BMJ Open Effectiveness of cognitive stimulation for individuals with mild cognitive impairment: a systematic review and meta-analysis

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ABSTRACT

Objective Cognitive stimulation (CS) is a nonpharmacological intervention aimed at enhancing cognitive function. However, the effectiveness of CS in individuals diagnosed with mild cognitive impairment (MCI) remains inconclusive. Therefore, this study aimed to assess the effectiveness of CS in improving cognitive function, psychological well-being, instrumental activities of daily living (IADL) and quality of life (QoL) in individuals with MCI, based on randomised controlled trials (RCTs). **Design** Systematic review and meta-analysis.

Data sources Six English databases were systematically searched, including PubMed, Web of Science, Embase, Cumulative Index to Nursing and Allied Health Literature, American Psychological Association PsycInfo and Academic Search Premier.

Eligibility criteria RCTs about CS for individuals with MCI, published between January 2003 and December 2024. Data extraction and synthesis Data were extracted and assessed using the revised Cochrane risk of bias tool for randomised trials by independent researchers. The metaanalysis was conducted using the standardised mean difference (SMD) and 95% CIs of the included studies. Results The meta-analysis included five eligible studies for the primary outcomes of cognitive function and three eligible studies for the secondary outcomes of psychological wellness. In the pooled samples, the CS intervention had a significant effect on cognitive function (SMD=0.63, 95% CI 0.25 to 1.01; p=0.001) and depression symptoms (SMD=-0.29, 95% CI -0.55 to -0.03; p=0.03) in individuals with MCI. However, no significant improvements in anxiety symptoms were identified after the CS intervention (SMD=-0.05; 95% CI -0.31 to 0.21; p=0.71).

Conclusion The CS intervention can effectively improve cognitive function and alleviate depression symptoms. Although a meta-analysis was not conducted for IADL and QoL due to the limited number of included studies, positive trends in enhancing IADL performance and augmenting QoL were observed in individuals with MCI. However, due to the scarcity of relevant studies in this research field, more comprehensive RCTs are warranted to provide a better understanding of the potential benefits of CS and to guide its clinical application in the future.

PROSPERO registration number CRD42023494685.

STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ Conduct a comprehensive and up-to-date systematic review with clear eligibility criteria and extensive database searches.
- ⇒ Apply rigorous methodology, including assessing the risk of bias, performing meta-analyses and evaluating the certainty of evidence.
- ⇒ Highlight key findings and their implications for future research.
- ⇒ Demonstrate limited statistical power for metaanalysis due to the small number of studies ultimately included.

INTRODUCTION

Protected by copyright, including for uses related to text and As the global population ages, the incidence of age-related neurodegenerative conditions increases. Mild cognitive impairment (MCI) has garnered significant attention from researchers due to its high prevalence and the potential risk of progressing to more severe forms of cognitive impairment. MCI ≥ is characterised by a cognitive decline that surpasses what is anticipated for normal ageing, yet it is not severe enough to fulfil the diagnostic criteria for dementia. According to the definition of the Diagnostic and Statistical Manual of Mental Illnesses, fifth edition (DSM-5), MCI is a condition that results in a modest decline in one or more cognitive domains without significantly impeding an individual's ability to independently carry out daily activities.² Individuals with MCI may exhibit subtle yet discernible declines in **3** cognitive function, setting them apart from their healthy, age-matched counterparts. The cognitive domains commonly impacted include memory, attention, language and executive functions.³

The global prevalence of MCI is 15.56% among community-dwelling adults aged ≥50 years, indicating that its status is a significant public health issue.⁴ It should be noted that



more than 60% of individuals with MCI ultimately develop dementia, such as Alzheimer's disease (AD), within their lifetime.⁵ Consequently, investigating the efficacy of various MCI treatments to delay or reverse its progression is of paramount importance. The US Food and Drug Administration (FDA) recently approved pharmacological interventions such as lecanemab and donanemab, which are amyloid beta-directed antibodies, for the treatment of MCI. However, they are too expensive for many patients to afford. Although some other AD medications have been used to manage symptoms and slow dementia progression, their clinical effectiveness varies and side effects are common.⁶ Thus, the current focus in MCI treatment has shifted towards non-pharmacological interventions, owing to their potential efficacy and superior safety profile.

Cognitive stimulation (CS), a non-pharmacological intervention strategy for managing MCI, encompasses a variety of engaging activities designed to stimulate cognitive function, such as thinking, concentration and memory. These activities are typically, but not exclusively, conducted in social settings. The origins of CS can be traced back to reality orientation (RO), a therapeutic technique that involves presenting orientation and memory information related to time, place and person. ¹⁰ CS incorporates the beneficial aspects of RO, such as reducing confusion and disorientation, while emphasising the importance of person-centredness, sensitivity and respect. 11 A typical CS programme involves small groups of participants meeting twice a week for 14 sessions, each lasting approximately 45 min and featuring different activity themes. These stimulating activities can range from reminiscence and discussions on topics of interest to word games, puzzles, music and expressive creative activities. 12 It is important to distinguish CS from other cognitive interventions. Unlike 'cognitive training', which involves guided repetitive practice aimed at maintaining or enhancing specific cognitive function, and 'cognitive rehabilitation', which identifies personal goals and employs relevant strategies for goal achievement, CS is grounded in the principle of engaging participants in enjoyable activities. 9 This distinction underscores the unique approach of CS in managing cognitive impairment.

Several recent studies have highlighted the potential benefits of CS for individuals with MCI. For instance, Arshad et al¹³ reported favourable outcomes of CS in enhancing cognitive function among individuals with MCI. Similarly, Djabelkhir-Jemmi et all suggested that CS was effective in improving memory, phonemic fluency and visuospatial processing in older adults with MCI. Furthermore, CS has been associated with improved psychological wellness and quality of life (QoL), ¹⁵ as well as enhanced performance in instrumental activities of daily living (IADL). 15 16 This evidence collectively underscores the potential of CS as a beneficial intervention for individuals with MCI.

Although existing research has provided valuable insights into the effects of CS, these studies often suffer

from small sample sizes, potentially limiting the generalisability and statistical power of the findings. For example, Arshad et al¹³ recruited only 20 subjects in their study, which may have compromised the reliability of the study due to potential bias. Additionally, there are inconsistent findings in the literature. For example, Carcelén-Fraile et al^{17} reported no significant changes in cognitive function among individuals with MCI following a CS programme; on the contrary, Arshad et al¹³ observed a significant improvement in cognitive function. These discrepancies highlight the need for further investigations to yield more comprehensive and robust conclusions regarding the overall effect of CS on the MCI population. A systematic review and meta-analysis, which are crucial for synthesising available evidence and providing more accurate and reliable conclusions, are therefore warranted. However, to date, this research area is void and lacks a unified conclusion. To fill this gap, we conducted a comprehensive systematic review and meta-analysis on the effectiveness of CS in individuals with MCI based on randomised controlled trials (RCTs), focusing on four

aspects of outcome measurements: (1) cognitive function, (2) psychological wellness, (3) IADL and (4) QoL.

METHODOLOGY

The systematic review was conducted in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Search method

The search encompassed the following databases: as

The search encompassed the following databases: PubMed, Web of Science, Embase, Cumulative Index to Nursing and Allied Health Literature, American Psychological Association PsycInfo and Academic Search Premier. The search was conducted exclusively in English using the following terms: ('cognitive stimulation therapy' OR 'cognitive stimulation programme' OR 'cognitive stimulation programme' OR 'cognitive stimulation' OR 'cognitive stimulation activity' OR 'CST' OR 'CS') AND ('mild cognitive impairment' OR 'MCI' OR 'mild neurocognitive disorder (NCD)' OR 'mild NCD') AND ('randomised controlled trial' OR 'RCT' OR 'randomised' OR 'randomly' OR 'trial' OR 'groups') (online supplemental appendix 1: search strategy). This study was duly registered in the International Prospective Register of Systematic Reviews (reference number: CRD42023494685).

Inclusion criteria and exclusion criteria

Inclusion criteria

(1) CS RCTs were conducted for individuals with MCI. (2) Individuals with MCI in the studies met the American Psychiatric Association's Diagnostic and Grading Criteria (DSM-5) or Petersen's criteria or had a definitive diagnosis of MCI based on other comparable criteria. (3) The design of the intervention fulfilled the criteria for CS in terms of content: a range of enjoyable group activities providing general stimulation for multiple cognitive function domains, including memory, thinking, concentration, executive function and problem-solving, usually in a social setting. The multiple stimulation sessions can be conducted as games, discussions, puzzles, music, reminiscence and so on.⁹ (4) CS intervention in the studies was compared with either 'no treatment', 'activity as usual' or 'placebo' group. Placebo conditions were defined as involving some activity sessions where general support was provided but without any structured intervention. (5) The CS intervention had a minimum duration of 10 sessions to ensure it was long enough to have an impact. (6) The primary outcome was cognitive function; secondary outcomes included psychological wellness, IADL and QoL. All outcomes needed to be measured with verifiable measurement tools as listed here: the Montreal Cognitive Assessment (MoCA)¹⁸ or Mini-Mental State Examination (MMSE)¹⁹ for measurement of cognitive function; the Goldberg Anxiety and Depression Scale (GADS)²⁰ or Geriatric Depression Scale-15 (GDS-15)²¹ for measurement of depression symptoms; the GADS or the Hamilton Anxiety Rating Scale (HAM-A)²² for measurement of anxiety symptoms; the Lawton-Brody Instrumental Activities of Daily Living Scale (Lawton IADL)²³ for measurement of IADL; the QoL in Alzheimer's Disease Scale (QoL-AD)²⁴ or 12-item Short Form Survey (SF-12)²⁵ for measurement of QoL. (7) The years of publication ranged from January 2003 to December 2024. This publication period ensured that all relevant articles were included, starting from when the first CS-related RCT was reported in 2003, ²⁶ while also capturing the most up-to-date information.

Exclusion criteria

(1) CS was combined with other interventions. (2) The means and SD were not provided or could not be calculated. (3) Complete data were not available after contacting the corresponding authors. (4) Papers written in languages other than English.

Study selection and data extraction

Two researchers (STN and YHZP) independently conducted the database search using the search strategy detailed above. Duplicate studies were removed before screening the retrieved studies. Three researchers (TM, OLL and YWL) independently screened the studies by reviewing the titles and abstracts. Subsequently, two researchers (OLL and YWL) independently conducted full-text screening for eligibility and extracted key information from the eligible studies. The key information included the authors, year of publication, country, study design, sample size, participant demographics (eg, number of participants, number of males and females and age), intervention details (eg, the content of the intervention, frequency and duration of the intervention and follow-up period), outcome measures and additional information related to the randomisation procedure and blinding. In instances where disagreements arose among the two researchers, a third researcher (LHC) mediated and resolved the disputes through discussion.

Risk of bias assessment

Two independent researchers (OLL and SYEN) assessed each study using the revised Cochrane risk of bias tool for randomised trials (RoB-2).²⁷ The RoB-2 tool encompasses five domains: (1) the randomisation process; (2) deviations from the intended interventions; (3) missing outcome data; (4) measurement of the outcome and (5) selection of the reported result. The risk of bias was graded based on three categories: 'low risk', 'some concerns' and 'high risk'. A study was deemed to have a high risk of bias if it was considered high risk in at least 5 three out of the five domains. In instances where discrepancies arose between the two researchers' assessments, a third researcher (LHC) was consulted to resolve the disagreement, ensuring a rigorous and unbiased evaluation process.

Publication bias assessment

These funnel plots, which graphically represent the study effect size in relation to the SE, provide a visual means of assessing systematic heterogeneity or bias. This method allows for a critical examination of the distribution of effect sizes, aiding in the identification of potential asymmetry that could indicate publication bias.

Certainty of evidence assessment

The overall quality of evidence and the strength of the recommendations were assessed by one researcher (LHC) using the Grading of Recommendations, Assessment, Development and Evaluations (GRADE) approach.²⁸ This approach rates the quality of evidence by considering six factors, including study design (RCTs vs observational studies), risk of bias, inconsistency, indirectness, imprecision and publication bias. The evidence was then graded as 'very low', 'low', 'moderate' or 'high', which represents the quality of evidence gradually ranging from uncertain to certain.20

Data synthesis and statistical analysis

Data sorting, processing and analysis were carried out using Cochrane Review Manager (Cochrane, RevMan, V.5.4, Oxford, UK) (https://training.cochrane.org/ online-learning/core-software/revman). The analysis was performed using the standardised mean difference (SMD) and 95% CIs. The SMD, which represents the effect size of different scales assessing the same outcome, was calculated using the equation below.³⁰

Standardized mean difference =

Difference in mean measurement between group Standard deviation of measurement among participants

The SMD was presented as Hedges' adjusted g (as implemented in RevMan) using post-CS scores (measured immediately following the intervention) for both primary and secondary outcomes. All these steps followed the Cochrane Handbook for Systematic Reviews of Interventions.³¹ For outcomes where higher scores are beneficial (eg, cognitive function), a positive SMD indicates that the CS intervention group had a higher mean score than the control group. For outcomes where lower scores are beneficial (eg, depression symptoms and anxiety symptoms), a negative SMD indicates that the CS intervention group had a lower mean score compared with the control group. An SMD value of 0.2, 0.5 and 0.8 suggests small, medium and large effects between the groups relative to the variability within the groups, respectively.³² The random-effects model was applied for the meta-analysis of the primary and secondary outcomes due to the expected heterogeneity in populations, clinical settings and intervention protocols among the included studies. Heterogeneity was evaluated using I^2 , τ^2 and the O-test to characterise the magnitude and uncertainty of between-study variability. 33 A p value < 0.05 was regarded as statistically significant for the pooled effect in the meta-analysis.

RESULTS

Literature retrieval

A total of 7039 pertinent studies were initially retrieved for review. From this pool, 1351 were identified as duplicates and subsequently excluded, and an additional 5609 were excluded following a thorough screening of their respective titles and abstracts. This left a remaining 79 references, of which only five met the established study inclusion criteria. The process of literature screening is

represented in figure 1, using a PRISMA flow diagram.

Characteristics of included studies

The five qualifying papers were published recently, from 2015 to 2023. 13 15-17 34 Three of these studies originated from Spain, one originated from Italy, and the remaining study was conducted in Pakistan. All the articles employed

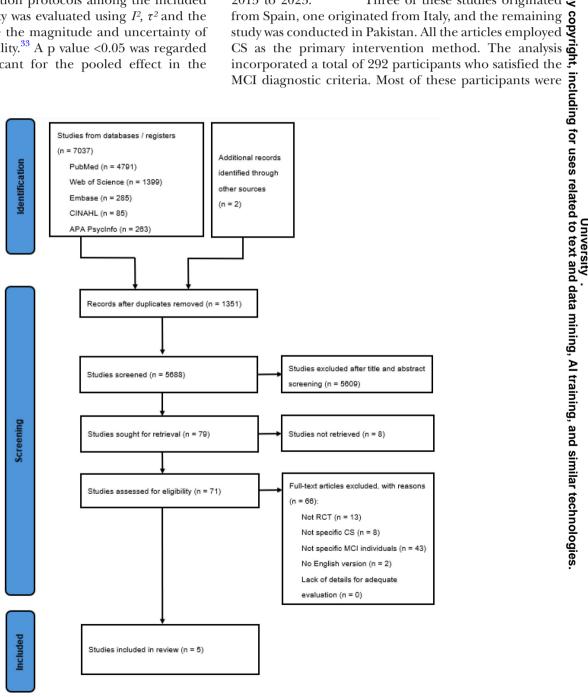


Figure 1 Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram.



female, comprising 222 out of 292 participants. The age range of the participants spanned from 50 to 81 years. The five studies implemented CS through various methods, as detailed in table 1. The frequency and duration of the interventions varied, ranging from one to three times per week, with each session lasting between 45 and 60 min. The total length of the intervention period ranged from 5 to 12 weeks (table 1).

Among the five papers with primary outcomes of cognitive function, three had secondary outcomes of psychological wellness (depression and anxiety symptoms), and only two had secondary outcomes of IADL and QoL. Considering the potential for high bias and low statistical power with only two papers, the subsequent meta-analysis was conducted only for the outcome indicators of cognitive function and psychological wellness.

Risk of bias analysis

Overall, the quality of the studies included in the analysis was good (figure 2). Four of the studies were evaluated as having a low risk of bias, ¹³ ¹⁵ ¹⁶ ³⁴ whereas one study was identified as having some concerns. 17 The study from Carcelén-Fraile et al raised some concerns regarding the measurement of the outcome, as it could have been influenced by the assessors.¹⁷

Publication bias analysis

Publication bias analysis was conducted for outcome indicators included in the meta-analysis, including cognitive function and psychological wellness (depression and anxiety symptoms). The visualised funnel plots were all symmetrical, suggesting a low risk of publication bias among the included studies (figure 3). However, due to the limited number of studies, this observation should be interpreted with caution (n=5 for cognitive function studies and n=3 for depression and anxiety symptoms studies, respectively).

Meta-analysis of outcomes

Cognitive function following CS (primary outcomes)

Two studies measured the effect of CS on cognitive function in individuals with MCI using the MoCA, 13 34 and three studies used the MMSE¹⁵⁻¹⁷ (figure 4). These studies involved 292 participants (138 in the intervention group and 154 in the control group). CS was significantly associated with the cognitive function of MCI individuals (SMD=0.63, 95% CI 0.25 to 1.01, p=0.001) among the pooled participants. A positive SMD of 0.63 indicates improved cognitive function in the CS intervention group compared with the control group (medium effect). Meanwhile, moderate heterogeneity was observed (I²=55%, τ^2 =0.10; Q=8.91, p=0.06) among the studies, which may be due to differences in population characteristics, intervention protocols and clinical settings.

Psychological wellness following CS (secondary outcomes)

Three studies evaluated depression symptoms in individuals with MCI using the GDS-15¹⁵⁻¹⁷ (figure 5A). These studies included a total of 228 participants, with 106 in

the intervention group and 122 in the control group. The meta-analysis revealed statistically significant improvements in the depression symptoms of individuals with MCI after CS intervention (SMD=-0.29, 95% CI -0.55 to -0.03, p=0.03). A negative SMD of -0.29 indicates fewer depression symptoms in the CS intervention group compared with the control group (small effect). Although no statistical heterogeneity was observed among the included studies (I²=0%, τ ²=0.00; Q=0.67, p=0.72), results should be interpreted cautiously due to the small number of

included studies (n=3).

Three studies assessed anxiety symptoms using the GADS, 15 16 and one study assessed anxiety symptoms using the HAM-A¹⁷ in individuals with MCI (figure 5B). These studies included a total of 228 participants, with 106 in the CS intervention group and 122 in the control group. However, the analysis indicated that improvements in anxiety symptoms (with a negative SMD suggesting fewer anxiety symptoms in the CS intervention group compared with the control group) were not significant among the pooled participants (SMD=-0.05, 95% CI -0.31 to 0.21, p=0.71). Similar to the studies assessing depression sympfor uses related to toms, no heterogeneity was identified among the three included studies (I²=0%, τ ²=0.00; O=0.73, p=0.70).

Narrative synthesis of outcomes

IADL following CS (secondary outcomes)

Two studies evaluated IADL in individuals with MCI using the Lawton IADL. 15 16 Although a meta-analysis was not conducted for IADL due to the limited number of eligible studies, a positive trend in enhancing IADL performance was observed in individuals with MCI (Gomez-Soria et al. 2020: mean=7.26 in the CS intervention group vs mean=6.36 in the control group; Gómez-Soria et al, 2023: mean=7.24 in the CS intervention group vs mean=6.36 in the control group).

QoL following CS (secondary outcomes)

One study assessed QoL using the QoL-AD, 13 and one study assessed QoL using the SF-12¹⁷ in individuals with MCI. Similar to IADL, a meta-analysis was not conducted for QoL due to the limited number of eligible studies; however, a potential positive impact on improving QoL was observed in individuals with MCI (Arshad et al, 2020: mean=36.2 in the CS intervention group vs mean=23.6 in the control group; Carcelén-Fraile et al, 2022: mean=87.35 in the CS intervention group vs mean=78.2 in the control group).

Certainty of evidence analysis

The certainty of evidence was assessed for outcome indicators of cognitive function as well as psychological well-being (depression and anxiety symptoms). For the outcome indicator of cognitive function, the evidence was downgraded by one level to moderate due to the inconsistency observed among the included studies. In contrast, the evidence for the outcome indicators related to symptoms of depression and anxiety was deemed high,

Sample Author (year) Country Design Translation criterion) Intervention Intervention Age (years)/7 (4 £ 1.7) Article (years) Country Design Translation Criterion) Age (years)/7 (4 £ 1.4) Article (years)/7 (4 £ 1.4) Age (years)/7 (4 £ 1.4) Article (years)/7 (4 £ 1.4) Art	Table 1 Summ	Summary of the study characteristics	study char	acteristics			
Peterson's criteria for MC P. CS group: each session included three parts: reality Peterson's criteria for MC P. CS group (22) Control group (23) Control group (23) Control group (24) Control group (36) Control group (36	Author (year)	Country	Design	Sample (inclusion criterion)	Intervention	Outcomes (scale) (assess	ed at)
Pakistan RCT	Polito <i>et al</i> (2015)	Italy	RCT	 ▶ Peterson's criteria for MCI ▶ CS group (22) Gender (male/female): 17/5 Age (years):74.0±1.4 ▶ Control group (22) Gender: (male/female): 14/8 Age (years):74.3±1.7 	 ► CS group: each session included three parts: reality orientation, exercises designed to stimulate attention (auditory and visual) on the targeted cognitive function (executive reasoning, language-verbal fluency, semantic memory, visual perception, encoding, information storage, non-verbal learning and executive problem solving) and group reflection of exercises. Sessions: 10 sessions, two times a week, 5 weeks, 60 min/session ► Control group: two interactive 60-min meetings focusing on lifestyle education and brain functioning. 	MocA	▶ Pre-CS ▶ Post-CS
PCS group (36) Scored 24–26 on MMSE and scored 18–26 on MoCA Scored 24–27 on MEC-35 Scored 24	Arshad et al (2020) ¹³	Pakistan	RCT	 ▶ Peterson's criteria for MCI ▶ Age (years): 56.48±7.09 ▶ CS group (10) Gender (male/female): 5/5 ▶ Control group (10) Gender (male/female): 4/6 	► CS group: each session included general (group song, names calling, ball throwing, etc) and session-specific activities. Themes included physical and number games, sound recognition, memories, categorising food objects, faces/places and current affairs and word games as well as using money. Sessions: 14 sessions, two times a week, 8 weeks, 45 min/ session ➤ Control group: no intervention.	A A	► Pre-CS ► Post-CS ► Follow- up at 2 months
RCT ► Scored 24–27 on MEC-35 ► CS group: each session included four parts: reality orientation, explanation of the cognitive aspects to be focused on (memory, orientation, language, praxis, gnosis, Porntrol group (68)	Carcelén-Fraile et al (2022) ¹⁷	Spain	RCT	3 2 3	► CS group: each session trained a cognitive domain, including three parts: orientation to reality, exercises of cognitive domains (memory, language, calculation, praxis and gnosis and executive functions) and group correction of practical exercises. Sessions: 36 sessions, three times a week, 12 weeks, 60 min/session ► Control group: no intervention.		▼ Pre-CS ▼ Post-CS
	Gomez-Soria e. al (2020) ¹⁵	t Spain	RCT	► Scored 24–27 on MEC-35 ► CS group (54) Gender (male/female): 7/47 Age (years):74.3±5.8 ► Control group (68) Gender: (male/female): 21/47 Age (years):75.6±6.2	► CS group: each session included four parts: reality orientation, explanation of the cognitive aspects to be focused on (memory, orientation, language, praxis, gnosis, calculation, perception, reasoning, visual attention and executive function), practical work and group correction of practical exercises. Sessions: 10 sessions, once a week, 10 weeks, 45 min/session Control group: no intervention.		▼ Pre-CS ▼ Post-CS ▼ Follow- up at 6 months

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Author (year) Count	ry Design	Sample Author (year) Country Design (inclusion criterion)	Intervention	Outcomes (scale) (assessed at)	ed at)
Gómez-Soria et Spain al (2023) ⁶¹	RCT	 ▶ Scored 20–35 on MEC-35, classified into four subgroups, where level deterioration group scoring 24–27 belonging to MCI ▶ CS group (49) Gender (male/female): 7/42 Age (years): 74.16±0.8 ▶ Control group (59) Gender (male/female): 20/39 Age (years): 75.15±0.78 	► CS group: performed 40 activities classified into four exercises for memory, orientation, language, praxis, gnosis, calculation, perception, logical reasoning, attention-concentration and executive function. Sessions: 10 sessions, once a week, 10 weeks, 45 min/session. ► Control group: no intervention.	► MEC-35 ► GDS-15 ► Anxiety subscale of GADS ► Lawton IADL	▼ Pre-CS ▼ Post-CS ▼ Follow-up at 6 and 12 months

nstrumental Activities of Daily Living Scale; MCI, mild cognitive impairment; MEC-35; Spanish version of MMSE, Mini-Examen Cognoscitivo-35 points; MMSE, Mini-Mental State Examination;

MoCA, Montreal Cognitive Assessment Scale; QoL-AD, quality of life in Alzheimer's disease; RCT, randomised controlled trial;

Short Form-12 Generic Health Questionnaire.

suggesting the certainty of the effect of CS (online supplemental appendix 1, table 1).

DISCUSSION

This meta-analysis investigated the clinical effectiveness of CS in improving cognitive function, psychological wellness, IADL and QoL among individuals with MCI by systematically reviewing RCTs. The results specifically indicate that CS significantly ameliorates cognitive function and depressive symptoms, but not anxiety symptoms, based on pooled samples. Although a meta-analysis was not conducted for IADL and QoL due to the limited number of included studies (n=2), positive trends in enhancing IADL performance and augmenting QoL were observed in individuals with MCI.

Our findings suggest a significant positive impact of CS on cognitive function among individuals with MCI. CS encourages the active involvement of individuals with MCI in structured and stimulating activities that target various cognitive domains. This active involvement furnishes opportunities for essential brain stimulation. By actively participating in brain-stimulating games and tasks, the brain's connectivity and the formation of new synapses can be augmented, thereby strengthening neural circuits.³⁵ The brain's neuroplasticity facilitates the reorganisation of its structures, thereby enabling potential cognitive improvement through CS.³⁶ Moreover, the group-based nature of CS activities provides opportunities for social interaction among individuals with MCI. According to Krueger et al, increased social engagement is associated with improved cognitive functioning.³⁷ This is because being socially engaged can offer ongoing CS by demanding a high level of comprehension, memory and problem-solving skills necessary to maintain and nurture social connections.³⁸ Therefore, the additional social elements of CS may further foster cognitive benefits through the positive influence of social interaction. Consequently, the findings of our meta-analysis support that CS plays a pivotal role in enhancing cognitive function among individuals with MCI.

Another noteworthy finding is that CS significantly mitigates depression levels among individuals with MCI. Although the individual results of three studies indicated improvement in depressive levels after CS intervention, statistical significance was not achieved. However, through meta-analysis, these individually insignificant results were amalgamated, thereby increasing the overall sample size (figure 5A). This approach yielded a significant positive effect of CS in alleviating depression symptoms. A relatively larger sample size provides greater statistical power, enabling the identification of differences and the detection of significant effects, as well as minimising potential deviations. ³⁹ Depression is prevalent in individuals with MCI, with rates varying from 16.9% to 55%. ⁴⁰ The observed positive alterations in depression levels based on pooled samples are postulated to be associated with the social interactions and group dynamics

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Study ID	<u>D1</u>	<u>D2</u>	<u>D3</u>	<u>D4</u>	<u>D5</u>	Overall
Polito 2015	+	+	+	+	+	+
Arshad 2020	+	!	+	+	+	+
Carcelén-Fraile 2022	+	+	+	!	+	!
Gomez-Soria 2020	+	+	+	+	+	+
Gómez-Soria 2023	+	+	+	+	+	+

+	Low risk
1	Some concerns
	High risk

process

- D3 Missing outcome data
- D4 Measurement of the outcome
- D5 Selection of the reported result

Figure 2 Risk of bias summary.

inherent in the reviewed studies. ^{15–17} The intensive social components during CS sessions could stimulate positive feedback and engender joyful feelings, thereby diminishing negative emotions and alleviating depression symptoms. ⁴¹ ⁴² Moreover, the presence of peer support in CS groups contributes to a reduction in depression symptoms. According to Carcelén-Fraile's research, ¹⁷ the inclusion of group peers with similar backgrounds in intervention sessions facilitates the formation of new friendships, the sharing of similar experiences, and the

exchange of practical advice. By receiving support and understanding from group peers, individuals with MCI can enhance their feelings of happiness. Additionally, the improvement in cognitive function brought about by CS could also indirectly contribute to the amelioration of depression symptoms, as Clare *et al* demonstrated in a previous study that cognitive enhancement is associated with reduced depression symptoms.⁴³ The significant improvement in depressive symptoms in individuals with MCI after CS intervention, as evidenced by

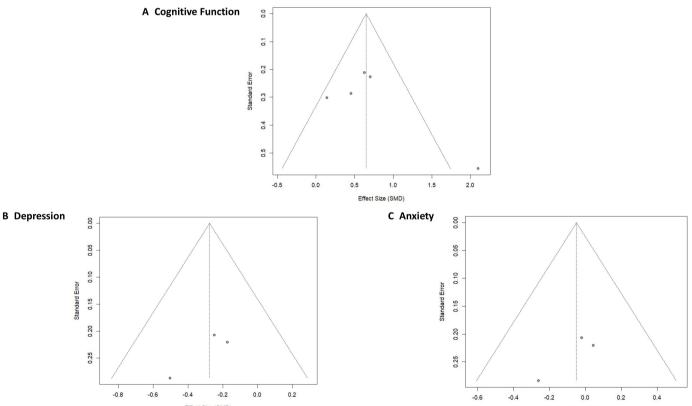


Figure 3 Funnel plots of publication bias analysis. (A) Cognitive Function; (B) depression symptoms and (C) anxiety symptoms.

Effect Size (SMD)

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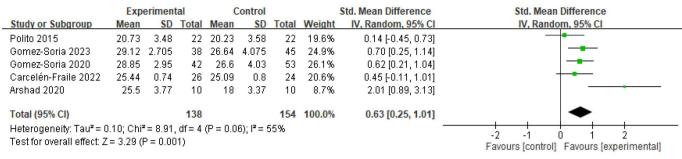


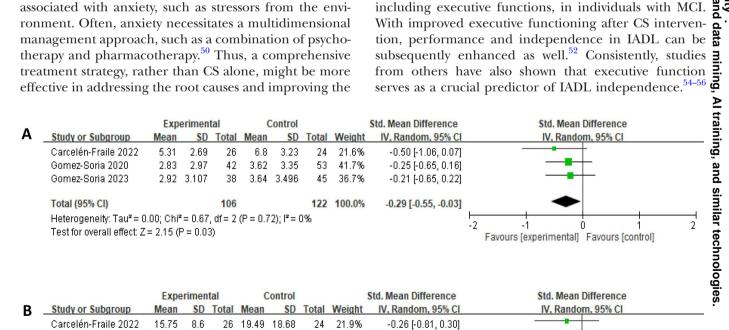
Figure 4 Meta-analysis of the effectiveness of cognitive stimulation on cognitive function of mild cognitive impairment individuals.

our meta-analysis, is a novel finding that diverges from previous individual literature.

In contrast to evidence on depression symptoms, the existing evidence does not support the therapeutic effects of CS in mitigating anxiety symptoms. The literature has demonstrated a robust association between MCI and anxiety, with prevalence rates ranging from 9.9% to 52%. 44-48 However, our meta-analysis did not indicate a significant improvement in anxiety symptoms among individuals with MCI following CS intervention based on the pooled samples. This finding may be attributed to the complex nature of anxiety. Thibaut⁴⁹ posited that anxiety is a multifaceted condition influenced by numerous factors, including genetic predisposition, neurochemical imbalances, personality traits and environmental stressors. CS alone might not be sufficiently effective in addressing the underlying causes and psychological disturbances associated with anxiety, such as stressors from the environment. Often, anxiety necessitates a multidimensional management approach, such as a combination of psychotherapy and pharmacotherapy.⁵⁰ Thus, a comprehensive treatment strategy, rather than CS alone, might be more effective in addressing the root causes and improving the

severity of anxiety. Our meta-analysis underscores the need for more experimental studies to explore the effectiveness of CS in improving anxiety levels in individuals with MCI.

Although a meta-analysis was not conducted for IADL due to the limited number of eligible studies, a positive trend in enhancing IADL performance was observed in individuals with MCI. This may be elucidated by the association between IADL and cognitive function. ⁵¹ ⁵² Executive function, a facet of cognition, encompasses high-level cognitive abilities such as working memory, problemsolving, decision-making and planning. ⁵³ This higher-order cognitive function is instrumental in facilitating the performance of complex daily tasks, known as IADL, which involves meal preparation, home maintenance, community mobility, and financial management. CS has been demonstrated to significantly enhance cognition, including executive functions, in individuals with MCI. With improved executive functioning after CS intervention, performance and independence in IADL can be subsequently enhanced as well. ⁵² Consistently, studies from others have also shown that executive function serves as a crucial predictor of IADL independence. ^{54–56}



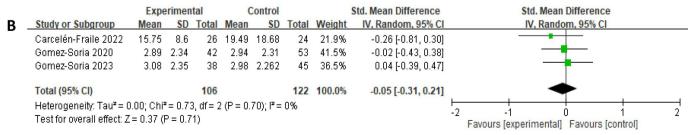


Figure 5 (A) Meta-analysis of the effectiveness of CS on depression symptoms of MCI individuals. (B) Meta-analysis of the effectiveness of CS on anxiety symptoms of MCI individuals. CS, cognitive stimulation; MCI, mild cognitive impairment.

Therefore, by enhancing cognitive function through CS, the IADL independence of individuals with MCI can be potentially augmented, as observed by the present study. However, larger samples and additional studies are warranted for more credible conclusions in the future.

Similar to IADL, the findings of the present study suggest that CS may have a potential positive impact on the QoL of individuals with MCI. As defined by the WHO Quality of Life (WHOQOL)-group,⁵⁷ QoL encompasses various dimensions, including physical, psychological, independence, social, environmental and spiritual domains. It is reasonable to postulate that enhancing any of these domains can contribute to an overall improvement in QoL. The WHOQOL-Group⁵⁷ emphasised that psychological wellness is determined by individuals' perceptions of their cognitive and affective states. Given the previous discussion, as CS promotes active brain use and dynamic group interactions, it leads to improvements in cognitive function and a reduction in depressive symptoms. Therefore, the amelioration of cognition and depression resulting from CS may consequently lead to an enhancement in QoL. This potential impact also aligns with previous studies indicating that individuals with better cognitive function and lower levels of depression tend to have greater QoL.⁵⁸ Additionally, the social domain, which involves perceptions of social relationships, plays a critical role in maintaining QoL.⁵⁷ As previously discussed, CS provides a platform for individuals with MCI to engage in group-based activities, reducing their social isolation. Socialisation during CS contributes to a greater level of connectedness and life satisfaction, positively influencing QoL.⁵⁹ In line with this, Siette et al⁶⁰ demonstrated a positive relationship between social engagement and QoL outcomes. In summary, the findings of the study suggest a positive trend in the improvement of QoL among individuals with MCI, which may be attributed to multiple dimensions facilitated by CS, including cognitive function, psychological wellness and social participation. However, these findings require further validation via future RCTs with larger sample sizes.

Although this study provides valuable insights, it has several limitations. First, the meta-analysis was constrained by the limited number of eligible articles included (only five) due to the scarcity of relevant studies focusing on individuals with MCI in this field of research. Meanwhile, considering that RCT-based meta-analyses have high value in minimising bias, establishing causality and guiding clinical evidence-based decisions, a study with an RCT design was an important inclusion criterion, which further reduced the number of eligible articles for the present meta-analysis. Although our meta-analysis of five studies provides a structured synthesis of existing evidence, its statistical power and reliability are inherently limited, and results should be interpreted with caution. Future research should focus on conducting more relevant RCTs to investigate the effectiveness of CS in individuals with MCI. By incorporating more relevant RCT studies, a larger sample size and consequently higher

statistical power can be achieved to further validate the conclusions of our meta-analysis. Second, one included study by Carcelén-Fraile et al was found to have some concerns during the risk of bias assessment due to the outcome measurement being influenced by the assessors. Although its effect estimate aligned with those of the other included studies, this methodological uncertainty highlights the need for cautious interpretation of the meta-analysis results. Future studies with rigorous methodological designs are required to confirm these T findings. Third, although high certainty was rated for the secondary outcomes of psychological well-being by the GRADE assessment, the evidence for the effect of CS on the primary outcomes of cognitive function was deemed ξ moderate. The downgrade in certainty for cognitive ? outcomes not only highlights the challenge of synthesising studies with heterogeneous methodologies and populations but also suggests a potential signal warranting further investigation and validation. Fourth, the lack of follow-up data in the included studies resulted in a dearth of reliable evidence regarding the long-term effects of CS. This highlights the need for more high-quality RCTs that encompass comprehensive datasets to demonstrate both the short- and long-term efficacy of CS interventions. Future studies should incorporate long-term data to better comprehend the sustained effectiveness of CS in individuals with MCI. Fifth, subgroup analysis, such as differences in age and sex, was not performed in this meta-analysis due to the limited number of eligible RCTs included. Future research should investigate these factors that may moderate the effectiveness of CS, enabling therapists to tailor CS interventions for specific groups, thereby amplifying the potential benefits for the MCI population. Finally, this study was restricted to reviewing studies published in English due to resource constraints for translation, potentially omitting significant data from original papers published in other languages.

CONCLUSION

This systematic review investigated the effectiveness of CS on cognition, psychological wellness, IADL and QoL in individuals with MCI. The findings of the subsequent meta-analysis suggest that CS can significantly enhance cognitive function and alleviate depressive symptoms, thereby indicating the practicality and effectiveness of CS for this population. However, studies in this field are quite scarce, which leads to a limited number of eligible RCTs being included in this meta-analysis. Thus, the meta-analysis findings must be interpreted with caution due to limited power and some concerns regarding the risk of bias. Future RCTs that are more comprehensive and in depth, as well as have rigorous methodological designs, are warranted to facilitate a better understanding of the potential benefits of CS for individuals with MCI.

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