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Effect of Occupational Therapy on Cognition in Patients with Mild Alzheimer's Disease: A Systematized Literature Review

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Abstract

Introduction: *Mild Alzheimer's Disease (AD), the most prevalent form of dementia, substantially burdens patients and caregivers. With only symptomatic treatments currently available, the potential of Occupational Therapy (OT) in aiding mild AD patients is increasingly recognized. This review evaluates OT's role in preserving cognitive function in mild AD.*
Methods: *We used PubMed and HINARI platforms to explore the effect of OT on mild AD. Studies in English, with observational or clinical trial designs involving patients with AD, were included. Case studies and literature reviews were excluded. Two authors independently selected the study, with a third resolving disputes.*
Results: *43 studies were initially retrieved. Post-duplicate removal, 34 abstracts were screened, 21 were selected for full review, and five met the inclusion criteria. Of these, three reported positive results, and two reported adverse effects. Those with positive results are observational studies with a low risk of bias and one RCT with a high risk of bias. The two remaining RCTs with negative consequences showed a low risk of bias.*
Discussion: *Our review suggests no benefit on cognition in mild AD from OT, although methodological variability led to inconsistent findings. Certain OT interventions, like Recollection-Based and Group Cognitive Therapy, showed promise in cognitive improvement for mild AD. Future research should include larger samples, extended interventions, and follow-up periods for a more comprehensive insight into OT's effects on cognition in mild AD patients.*

Introduction

Alzheimer's disease (AD) is the most common form of dementia, accounting for 2/3 of cases globally (Kumar et al., 2022). It is also one of the most common causes of disability among older adults, accounting for approximately 2% of all causes of years lived with disability, leading to an immense economic burden for society ("Alzheimer's Disease Facts and Figures,"; Gauthier et al., 1997; Guilbert, 2003).

AD profoundly impacts patients, leading to a marked decrease in their quality of life and functional capacity. This, in turn, has consequential implications for caregivers and reverberates broadly, affecting societal structures. Currently, the therapeutic landscape for this disease is limited to symptom management, yet existing pharmacological strategies remain inadequate in preventing disability progression among patients (Birks, 2006). Therefore, there is a critical need for accessible interventions aimed at slowing cognitive deterioration in Mild AD, thus extending

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periods of functional autonomy within this patient population.

Occupational Therapy (OT) is a multidisciplinary branch of healthcare that underscores the therapeutic use of everyday life activities, or "occupations," to increase or restore individual functional capacity (Janssen & Grabanski, 2023). OT focuses on enabling individuals to participate in the tasks and roles that are essential to them, despite any physical, cognitive, or social restrictions they may experience. OT specialists use extensive assessments and individualized intervention strategies to assist skill development, adjust settings, or adapt activities. The goal is to improve an individual's capacity to live independently and maintain a good quality of life.

Occupational therapy (OT) is recognized in the standard care protocol of Mild AD, addressing behavioral and psychological manifestations and supporting daily care needs (Bennett et al., 2019). However, emergent research highlights the potential of these interventions to enhance associated outcomes, such as cognitive functions (Stavrinou et al., 2022). This review evaluated whether OT could preserve cognitive function in patients with Mild AD and delay functional decline in daily activities.

Materials and Methods

We performed a systematized literature review (Grant & Booth, 2009). A search of studies was conducted in Cochrane Central, CINAHL, and Scopus through the HINARI search platform, in addition to PubMed. The following keywords were used: "Alzheimer's disease," "dementia," "occupational therapy," "cognitive manifestations," "cognitive behavior therapies," and "randomized controlled trials." No time restriction was applied. The selected studies were published between 2011 and 2021.

Studies were included if 1) they were conducted on patients aged 50–80 years with a diagnosis of AD, in other words, no early AD (<50 years) due to different mechanisms of disease, 2) OT interventions were used as an active treatment for cognitive improvement; 3) they used control standard therapy or placebo; 4) they assessed the effectiveness of the intervention using the Mini-Mental State Exam (MMSE), Montreal Cognitive Assessment (MoCA), Rivermead Behavioral Test, ADAS-Cog questionnaires or any similar validated scale for memory and cognition 5) they were randomized clinical trials (RCTs), case controls or cohort studies; and 6) they recruited patients from any clinical or general population setting. We only included articles published in English.

Articles with no clinical profiles or high clinical suspicion of AD were excluded. We also excluded 1) case studies 2) and literature reviews.

A step-by-step selection process flowchart was used to summarize the screening process (Figure 1). Study selection was performed by two authors independently, and the results were compared. A third author resolved any discrepancies. We used the Rayyan web application software for title, abstract, and full-text evaluation. We included variables of interest in the following categories: epidemiology, diagnosis, pre-intervention cognitive status, intervention, and outcomes.

Selected studies were classified according to patients, intervention, comparison, outcome, cognitive assessment tools, and duration. Patient characteristics are reported in the following order: sex, age, sample size, intervention methods, number of treatment sessions, location of treatment sessions, instruments used, and caregiver involvement. The primary outcomes were changes in cognitive assessment global scores before and after intervention and changes in any category of the cognitive assessment tool. Secondary outcomes were quality of life and functional disability.

We reviewed a wide range of studies and used the RoB 2 Cochrane risk-of-bias revised instrument for RCTs and the Newcastle-Ottawa scale for cohort and case-control studies. The Cochrane risk-of-bias instrument (Sterne et al., 2019) contains six domains: randomization process, deviation from intended interventions, missing outcome data, measurement of the outcome, and selection of the reported result. The New Castle Ottawa scale contains three domains: selection, comparability, and exposure/outcome (Wells G et al., 2013). Both scales are graded as low risk of bias, some concerns, and high risk of bias. Two researchers independently performed quality assessments, and a third researcher resolved discrepancies.

Results

Study selection

A total of 43 studies were retrieved from the initial search (13 studies from PubMed/MEDLINE and 30 from HINARI). After duplicates (n = 9) were removed, abstracts from the 34 studies were screened, and 21 were selected for full-text review. Ultimately, five studies were included in the review based on the inclusion and exclusion criteria (Callahan et al., 2017; Clare et al., 2010; Kim, 2020; Matsuzono et al., 2016; Tokuchi et al., 2016). Of all selected studies, three were RCTs (Callahan et al., 2017; Clare et al., 2010; Kim, 2020), and two were a retrospective cohort studies field(Matsuzono et al., 2016; Tokuchi et al., 2016) with cognition as the primary and secondary outcome.

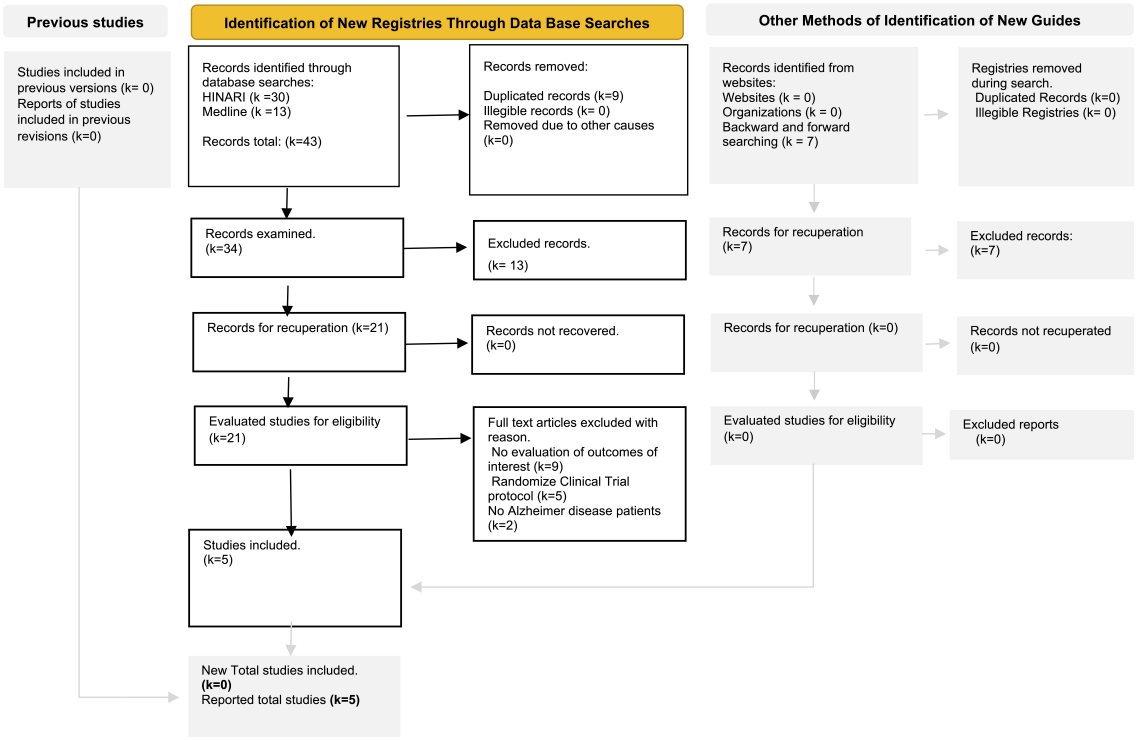

Figure 1: *Flowchart of the selection process.*

Study characteristics

Study characteristics are summarized in Table 1. Included studies had 425 participants, 234 of whom were not treated with OT and 191 who were treated with OT. Included participants were aged at least 65 years and were mainly female. The studies were conducted in Japan, the United Kingdom, South Korea, and the USA. Study sample sizes ranged from 35 to 180 participants. Four studies (Callahan et al., 2017; Kim, 2020; Matsuzono et al., 2016; Tokuchi et al., 2016) compared standard therapy plus OT and standard therapy only, whereas one (Clare et al., 2010) compared OT with no treatment. Each study employed different variations of similar OT approaches, which is expected as OT is a broad field with diverse strategies.

Risk of bias in studies

Regarding the observational study, we found a low overall risk of bias (Table 2). Both retrospective cohorts showed good performance in the selection and outcome categories, with low performance in the comparability category. The risk of bias of the three RCTs is described in Figure 2. Two studies (Callahan et al., 2017; Clare et al., 2010) showed a low risk of bias, while one showed a high risk of bias (Kim, 2020).

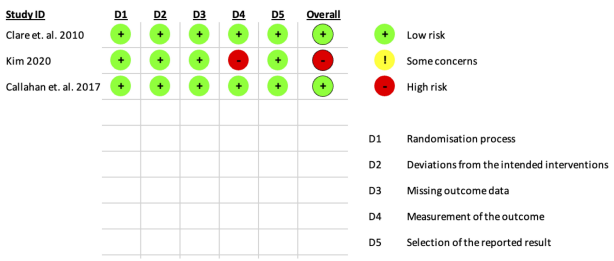

Figure 2: *RoB risk of bias assessment of Clinical Trials.*

Synthesis of the article's results

Three studies reported positive results for the intervention (Kim, 2020; Matsuzono et al., 2016; Tokuchi et al., 2016), while two reported insignificant results (Callahan et al., 2017; Clare et al., 2010). These studies had small sample sizes ranging from 35 to 86 participants. The interventions used were cognitive rehabilitation and recollection-based therapy, both with the addition of exercise. One study used goal-oriented cognitive rehabilitation in combination with relaxation training (Clare et al., 2010). Three studies (Kim, 2020; Matsuzono et al., 2016; Tokuchi et al., 2016) used the MMSE scale as a tool for cognitive assessment, whereas the other two used the Rivermead Behavioural Memory Test II (RBMT-II) (Clare et al., 2010) and the cognitive domains of the Alzheimer's Disease Cooperative Study Group Activities of Daily Living Scale (ADCS ADL) (Callahan et al., 2017).

Study	Study design	Country	Age	Sample Size	Drop-out rate	Females (%)	Type of Occupational Therapy	Cognition assement tool	Results
Tokuchi et. al 2016	Retrospective Cohort Study	Japan	78.9 ± 7.3	86 (CG: 45, IG:41)	0	56 (65%)	Cognitive Rehabilitation	MMSE	At 6 months pre-post IG: +1.2±3.3, p=0.04. There was an improvement in cognition.
Matsuzono et. al. 2016	Retrospective Cohort Study	Japan	76.6 ± 8.5	55 (CG:23, IG: 32)	0	Not reported	Cognitive rehabilitation	MMSE	At 1 year, pre-post IG: +2.3, p<0.001. In the CG, there was no change in the MMSE.
Clare et. al 2010	Randomized Clinical trial	United Kingdom	77.78 ± 6.32	69 (CG: 23, IG:24, NI: 22)	5	41 (59.4%)	Cognitive rehabilitation	RBMT-II	Cognition was a secondary outcome. At 8 week, pre-port IG: +0.49, at 6 months: +1.84. Aparently improve in cognition, but results not statistical significant.
Kim 2020	Randomized Clinical trial	South Korea	79.2 ± 5.2	35 (CG: 17, IG: 18)	0	26 (73%)	Recollection-Based Occupational Therapy	Korean MMSE	After 5 weeks, IG changed from 18.7±1.68 to 19.56±2.17 (p<0.005). There was an improvement in cognition.
Callahan et. al 2017	Randomized Clinical trial	USA	78.4 ± 8.9	180 (CG: 89, IG: 91)	0	130 (72.2%)	Home-based Occupational therapy	ADCS ADL	After 2 years, at IG mean difference was 2.34, 95% CI (−5.27, 9.96). Aparently improve in cognition, but results not statistical significant.

CG: Control group, **IG:** Intervention group, **NI:** No internvention group, **MMSE:** Mini-Mental State Examination, **RBMT-II:** Rivermead Behavioural Memory Test II, **ADCS ADL:** Alzheimer's Disease Cooperative Study Group Activities of Daily Living Scale.

Table 1: *Summary of studies.*

Callahan et al. (Callahan et al., 2017) conducted an RCT with 180 participants and a follow-up of 2 years. They reported indeterminate effects on cognition using home-based OT. These results were thought to be due to the older age of the participants and because OT was not combined with other potential interventions. In addition, an observational study compared the effects of galantamine alone and galantamine combined with OT in 86 patients (Tokuchi et al., 2016). This study included physical therapy for 1-2 h once or twice a week and reported adverse effects at the 3-month assessment and positive impact at the 6-month evaluation.

Discussion

The results of this systematized review suggest no positive effect of OT interventions on cognition in patients with mild AD. The larger variability in study methodology resulted in high heterogeneity and inconsistent findings. Thus, the impact of OT on cognition in mild AD remains unclear. Future studies should employ standard methods and study designs to elucidate the effects of OT interventions on mild AD.

Cognitive changes might affect a wide range of functional domains, such as self-care abilities and the performance of daily tasks in domestic living. However, evidence from our review showed that while OT might not significantly affect cognition as measured by MMSE scores (Clare et al., 2010), there are significant changes in functionality outcomes such as goal attainment. This indicates that OT can be a clinically meaningful intervention to improve functionality in mild AD, despite insignificant effects on measures of cognition such as MMSE.

The two studies that reported adverse effects of OT on cognition employed cognitive rehabilitation and OT interventions with at-home components (Callahan et al., 2017; Clare et al., 2010). These studies had the largest sample sizes and less risk of bias. Home-based OT interventions are designed to be implemented by caregivers who lack the qualification and training of a professional occupational therapist and might be too overwhelmed with daily caretaking duties to implement the intervention. This suggests that the ineffectiveness of OT on cognition is confounded by poor implementation of home-based interventions rather than as a direct consequence of OT interventions.

The specific type of OT intervention might also affect the magnitude of cognitive changes. One study implemented Recollection-Based Cognitive Therapy (Kim, 2020), showing significant differences in MMSE scores in mild AD after just five weeks of intervention. In comparison, traditional cognitive training, such as guided practices on standardized tasks, has shown insignificant benefits for people with early-stage AD (Clare & Woods, 2003). Per-son-centered cognitive stimulation approaches may be superior in improving cognition in mild AD. OT interventions across the trials had a wide range of duration, lasting between 5 weeks and two years. Shorter intervention periods yielded significant changes in cognition compared with more extended intervention periods. This suggests that OT has a limited effect on cognition as AD progresses.

The five studies analyzed in the present review used different control groups. Two used drug-only (acetylcholinesterase inhibitors) controls (Matsuzono et al., 2016; Tokuchi et al., 2016), four studies used standard care (Callahan et al., 2017; Clare & Woods, 2003; Kim, 2020).

Studies reporting adverse effects of OT on cognition had control groups that received effective alternative interventions such as usual care (including the use of cholinesterase inhibitors). This suggests that significant effects of OT interventions on cognition might only be observed in specific experimental settings and are less conspicuous in clinical settings.

	SELECTION			COMPARABILITY		OUTCOME		
Study	Representativeness of the exposed cohort	Selection of the non exposed cohort	Ascertainment of exposure	Demonstration that outcome of interest was not present at start of study	Comparability of cohorts on the basis of the design or analysis	Assessment of outcome	Was follow-up long enough for outcomes to occur	Adequacy of follow up of cohorts
Tokuchi et. al 2016	-	-	★	★	-	★	-	★
Matsuzono et. al. 2016	-	-	★	★	-	★	★	★

★ refers to low risk of bias in this specific domain, - refers to high risk of bias in this specific domain.

Table 2: *Newcastle-Ottawa risk of bias assessment for cohort studies.*

Interpreting the results of this review is difficult because of significant heterogeneity owing to the differences in the type and frequency of OT interventions because of a lack of standardized OT regimens. Our review analyzed studies from different continents with diverse demographic and social characteristics, further increasing participants' heterogeneity. Furthermore, the small sample sizes result in heterogeneity of treatments in the control patients, making them less comparable.

The platforms used for this literature search were PubMed and HINARI, which were chosen primarily for their open access. HINARI comprises four primary databases: Cochrane Central, CINAHL, and Scopus (Saric, 2016). Therefore, one limitation of the study is that both published and gray literature, which may have met our inclusion criteria, may have been omitted from this search.

As with most non-pharmacological interventions in AD, strict implementation of blinding is complex and might have further increased the risk of bias of the RCTs. To the best of our knowledge, this is the first review that evaluates the effects of OT on cognition in patients with AD. Our results provide insight into the gaps in the relevant literature and provide direction for future research in OT as an intervention for cognitive changes in AD.

Conclusions

This review showed that OT interventions only provide modest and primarily nonsignificant benefits on cognition in people with mild AD. Therefore, OT implementation to improve cognition in this population is not supported. Nonetheless, specific types of OT interventions, such as Recollection-Based programs, showed promising results for enhancing cognition in mild AD. These OT interventions tended to be person-centered in design and employ social con-text-relevant cognitive stimulation approaches rather than standardized cognitive training methods. However, these trials had small sample sizes, non-placebo-controlled, short intervention durations, and needed more follow-up. Future studies should include larger sample sizes, longer interventions, and extended follow-up periods. OT interventions that use person-centered, cognition stimulation approaches performed by qualified OT professionals should be considered to produce more comprehensive data on the effects of OT on cognition in patients with mild AD.

Author Contributions

Conceptualization of the idea was made by L.R-W and N.P-B; methodology was developed by N.P-B; the search strategy was developed by M.S-B; article selection was made by N.P-B, L.R-W, M.S-B, A.B-R, A.E and S.A-A; data extraction was made by N.P-B, J.P.G.K, C.G, R.M, N.R, D.E, A.E, S.A-A, A.B-R and M.S-B; result synthesis by N.P-B, L.R-W; Discussion by S.Z, L.R-W and N.P-B; writing—original draft preparation N.P-B, L.R-W, S.Z, M.S-B, A.B-R; writing—review and editing L.R-W, D-E, N.P-B; project administration, L.R-W and N.P-B. All authors have read and agreed to the published version of the manuscript.

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Conflicts of Interest

The authors declare no conflict of interest.

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