



## Original Article

# Multisensory stimulation reduces neuropsychiatric symptoms and enhances cognitive function in older adults with dementia: A meta-analysis of randomized controlled trials

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## ABSTRACT

**Objective:** Multisensory stimulation defined as engaging multiple senses (visual, olfactory, auditory, gustatory, and tactile), has been demonstrated to improve older adults' general health. However, its effectiveness in mitigating neuropsychiatric symptoms (NPSs) and cognitive deficits in older adults with dementia remains unclear. This meta-analysis evaluated the efficacy of multisensory stimulation in ameliorating NPSs and improving overall cognitive function in older adults with dementia.

**Methods:** We searched eight databases to September 2024 without restriction. Older adults with all stages of dementia aged 65 years and above were included. To estimate the pooled effect size, Hedge's  $g$  ( $g$ ) values were calculated using a random-effects model. Heterogeneity was assessed using the  $Q$ ,  $I^2$ , and  $\tau^2$  statistics. Subgroup and meta-regression analyses were performed to identify moderators. Publication bias was assessed using Begg and Mazumdar's rank correlation and Egger's linear regression tests.

**Results:** This review included 16 studies (974 patients). Multisensory stimulation significantly reduced agitation ( $g = -0.96$ ; 95 %CI=  $-1.44, -0.48$ ), apathy ( $g = -1.27$ ; 95 %CI=  $-2.08, -0.46$ ), and depression ( $g = -0.28$ ; 95 %CI=  $-0.48, -0.07$ ). Moreover, the intervention significantly improved overall cognitive function ( $g = 0.30$ ; 95 %CI=  $0.09, 0.52$ ). However, multisensory stimulation had no significant effect on anxiety ( $g = -0.81$ ; 95 %CI=  $-1.79, 0.17$ ). Significant heterogeneity was observed in agitation, apathy, and anxiety. Moreover, meta-regression analyses by educational level (junior high school and above) revealed significant moderators in agitation.

**Conclusions:** Multisensory stimulation shows promise as a non-pharmacological intervention for older adults with dementia. It may effectively mitigate NPSs and improve cognitive function into clinical practice as an alternative therapeutic.

## 1. Introduction

Neuropsychiatric symptoms (NPSs) are common and often more distressing than cognitive symptoms in patients with dementia; approxi-

mately 80 % of all patients with Alzheimer's disease develop these symptoms [1]. The ageing process is intricately linked with the emergence of NPSs, which are significant predictors of cognitive decline and dementia [2]. NPSs include behavioral domains such as agitation, apathy, depres-

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sion, and anxiety [1]. NPSs, along with cognitive deficits, result in the loss of essential functions, substantially diminishing the quality of life for both patients and caregivers [1]. Interventions targeting NPSs can help improve the overall quality of life of patients with dementia and their caregivers by facilitating disease management and reducing caregiver burden.

Pharmacological treatment options for dementia often exhibit limited efficacy and can cause adverse effects. Therefore, nonpharmacological interventions, such as multisensory stimulation, have gained popularity as complementary therapeutic options [3]. Multisensory stimulation refers to stimulation of visual, auditory, tactile, olfactory, and gustatory senses, and that creates a space/ environment for enjoying a variety of sensory experiences and where gentle stimulation of the senses can be provided in a controlled way [4]. Visual stimuli, such as light effects from bubble tubes and fiber optic sprays, or the use of familiar images, can regulate the circadian rhythm, influencing both NPSs and cognitive function [4]. Olfactory stimuli, such as the aroma of spices and the fragrance of flowers, can aid in memory recall [5]. Auditory stimuli, such as music, serve as positive distractors and help stabilize agitated behaviors [6]. Gustatory stimuli, such as sweetened foods, address nutritional deficiencies in patients with dementia and increase food intake through appealing supplements [7]. Tactile stimuli, such as the warmth of a mug, can evoke positive emotional responses and memories [8].

Multisensory stimulation has been demonstrated to alleviate NPSs, such as agitation [9,10], apathy [11,12], depression [8], and anxiety [8,13] and improve cognitive function by reinforcing memory recall [2] among older adults with dementia. Therefore, multisensory stimulation holds promise as a nonpharmacological intervention for patients with dementia, particularly in ameliorating NPSs and improving cognitive function. Relevant meta-analyses have been conducted in various populations, such as children [14] and adults [15], and for various conditions, such as brain injury [16], autism [17], and stroke [18]. However, these meta-analyses have neither examined older adults or patients with dementia nor analyzed pooled estimates across a diverse range of outcome indicators (NPSs and cognitive function) or moderating factors. Thus, to address these research gaps and recognizing the importance of understanding the effect of multisensory intervention on the older adults with dementia population, given that this intervention has a positive impact on other populations, we conducted the present systematic review and meta-analysis of randomized controlled trials (RCTs) to investigate the effects of multisensory stimulation on NPSs and cognitive function in older adults with dementia. Our findings may aid health-care professionals, particularly nurses, in implementing effective nonpharmacological interventions for older adults with dementia.

## 2. Methods

### 2.1. Study design and eligibility criteria

This study adhered to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses guidelines [19]. The review protocol was registered in the International Prospective Register of Systematic Review database (registration ID: CRD42024507054). Ethical approval was not required because the analysis relied on published, anonymized, and aggregated data.

Studies were included if they (1) focused on older adults ( $\geq 65$  years) with all stages of dementia, diagnosed by neurologists or geriatricians on the *Diagnostic and Statistical Manual of Mental Disorders* criteria, *International Classification of Diseases* codes, Mini-Mental State Examination scores, Montreal Cognitive Assessment scores, Alzheimer's Disease Assessment Scale–Cognitive Subscale (ADAS-Cog), or Clinical Dementia Rating scores; (2) administered multisensory stimulation through  $\geq 2$  sensory modalities (such as visual, auditory, olfactory, gustatory, and tactile stimulation); (3) included a usual care, no treatment, or active control group; (4) assessed NPS subcategories (e.g., agitation, apathy, depression, and anxiety) and cognitive function; and (5) had an RCT

design. Articles were excluded if they (1) focused on an irrelevant topic or populations (such as pharmacotherapy, physical therapy, cognitive training, others), (2) were reviews, (3) were non-research articles, (4) were descriptions of study protocols, (5) were based on irrelevant study designs, or (6) provided insufficient data in spite of our attempts to obtain full-text information by email.

### 2.2. Search strategy

A comprehensive search strategy was developed in collaboration with a university librarian. Population- and intervention-focused keywords were used to capture a broad range of outcomes. The search spanned eight databases, including CINAHL, Cochrane, Embase, ProQuest, PsycINFO, PubMed, Scopus, and Web of Science. The databases were searched with no time, region, or language restrictions imposed. Relevant articles published from database inception to September 2024 were screened for eligibility. Medical Subject Headings, Subject Headings, Psychological Index Terms, Main Subject, Emtree, and keywords were combined with Boolean operators (“AND” or “OR”) to identify RCTs focusing on “multisensory stimulation” and “dementia.” The search terms and strategies are presented in **Tables S3** and **S4**. Forward citation searching was conducted, where databases were screened for articles that referenced published studies, and backward citation searching was also conducted, where studies in the reference lists of other systematic reviews and meta-analyses were screened for eligibility. Additional potentially eligible studies were identified through manual searches in Google Scholar (**Fig. 1**).

### 2.3. Study selection and data extraction

Two reviewers independently assessed relevant articles by using EndNote 20. After the removal of duplicate articles, titles and abstracts were screened on the basis of predefined inclusion and exclusion criteria. Then, a full-text review was performed to assess eligibility. Discrepancies were resolved through discussion with a third reviewer. The following information was extracted from each included study: author names, study country, dementia subtype/severity, diagnostic tool, study setting, sample characteristics, study design, group type, intervention characteristics (e.g., intervention setting, number of session, duration, and study period), and intervention outcomes (**Table 1**). The corresponding authors of eligible studies were contacted for clarification or additional information when necessary.

### 2.4. Outcomes measures and instruments

The primary study outcomes were the NPS which consists of agitation, apathy, depression, and anxiety. Agitation was evaluated using the Behavioral Pathology in Alzheimer's Disease Rating Scale, Cohen–Mansfield Agitation Inventory, Daily Observation Scale, and Pittsburgh Agitation Scale. Apathy was evaluated using the Apathy Evaluation Scale and the Scale for the Assessment of Negative Symptoms in Alzheimer's Disease. Depression was evaluated using the Cornell Scale for Depression in Dementia and Interact Scale. Anxiety was evaluated using the Beck Anxiety Inventory, Behavioral Pathology in Alzheimer's Disease Rating Scale, Hamilton Anxiety Scale, and Rating Anxiety in Dementia scale.

The secondary study outcome was cognitive function. It was assessed by measuring overall cognitive function or specific cognitive domains such as complex attention (sustained attention, divided attention, selective attention, and processing speed), executive function (planning, decision making, working memory, responding to feedback/ error correction, overriding habits/ inhibition, and mental flexibility), learning and memory (immediate memory, recent memory [including free recall, cued recall, and recognition memory], very-long-term memory [semantic; autobiographical], and implicit learning), language (expressive language [including naming, word finding, fluency, and grammar, and syn-

**Table 1**  
Multisensory stimulation interventions for older adults with dementia.

No	Author (year), country	Subtype/ severity of dementia, tool, study setting	Sample characteristics n (%); mean (SD)	Study design, group type	Intervention characteristics	Outcomes (tool)	Time point
1.	Andretta (2008), United States	Subtype: Alzheimer's dementia Severity: moderate dementia Tool: MMSE, 15.0 (2.3) Study setting: nursing home	Sample size Overall: 84 EG: 41 (48.8%) CG: 43 (51.2%) Mean age: 85.8 (10.1) Gender: M: 15 (17.9%) F: 69 (82.1%)	Study design: RCT EG: Snoezelen Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: no treatment	Intervention setting: Snoezelen room Number of sessions: 1 session Duration: 20 min/session Study period: 1 session	Primary outcomes: - Neuropsychiatric symptoms: Anxiety (BAI) - Cognition: NI	- Baseline - During treatment: NI - Post treatment: 1-session - Follow-up: 1-week 4-week
2.	Bakshi (2004), Canada	Subtype: NI Severity: moderate dementia Tool: MMSE, 9.5 (4.9) Study setting: hospital	Sample size Overall: 40 EG: 20 (50.0%) CG: 20 (50.0%) Mean age: 78.0 (7.3) Gender: M: 24 (60.0%) F: 16 (40.0%)	Study design: RCT EG: Snoezelen Visual: - Olfactory: + Auditory: + Gustatory: - Tactile: + CG: usual care	Intervention setting: activity room Number of sessions: 3 sessions/week Duration: 30-40 min/session Study period: 12 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (CMAI) - Cognition: NI	- Baseline - During treatment: 6-session - Post treatment: 12-session - Follow-up: NI
3.	Goyal et al. (2021), Ireland	Subtype: NI Severity: moderate to severe dementia Tool: MMSE, 8.7 (7.0) Study setting: nursing home	Sample size Overall: 88 EG: 48 (54.5%) CG: 40 (45.5%) Mean age: 84.8 (6.9) Gender: M: 20 (22.7%) F: 68 (77.3%)	Study design: RCT EG: Snoezelen Visual: + Olfactory: + Auditory: + Gustatory: + Tactile: + CG: usual care	Intervention setting: activity room Number of sessions: 2 sessions/week Duration: 45 min/session Study period: 48 sessions	Primary outcomes: - Neuropsychiatric symptoms: Depression (CSDD); Anxiety (RAID) - Cognition: NI	- Baseline - During treatment: 24-session - Post treatment: 48-session - Follow-up: NI
4.	Hong (2011), Korea	Subtype: Alzheimer's dementia Severity: moderate dementia Tool: MMSE-KC, 12.2 (4.7) Study setting: nursing home	Sample size Overall: 51 EG: 25 (49.0%) CG: 26 (51.0%) Mean age: 82.1 (6.5) Gender: M: 11 (21.6%) F: 40 (78.4%)	Study design: RCT EG: Multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: usual care	Intervention setting: activity room Number of sessions: 2 sessions/week Duration: 55 min/session Study period: 20 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (CMAI-K); Depression (CSDD) - Cognition: (MMSE-KC)	- Baseline - During treatment: 10-session - Post treatment: 20-session - Follow-up: NI
5.	Hutson et al. (2014), UK	Subtype: NI Severity: moderate to severe dementia Tool: DSM-IV MMSE, 4.9 (5.2) Study setting: nursing home	Sample size Overall: 39 EG: 21 (53.8%) CG: 18 (46.2%) Mean age: 86.6 (6.7) Gender: M: 5 (13.9%) F: 34 (86.1%)	Study design: RCT EG: Snoezelen Visual: + Olfactory: + Auditory: + Gustatory: + Tactile: + CG: usual care	Intervention setting: activity room Number of sessions: 2 sessions/week Duration: 45-60 min/session Study period: 14 sessions	Primary outcomes: - Neuropsychiatric symptoms: Depression (CSDD); Anxiety (RAID) - Cognition: NI	- Baseline - During treatment: NI - Post treatment: 14-session - Follow-up: NI
6.	Kor et al. (2024), Hong Kong	Subtype: NI Severity: moderate dementia Tool: ICD-10 Study setting: home	Sample size Overall: 241 EG: 121 (50.2%) CG: 120 (49.8%) Mean age: 83.0 (8.0) Gender: M: 98 (40.8%) F: 142 (59.2%)	Study design: RCT EG: multisensory (five senses box) Visual: + Olfactory: + Auditory: + Gustatory: + Tactile: + CG: usual care	Intervention setting: NI Number of sessions: 3 sessions/week Duration: 45 min/session Study period: 45 sessions	Primary outcomes: - Neuropsychiatric symptoms: NI - Cognition: (MoCA 5-min protocol)	- Baseline - During treatment: NI - Post treatment: 45-session - Follow-up: 12-week
7.	Li et al. (2024), China	Subtype: Alzheimer dementia Severity: mild to severe dementia Tool: CCMD-3 Study setting: hospital	Sample size Overall: 80 EG: 40 (50.0%) CG: 40 (50.0%) Mean age: 75.3 (5.7) Gender: M: 43 (53.8%) F: 37 (46.3%)	Study design: RCT EG: multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: regular rehabilitation training	Intervention setting: multisensory room Number of sessions: 2 sessions/week Duration: 60 min/session Study period: 24 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (BEHAVE-AD); Apathy (AES); Anxiety (BEHAVE-AD) - Cognition: NI	

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Table 1 (continued)

No	Author (year), country	Subtype/ severity of dementia, tool, study setting	Sample characteristics n (%); mean (SD)	Study design, group type	Intervention characteristics	Outcomes (tool)	Time point
8.	Maseda et al. (2014), Spain	Subtype: NI Severity: moderate dementia Tool: GDS, stage 5 Study setting: specialized elderly center	Sample size Overall: 20 EG: 10 (50.0%) CG: 10 (50.0%) Mean age: 87.0 (5.6) Gender: M: 2 (10.0%) F: 18 (90.0%)	Study design: RCT EG: multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: usual care	Intervention setting: Snoezelen room Number of sessions: 2 sessions/week Duration: 30 min/session Study period: 32 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (CMAI); Depression (CSDD) - Cognition (MMSE)	- Baseline - During treatment: 16-session - Post treatment: 32-session - Follow-up: 8-week
9.	Maseda et al. (2018), Spain	Subtype: NI Severity: severe dementia Tool: GDS, 6–7 Study setting: nursing home	Sample size Overall: 21 EG: 10 (47.6%) CG: 11 (52.4%) Mean age: 88.9 (6.7) Gender: M: 6 (28.6%) F: 15 (71.4%)	Study design: RCT EG: multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: music	Intervention setting: Snoezelen room Number of sessions: 2 sessions/week Duration: 30 min/session Study period: 24 sessions	Primary outcomes: - Neuropsychiatric symptoms: Depression (Interact Scale) - Cognition: NI	- Baseline - During treatment: NI - Post treatment: 24-session - Follow-up: NI
10.	Milev et al. (2008a), Canada	Subtype: NI Severity: NI Tool: DSM-IV Study setting: long-term care	Sample size Overall: 11 EG: 5 (45.5%) CG: 6 (54.5%) Mean age: 84.6 (6.7) Gender: M: 3 (27.3%) F: 8 (72.7%)	Study design: Pilot RCT EG: multisensory stimulation Visual: + Olfactory: - Auditory: + Gustatory: - Tactile: + CG: usual care	Intervention setting: Snoezelen room Number of sessions: 1 session/week Duration: 30 min/session Study period: 12 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (DOS) - Cognition (MMSE)	- Baseline - During treatment: 4-session, 8-session - Post treatment: 12-session - Follow-up: 24-week
11.	Milev et al. (2008b), Canada	Subtype: NI Severity: NI Tool: DSM-IV Study setting: long-term care	Sample size Overall: 13 EG: 7 (53.8%) CG: 6 (46.2%) Mean age: 85.5 (5.4) Gender: M: 2 (15.4%) F: 11 (84.6%)	Study design: Pilot RCT EG: multisensory stimulation Visual: + Olfactory: - Auditory: + Gustatory: - Tactile: + CG: usual care	Intervention setting: Snoezelen room Number of sessions: 3 sessions/week Duration: 30 min/session Study period: 36 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (DOS) - Cognition (MMSE)	- Baseline - During treatment: 12-session, 24-session - Post treatment: 36-session - Follow-up: 24-week
12.	Safavi et al. (2013), Iran	Subtype: Alzheimer's dementia Severity: moderate dementia Tool: DSM-IV-TR MMSE, 15.9 (3.2) Study setting: elderly women care center	Sample size Overall: 52 EG: 26 (50.0%) CG: 26 (50.0%) Mean age: NI Gender: M: 0 (0%) F: 52 (100%)	Study design: RCT EG: Multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: no treatment	Intervention setting: hall in elderly women care center Number of sessions: 2 sessions/day Duration: 45–60 min/session Study period: 20 sessions	Primary outcomes: - Neuropsychiatric symptoms: NI - Cognition (MMSE)	- Baseline - During treatment: NI - After treatment: 20-session - Follow-up: NI
13.	Sanchez et al. (2016), Spain	Subtype: NI Severity: severe dementia Tool: GDS, stage 6–7 Study setting: specialized dementia elderly center	Sample size Overall: 22 EG: 11 (50.0%) CG: 11 (50.0%) Mean age: 87.0 (6.7) Gender: M: 2 (9.1%) F: 20 (90.9%)	Study design: Pilot RCT EG: multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: activity group	Intervention setting: Snoezelen room Number of sessions: 2 sessions/week Duration: 30 min/session Study period: 32 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (CMAI); Depression (CSDD) - Cognition (SMMSE)	- Baseline - During treatment: 16-session - After treatment: 32-session - Follow-up: 8-week
14.	Solé et al. (2023), Spain	Subtype: NI Severity: NI Tool: FAST, NI Study setting: nursing home	Sample size Overall: 81 EG: 38 (46.9%) CG: 43 (53.1%) Mean age: 88.0 (6.1) Gender: M: 13 (16.0%) F: 68 (84.0%)	Study design: RCT EG: Snoezelen Visual: + Olfactory: + Auditory: + Gustatory: + Tactile: + CG: reminiscence	Intervention setting: Snoezelen room Number of sessions: 2 sessions/week Duration: 30 min/session Study period: 24 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (CMAI); Depression (CSDD); Anxiety (HAS) - Cognition: NI	- Baseline - During treatment: NI - After treatment: 24-session - Follow-up: NI

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Table 1 (continued)

No	Author (year), country	Subtype/ severity of dementia, tool, study setting	Sample characteristics n (%); mean (SD)	Study design, group type	Intervention characteristics	Outcomes (tool)	Time point
15.	Staal et al. (2007), United States	Subtype: NI Severity: moderate dementia Tool: MMSE, 15.5 (4.3) Study setting: hospital	Sample size Overall: 24 EG: 12 (50.0%) CG: 12 (50.0%) Mean age: 76.2 (4.4) Gender: M: 8 (33.3%) F: 16 (66.7%)	Study design: RCT EG: Snoezelen Visual: NI Olfactory: NI Auditory: NI Gustatory: NI Tactile: NI CG: usual care	Intervention setting: multisensory room Number of sessions: 3 sessions/week Duration: 25–30 min/session Study period: 15 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (PAS); Apathy (SANS-AD) - Cognition: NI	- Baseline - During treatment: 1 to 5 sessions - After treatment: 6-session - Follow-up: NI
16.	Verkaik et al. (2019), Netherlands	Subtype: NI Severity: moderate dementia Tool: GDS, stage 5–6 Study setting: nursing home	Sample size Overall: 47 EG: 24 (51.1%) CG: 23 (48.9%) Mean age: 87.0 (6.4) Gender: M: 12 (25.5%) F: 35 (74.5%)	Study design: Pilot RCT EG: multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: + Tactile: + CG: usual care	Intervention setting: multisensory room Number of sessions: 3 sessions/week Duration: 30 min/session Study period: 36 sessions	Primary outcomes: - Neuropsychiatric symptoms: Agitation (CMAI); Depression (CSDD); Apathy (AES) - Cognition: NI	- Baseline - During treatment: NI - After treatment: 36-session - Follow-up: NI
17.	Yan (2018) China	Subtype: Senile dementia Severity: mild dementia Tool: MoCA, 23.1 (3.3) Study setting: hospital	Sample size Overall: 66 EG: 33 (50.0%) CG: 33 (50.0%) Mean age: 72.7 (2.0) Gender: M: 42 (63.6%) F: 24 (36.4%)	Study design: RCT EG: multisensory stimulation Visual: + Olfactory: + Auditory: + Gustatory: - Tactile: + CG: routine rehabilitation training	Intervention setting: multisensory room Number of sessions: 2 sessions/week Duration: 30 min/session Study period: 24 sessions	Primary outcomes: - Neuropsychiatric symptoms - Cognition (MoCA)	- Baseline - During treatment: 12-session - After treatment: 24-session - Follow-up: NI

Abbreviations: AES, Apathy Evaluation Scale; BAI, Beck Anxiety Inventory; BEHAVE-AD, Behavioral Pathology in Alzheimer's Disease Rating Scale; CCMD-3, *Chinese Classification and Diagnostic Criteria of Mental Disorders, Third Edition*; CG, control group; CMAI, Cohen–Mansfield Agitation Inventory; CSDD, Cornell Scale for Depression in Dementia; DOS, Daily Observation Scale; DSM-IV-TR, *Diagnostic and Statistical Manual, Fourth Edition, Text Revision*; EG, experimental group; F, female; FAST, Functional Assessment Staging Tool; GDS, Global Deterioration Scale; HAS, Hamilton Anxiety Rating Scale; ICD, *International Classification of Diseases*; M, male; MMSE, Mini-Mental State Examination; MMSE-KC, Korean version of Mini-Mental State Examination; MoCA, Montreal Cognitive Assessment; NI, no information; NPS, neuropsychiatric symptom; PAS, Pittsburgh Agitation Scale; RAID, Rating Anxiety in Dementia; RCT, randomized controlled trial; SANS-AD, Scale for the Assessment of Negative Symptoms in Alzheimer's Disease; SMMSE, Severe Mini-Mental State Examination.

tax], and receptive language), perceptual-motor (abilities, subsumed under the term visual perception, visuo-constructional, perceptual-motor, praxis, and gnosis), and social cognition (recognition of emotions and theory of mind) [20]. Cognitive function was primarily evaluated by neurologists or geriatricians on the basis of the *Diagnostic and Statistical Manual of Mental Disorders* criteria or the *International Classification of Diseases* codes. Additional instruments included the Mini-Mental State Examination, Montreal Cognitive Assessment, and Severe Mini-Mental State Examination.

## 2.5. Data synthesis and analysis

The random-effects model in Comprehensive Meta-Analysis software (version 3.0) was used to account for statistically significant heterogeneity [21]. Hedge's *g* (*g*) values with 95 % confidence intervals (CIs) were calculated to estimate the pooled effect size for continuous data and incorporates a correction factor that addresses this bias, providing more accurate effect size estimates, especially when dealing with smaller sample sizes [22]. After treatment and follow-up analyses were performed using the pooled estimates for NPS subcategories (agitation, apathy, depression, and anxiety) and cognitive function. *g* providing more accurate effect size estimates, especially when dealing with smaller sample sizes [22]. *g* values were interpreted as follows: 0.20–0.49, small effect; 0.50–0.79, medium effect; and  $\geq 0.80$ , large effect. Statistical significance was set at  $p < 0.05$  [23,24]. A significant, negative *g* value indicated decreased NPSs, whereas a significant, positive *g* value indicated improved cognitive function.

Heterogeneity was assessed using the  $I^2$ ,  $\tau^2$ , and Cochrane Q statistics; a *p* value of  $< 0.10$  indicated significant heterogeneity.  $I^2$  values were interpreted as follows:  $< 25$  % indicated low heterogeneity,  $\geq 25$  % to  $< 75$  % indicated moderate heterogeneity; and  $\geq 75$  % indicated high heterogeneity [25]. Prediction intervals (95 % PI) were calculated to estimate the range of true effect sizes in similar future studies [26]. Moderator analyses—subgroup and meta-regression analyses—were performed to identify potential sources of significant heterogeneity. Categorical variables were subject to subgroup analyses; specifically, the included studies were segmented by the setting of the study; the setting, number of session, and length of the intervention; and the number of senses targeted (all five senses, four senses [visual, olfactory, auditory, and tactile], or three senses [visual, auditory, and tactile or olfactory, auditory, and tactile]). Continuous variables were subjected to meta-regression analyses [27]. A  $p < 0.05$  indicated significant moderation. For each outcome category with  $\geq 10$  studies, publication bias was independently evaluated using Begg and Mazumdar's rank correlation test [28,29] and Egger's linear regression test [28,29]; a  $p > 0.10$  indicated no publication bias [30]. The trim-and-fill method was used to adjust for publication bias [31]. Furthermore, a sensitivity analysis was conducted to assess the robustness of our findings. This involved excluding studies with large and small contribution (identified by *g* values) to determine if the overall effect size was sensitive to individual studies, indicating potential instability or heterogeneity [32]. The results were compared with those of the initial pooled effect size analysis to validate the robustness of our findings. The present systematic review and meta-analysis adhered to prevailing standards on participant charac-

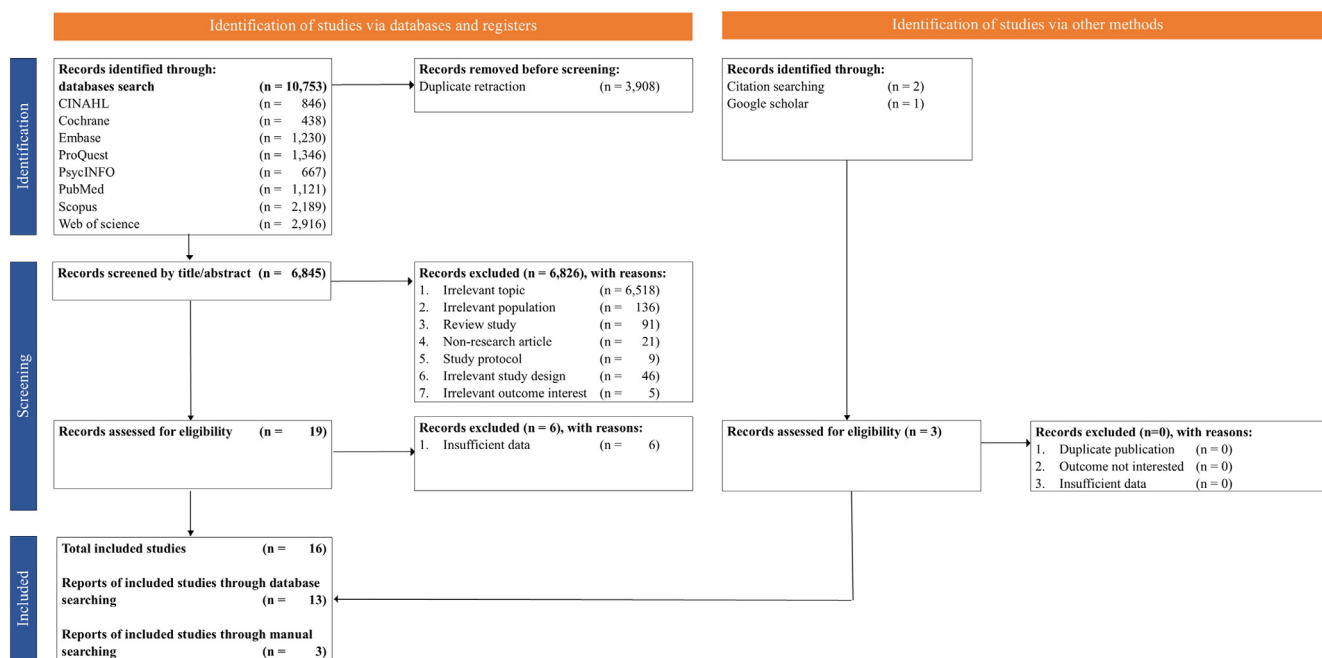


Fig. 1. Preferred reporting items for systematic reviews and meta-analyses flow diagram.

teristics, intervention characteristics, comparators, outcomes, study designs, time-to-event data, continuous data, ordinal scales, cluster-RCTs, cross-over trials, and any additional analyses [33].

## 2.6. Quality assessment

Two reviewers independently evaluated the quality of the included RCTs by using the revised Cochrane risk-of-bias tool (version 2) [34]. Discrepancies were resolved through discussion with a third reviewer. Studies were classified as having a high risk of bias, some concerns, or a low risk of bias on the basis of the final quality assessment results.

## 3. Results

### 3.1. Study inclusion and characteristics

The literature search returned 10,753 articles. After the removal of 3908 duplicate articles, 6845 were subjected to title and abstract screening. From these, 6826 articles were excluded for the following reasons: irrelevant topics (n = 6518), irrelevant populations (n = 136), reviews (n = 91), non-research articles (n = 21), study protocol (n = 9), irrelevant study designs (n = 46), and irrelevant outcome measures (n = 5). A full-text review was performed for 19 studies. Six articles were excluded because of the unavailability of the full text despite attempts to contact the authors. Citation searches and manual searches through Google Scholar returned three additional articles. Ultimately, 16 studies were included in the meta-analysis; a complete list of references is presented in Table S5. Among the included studies, one [35] had a three-arm design; this resulted in findings on a total of 17 effect sizes (Fig. 1). Among the included RCT articles, none were double-blinded. This absence is primarily attributable to the nature of multisensory stimulation interventions.

The sample sizes of the studies ranged from 11 to 241; the total number of patients (sum of the experimental and control groups) was 974. Dementia was the most common condition, accounting for 11 (68.8%), followed by Alzheimer disease accounting 4 (25.0%), and 1 (6.3%) of Senile dementia. Approximately 68.7% of the patients were women. The patients' mean age was  $82.7 \pm 8.4$  years. Their mean Mini-Mental State Examination score (on the basis of seven studies) was  $11.7 \pm 6.0$ .

The studies were conducted across America (4 studies), Asia (5 studies), and Europe (7 studies). As shown in Table S7, most patients resided in nursing homes or long-term care facilities (62.5%).

Multisensory stimulation targeted all five senses in five studies (31.3%). Most interventions were administered in multisensory rooms (68.8%). The session duration of multisensory stimulation ranged from 4 to 24 weeks. The number of sessions were held 1–3 times a week, and each session lasted 20–60 min. The study period ranged from 1 to 48 sessions and the follow-up period ranged from 1 to 24 weeks (Table 1).

### 3.2. Results of quality assessment

Study quality was assessed using the latest Cochrane risk-of-bias tool. Among the 16 included studies, 15 used an intention-to-treat analysis, whereas one used a per-protocol analysis. Among the 15 studies that used an intention-to-treat analysis, 4 (26.7%) had a low risk of bias, whereas another 4 (26.7%) had some concerns of bias (Figure S2).

### 3.3. Effect of multisensory stimulation on NPSs

Multisensory stimulation significantly reduced the severity of the NPSs including agitation, apathy, and depression, with no significant effect on anxiety (Fig. 2).

#### 3.3.1. Agitation

The meta-analysis revealed that multisensory stimulation considerably reduced agitation in older adults with dementia, with a large effect size. A total of 10 effect sizes from 9 studies [11–13,35–40] involving 386 patients were evaluated to investigate the effects of multisensory stimulation on agitation. The random-effects model indicated that multisensory stimulation significantly alleviated agitation ( $g = -0.96$ ; 95%CI =  $-1.44$  to  $-0.48$ ;  $p < 0.001$ ). Significant heterogeneity was observed for agitation ( $Q = 41.98$ ;  $p = < 0.001$ ,  $I^2 = 78.56\%$ ;  $\tau^2 = 0.45$ ; Table 2). Subgroup analyses by study setting; intervention setting, number of session, or length; and number of senses revealed no significant moderators. Moreover, meta-regression analyses by educational level (junior high school and above) revealed significant moderators, while age, gender (male, female), and educational level (elementary school and below) revealed no significant moderators (Table 3).

1. NPS – Agitation

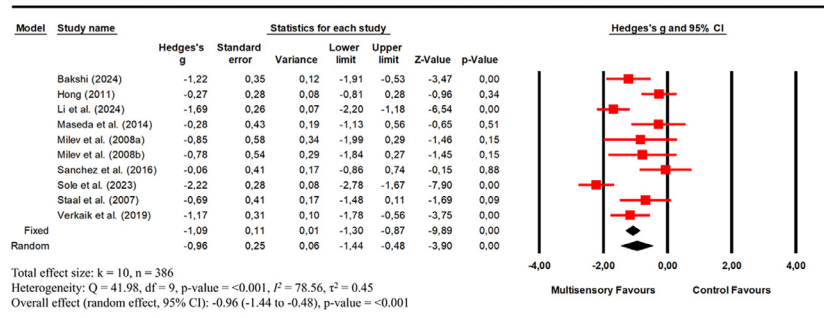
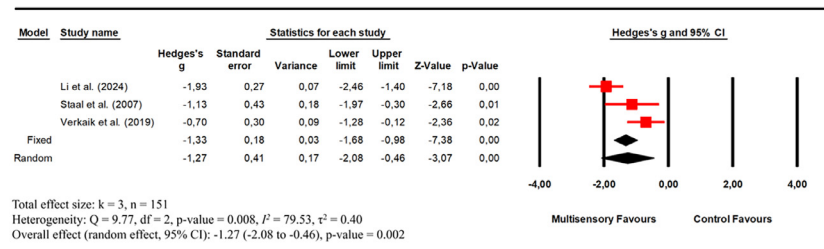
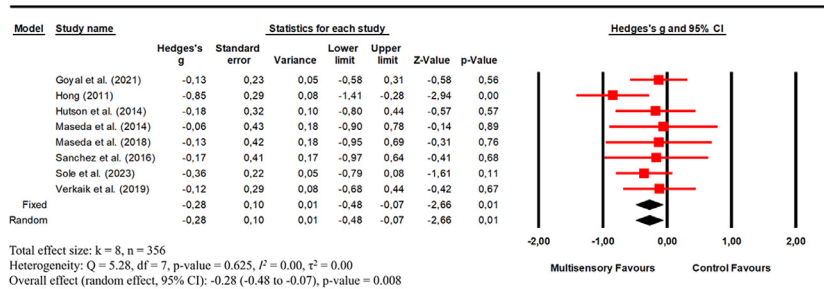


Fig. 2. Main findings of this study.

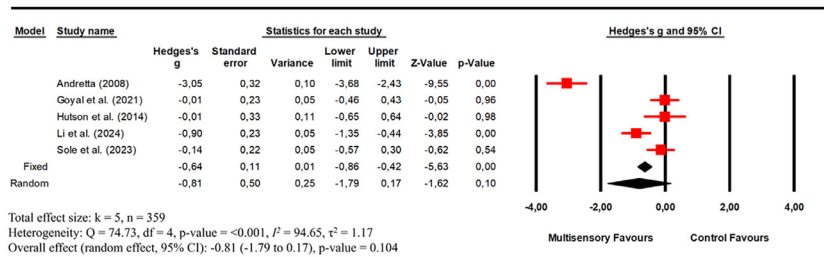
2. NPS – Apathy



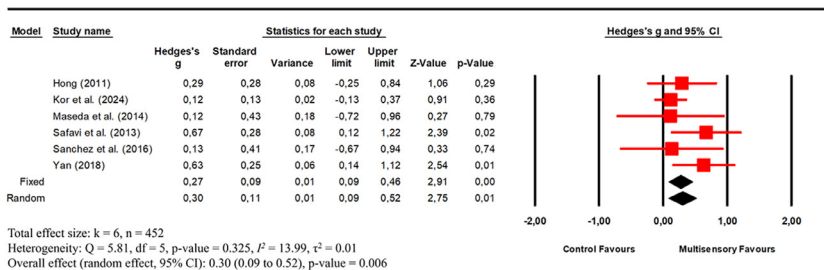
3. NPS – Depression



4. NPS – Anxiety



5. Cognitive Function



No publication bias was detected. A Begg and Mazumdar's rank correlation test, performed using Kendall's tau without continuity correction, yielded a  $p = 0.420$ , whereas an Egger's linear regression test yielded a  $p = 0.194$  (95 %CI =  $-2.32$  to  $9.74$ ; Figure S1).

3.3.2. Apathy

The meta-analysis revealed that multisensory stimulation significantly reduced apathy in older adults with dementia, with a large effect size. Three studies [11,12,40] involving 151 patients investigated the

**Table 2**  
Effects of multisensory stimulation on neuropsychiatric symptoms and cognitive function.

No.	Outcomes	Time point	k (n)	Effect size					Heterogeneity				
				Hedges' g	95 %	CI	Z value	p value	Q statistic	df (Q)	p value	I <sup>2</sup> (%)	τ <sup>2</sup>
1.	Neuropsychiatric symptoms												
	(a) Agitation	Posttest	10 (386)	-0.96	-1.44	-0.48	-3.90	<0.001	41.98	9	<0.001	78.56	0.45
	(b) Apathy	Posttest	3 (151)	-1.27	-2.08	-0.46	-3.07	0.002	9.77	2	0.008	79.53	0.40
	(c) Depression	Posttest	8 (356)	-0.28	-0.48	-0.07	-2.66	0.008	5.28	7	0.625	0.00	0.00
	(d) Anxiety	Posttest	5 (359)	-0.81	-1.79	0.17	-1.62	0.104	74.73	4	<0.001	94.65	1.17
2.	Cognitive function												
		Posttest	6 (452)	0.30	0.09	0.52	2.75	0.006	5.81	5	0.325	13.99	0.01
		Follow-up	5 (307)	0.42	0.20	0.64	3.70	<0.001	1.15	4	0.886	0.00	0.00

Effects were analyzed using a random-effects model.

**Abbreviations:** CI, confidence interval; k, number of studies; n, number of patients.

**Table 3**  
Results of the moderator analysis for the effect of multisensory stimulation on agitation and anxiety.

Categorical variables	Agitation					Anxiety				
	k	Hedge's g	95 %	CI	p value	k	Hedge's g	95 %	CI	p value
Study setting										
Noninstitutional	3	-1.26	-1.83	-0.69	0.327	2	-0.48	-1.35	0.39	0.555
Institutional	7	-0.83	-1.49	-0.16		3	-1.05	-2.73	0.63	
Number of senses targeted										
5 senses	2	-1.70	-2.74	-0.67	0.228	3	-0.06	-0.34	0.22	0.081
4 senses	5	-0.63	-1.31	0.05		2	-1.96	-4.08	0.15	
3 senses	3	-1.04	-1.56	-0.53		0	0	0	0	
Intervention setting										
Activity room	2	-0.72	-1.65	0.22	0.583	2	-0.01	-0.38	0.36	0.096
Multisensory room	8	-1.02	-1.57	-0.47		3	-1.35	-2.87	0.18	
Intervention frequency										
Twice a week	6	-0.92	-1.71	-0.14	0.655	NA	NA	NA	NA	NA
More than twice a week	3	-1.13	-1.55	-0.71		NA	NA	NA	NA	NA
Intervention length (min/session)										
≤30 min	7	-0.90	-1.54	-0.26	0.778	2	-1.59	-4.44	1.27	0.396
>30 min	3	-1.06	-1.95	-0.17		3	-0.32	-0.94	0.29	
<b>Continuous variable</b>	<b>k</b>	<b>Coefficient</b>	<b>95 %</b>	<b>CI</b>	<b>p value</b>	<b>k</b>	<b>Coefficient</b>	<b>95 %</b>	<b>CI</b>	<b>p value</b>
Mean age	10	0.03	-0.09	0.15	0.580	5	0.02	-0.23	0.27	0.868
Male (%)	10	-0.02	-0.04	0.01	0.270	5	-0.00	-0.08	0.07	0.934
Female (%)	10	0.02	-0.01	0.04	0.270	5	0.00	-0.07	0.08	0.933
Elementary school and below (%)	4	-0.06	-0.17	0.05	0.278	NA	NA	NA	NA	NA
Junior high school and above (%)	4	-0.05	-0.09	-0.01	0.022	NA	NA	NA	NA	NA

A p value of <0.05 indicates a significant effect; k denotes the number of effect size.

**Abbreviation:** CI, confidence interval; NA, not applicable.

effect of multisensory stimulation on apathy. The random-effects model indicated that multisensory stimulation significantly alleviated apathy (g = -1.27; 95 %CI = -2.08 to -0.46; p = 0.002). Significant heterogeneity was observed for apathy (Q = 9.77; p = 0.008, I<sup>2</sup> = 79.53 %; τ<sup>2</sup> = 0.40; Table 2). Given the limited number of studies and the presence of significant heterogeneity, no moderator analysis was performed for this outcome.

### 3.3.3. Depression

The meta-analysis revealed that multisensory stimulation significantly reduced depression in older adults with dementia. Eight studies [8,12,13,37–39,41,42] involving 356 patients investigated the effect of multisensory stimulation on depression. The random-effects model indicated that multisensory stimulation significantly alleviated depression (g = -0.28; 95 %CI = -0.48 to -0.07; p = 0.008). No significant heterogeneity was observed for depression (Q = 5.28; p = 0.625; I<sup>2</sup> = 0.00 %; τ<sup>2</sup> = 0.00; Table 2).

### 3.3.4. Anxiety

The meta-analysis suggested that multisensory stimulation reduced anxiety in older adults with dementia; however, further studies are needed to confirm this effect. Five studies [8,11,13,41,43] involving 359 patients investigated the effect of multisensory stimulation on anxiety. The random-effects model indicated that multisensory stimula-

tion nonsignificantly alleviated anxiety (g = -0.81; 95 %CI = -1.79 to 0.17; p = 0.104). Significant heterogeneity was observed for anxiety (Q = 74.73; p <0.001; I<sup>2</sup> = 94.65 %; τ<sup>2</sup> = 1.17; Table 2). Subgroup analyses by study setting; intervention setting, number of session, or length; and number of senses revealed no significant moderators. Similarly, meta-regression analyses by age, gender (male, female), and educational level (elementary school and below; junior high school and above) revealed no significant moderators (Table 3).

### 3.4. Effect of multisensory stimulation on cognitive function

The meta-analysis revealed that multisensory stimulation significantly improved cognitive function in older adults with dementia (Fig. 2). Six studies [2,37–39,44–46] involving 452 patients investigated the effect of multisensory stimulation on cognitive function. The random-effects model indicated that multisensory stimulation significantly improved cognition at post-test (g = 0.30; 95 %CI = 0.09 to 0.52; p = 0.006). No significant heterogeneity was observed for cognitive function (Q = 5.81; p = 0.325; I<sup>2</sup> = 13.99 %; τ<sup>2</sup> = 0.01; Table 2). By contrast, five effect sizes in four studies [2,35,38,39] involving 307 patients reported a significant effect at follow-up (analyzed using a random-effects model: g = 0.42; 95 %CI = 0.20 to 0.64; p < 0.001); no significant heterogeneity was observed (Q = 1.15; p = 0.886; I<sup>2</sup> = 0.00 %; τ<sup>2</sup> = 0.00; Table 2).

### 3.5. Results of sensitivity analysis

Sensitivity analysis was conducted by removal one study with large or small contributions. Solé, Celdrán [13] in agitation, Yang, Yu [11] in apathy, Andretta [43] in anxiety, and Safavi, Yahyavi [45] in cognitive function were excluded due to large contributions, while Maseda, Sánchez [38] was excluded due to small contribution. The results remained stable, indicating the robustness of the results of this meta-analysis (Table S8).

## 4. Discussion

This study revealed that multisensory stimulation significantly reduced various NPSs, particularly agitation, apathy, and depression, in older adults with dementia. Furthermore, it substantially improved cognitive function in this population. However, multisensory stimulation exerted no significant effect on anxiety.

### 4.1. Effect of multisensory stimulation on NPSs

Multisensory stimulation effectively mitigated the following NPS subcategories: agitation, apathy, and depression. It exhibited a large effect in reducing agitation. The amygdala, a limbic brain region sensitive to threats, activates areas that regulate the release of stress hormones, contributing to agitation [47]. Multisensory stimulation can influence these brain areas, leading to a reduction in agitation [9,10]. Visual stimulation, such as exposure to calming visual stimuli and engaging activities, can redirect attention and reduce agitation [13]. Olfactory stimulation, such as smelling pleasant and familiar scents, can evoke positive emotions and memories, thereby alleviating agitation [12]. Auditory stimulation, such as listening to calming music and familiar sounds, can induce relaxation and reduce stress, ultimately reducing agitation [10]. Gustatory stimulation, such as consuming familiar and palatable foods, can enhance comfort and reduce agitation [13,48]. Tactile stimulation, such as gentle touch and exposure to familiar textures, can promote relaxation and reduce anxiety, thereby improving overall well-being [10,49]. Overall, a multisensory approach that combines calming visual stimuli, pleasant scents, gentle sounds, familiar tastes, and comforting touch is often the most effective approach to reduce agitation in older adults with dementia. Our moderator analysis indicated that higher levels of education in older adults were significant moderator with a greater reduction in agitation. Previous study has revealed that older adults with higher education levels may exhibit lower levels of neuropsychiatric symptoms, potentially due to better cognitive reserve and emotional intelligence [50]. Meanwhile, study setting, intervention setting, number of session or length of intervention, number of senses stimulated, age, gender (male, female), and educational level (elementary school and below) did not emerge as significant moderators of agitation among older adults with dementia in our analysis.

Multisensory stimulation exhibited a large and significant effect in reducing apathy, with significant reductions in this NPS observed across the studies. It reduced the level of apathy in the intervention group [11]. People with apathy, which is associated with a lack of motivation, often exhibit similar changes in specific brain areas, such as the medial frontal cortex (including the anterior cingulate cortex, medial orbitofrontal cortex, and ventral striatum) and subcortical structures [51]. By combining various stimulation techniques, multisensory stimulation interventions create a calming and engaging environment to improve mood, reduce feelings of isolation, and counter the sensory deprivation associated with dementia and apathy [11,12]. These effects align with the prevailing understanding that multisensory stimulation, by offering relaxing aromas, real touch, lighting effects, and meditation music, stimulates patients' sensory organs, such as those associated with smell, touch, vision, hearing, and taste; thus, multisensory stimulation effectively promotes activity in brain regions such as the orbitofrontal cortex and amygdala, which regulate emotion and motivation and are influenced by sensory

input [11,52]. These findings suggest that multisensory environments help reduce passive behaviors by encouraging interaction with sensory stimuli, which, in turn, enhances motivation and engagement.

Multisensory stimulation also alleviated depressive symptoms. It considerably reduced depression in the intervention group [8]. The prefrontal cortex, which regulates executive function, decision-making, and mood regulation, exhibits reduced activity and altered connectivity in people with depression [53]. Patients with Alzheimer's disease lacking environmental stimulation are highly susceptible to depression, and their diminishing sensory perception with age indicates disease deterioration or progression [11]. However, interventions engaging multiple senses—for example, those combining auditory stimulation (music), olfactory stimulation (aromatherapy), and tactile stimulation (relaxation massage)—may help improve mood and create a stimulating and supportive environment to increase engagement and interaction, which can counteract feelings of sadness and withdrawal [8]. Furthermore, intervention settings and materials in multisensory rooms foster pleasant experiences and sensations and create a calming ambience [54]. Our meta-analysis indicated that multisensory stimulation significantly ameliorated depressive symptoms; thus, it holds promise as an adjunct treatment for depression in patients with dementia.

Although multisensory stimulation alleviated anxiety, the result was nonsignificant. This finding is consistent with others in the literature; minimal effects on anxiety may be attributable to the short-term effect of the intervention [8]. However, a study indicated that familiar, calming stimuli such as music and tactile objects can help reduce feelings of fear or anxiety in patients with dementia [4]. Consistent, gentle sensory input from multisensory stimulation may soothe anxiety by creating a predictable and comfortable environment. Our moderator analysis indicated that among the interventions that were delivered in institutional settings, those that were administered in multisensory rooms, engaged four of the five senses, and lasted <30 min were more effective than others in reducing anxiety, particularly in younger individuals. However, the overall effect was nonsignificant.

### 4.2. Effect of multisensory stimulation on cognitive function

We found that multisensory stimulation significantly improved cognitive function in older adults with dementia. Similar findings have been reported by other studies [2,3,37]. The cerebrum regulates various cognitive abilities, such as attention, executive function, memory, language, and visuospatial skills [55]. Multisensory stimulation interventions based on familiarity stimulate multiple senses to recall long-held memories and engage patients in games or activities that they had participated in when younger. For instance, each session begins with a reality orientation to familiarize patients with time, place, and people; this is followed by various activities (e.g., creating handicrafts, garnishing fruits/vegetables, compiling photograph albums, and engaging in horticulture) to stimulate attention, executive function, and visuospatial skills. Then, additional activities such as guessing songs, singing or dancing to musical instruments, and compiling photographs are conducted to reinforce memory [2]. Some activities include discussions on items, their names, and purposes, encouraging patients to access implicit memories by recalling the past. Thus, cognitively stimulating activities in a multisensory context activate neuronal pathways in patients with dementia [56]. Although our study indicated modest improvements in cognition, the finding suggests that multisensory stimulation can help preserve or slightly enhance cognitive processing, likely by promoting neural engagement and plasticity. Follow-up analyses, particularly in studies with relatively long intervention durations, revealed that the aforementioned cognitive benefits persist over time.

### 4.3. Strengths and limitations

Our study has several strengths. First, this is the most comprehensive meta-analysis to date, providing data on the efficacy of multisensory

stimulation in managing NPSs and cognitive deficits in older adults with dementia. Second, specific outcomes related to NPS subcategories and cognitive function were determined in this study. Third, eight databases were searched to identify all eligible RCTs; moreover, reference lists were manually reviewed without imposing any restrictions on language, region, or publication year. Finally, moderator analyses were performed to explore the heterogeneity between the included studies. However, this study also has some limitations. The exclusion of articles with insufficient data might have affected the estimated effect sizes, although attempts were made to contact corresponding authors to obtain missing data. The included studies were not double-blinded, as this limitation is inherent in studies involving multisensory stimulation interventions, given the difficulty of blinding both participants and intervention providers due to the nature of the stimuli involved. Future research could incorporate a sham condition with minimal multisensory stimulation as a potential solution to enhance methodological rigor. Measuring cognitive function using MMSE has limitations in sensitivity and specificity, particularly in detecting subtle cognitive changes in people with dementia. Furthermore, this meta-analysis did not present the results of the effects of multisensory stimulation on specific domains of cognitive function due to the limited amount of data available from Randomized Controlled Trials. The current findings suggest that multisensory stimulation enhances cognitive function; however, the evidence remains preliminary and requires cautious interpretation. Future research should utilize more precise cognitive assessment tools, such as the ADAS-Cog, to provide a more reliable and standardized measure of cognitive outcomes. Similarly, we did not present the results for overall NPSs and other domains (except agitation, apathy, depression, and anxiety) due to limited available data. This study was limited by the number of included studies and the presence of heterogeneity, which impacts generalizability. Consequently, it is challenging to conclude which specific multisensory stimulation targeting particular sensory modalities will be the most effective for NPSs and cognitive function. Including a larger number of studies in future research could enhance the robustness of the results. Furthermore, the lack of follow-up analyses in some of the included studies limited our ability to evaluate the effects of multisensory stimulation on the study outcomes. Future studies should include follow-up analyses to clarify the short- and long-term effects of multisensory stimulation and the sustainability of these effects over time.

## 5. Conclusion

Our meta-analysis provides compelling evidence that multisensory stimulation serves as an effective nonpharmacological intervention for managing NPSs and cognitive functions in older adults with dementia. The findings indicate that this intervention exerts large and significant effects in alleviating agitation and apathy and a significant effect in alleviating depression. Furthermore, multisensory stimulation significantly improved cognitive function, with benefits sustained over follow-up periods. However, the intervention exerted no significant effect on anxiety. Nonetheless, multisensory stimulation holds promise as a valuable complementary therapy in dementia care. The intervention's ability to address multiple NPSs while supporting cognitive function makes it as a promising strategy for enhancing patients' quality of life and reducing caregiver burden. Future studies should focus on optimizing intervention protocols, exploring factors that influence intervention efficacy, and investigating long-term outcomes. Combining multisensory stimulation with other nonpharmacological approaches may amplify its therapeutic potential. In conclusion, multisensory stimulation offers a safe and effective strategy for managing the complex symptoms of dementia. Integrating it into comprehensive care plans may significantly enhance the well-being of patients with dementia and provide support to their caregivers. By mitigating challenging behaviors and promoting patient engagement, health-care professionals, particularly nurses, can holistically meet patients' psychological and cognitive needs. This approach also offers a viable alternative to pharmacological therapy, reducing re-

liance on medications and minimizing their adverse effects. Overall, this meta-analysis highlights multisensory stimulation as a promising intervention exerting significant positive effects on NPSs (particularly agitation, apathy, and depression) and cognitive function.

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## Declaration of generative AI

I confirm that I have not used any AI at all.

## 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 authorship contribution statement

**Tiara Octary:** Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Melati Fajarini:** Writing – review & editing, Validation. **Hidayat Arifin:** Writing – review & editing, Visualization. **Ruey Chen:** Writing – review & editing, Visualization. **Chien-Mei Sung:** Validation, Formal analysis. **Li-Fang Chang:** Writing – review & editing, Validation. **Chia-Hui Wang:** Writing – review & editing, Validation. **Kondwani Joseph Banda:** Writing – review & editing, Validation. **Kuei-Ru Chou:** Writing – review & editing, Validation, Supervision, Conceptualization.

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## Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.tjpad.2025.100091](https://doi.org/10.1016/j.tjpad.2025.100091).

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