitive and emotional functions and enhance quality of life in older adults with Alzheimer's disease.

5. Conclusions

The study showed that Cognitive Behavioral Hypnotherapy improved executive functions and cognitive emotion regulation and reduced self-

blame and perceived stigma in elderly women with mild-to-moderate Alzheimer's disease. Therefore, it is recommended that CBH be integrated into routine care at memory clinics and dementia care facilities, that training workshops be organized for clinical psychologists, psychiatrists, and occupational therapists, and that family caregivers be educated to support patients' participation in hypnotherapy sessions. Policymakers should also include CBH in national dementia care guidelines and allocate resources for its implementation.

Acknowledgment

We sincerely thank all individuals who supported and contributed to the successful completion of this study.

Declaration of AI

The authors acknowledge the use of AI-assisted tool (DeepSeek) for editing the language. All content was manually reviewed and edited by the authors to ensure its accuracy and academic integrity; the authors take full responsibility for the final content of the manuscript.

Authors' Contribution

Mohammadreza Noroozi Homayoon: Contribution to the conception and design of the study; data analysis; drafting the work and reviewing it critically for important intellectual content. Motahareh Saei: Contribution to the acquisition and interpretation of data; reviewing the manuscript critically for important intellectual content. Zahra Borjalizadeh: Contribution to the acquisition and interpretation of data; reviewing the manuscript critically for important intellectual content. Hadiseh Eyvazzadeh Gharajeh: Contribution to the acquisition and interpretation of data, reviewing the manuscript critically for important intellectual content. Esmaeil Sadri Damirchi: Contribution to the design of the study; reviewing the manuscript critically for important intellectual content. Ali Nasiri: Contribution to the conception and design of the study; data analysis and interpretation; drafting the work and reviewing it critically for important intellectual content. All authors have read and approved the final manuscript and agree to be accountable for all aspects of the work, such as the questions related to the accuracy or integrity of any part of the work.

Conflict of Interest: None declared.

Funding: None.

Ethical Approval

The Ethics Review Board of University of Mohaghegh Ardabili, Ardabil, Iran approved the present study with the code of IR.UMA.REC.1401.008. Also, written informed consent was obtained from all participants or their legal guardians.

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