



The Connection between Cognitive Training and Cognitive Reserve: A Systematic Review

VERSÃO FINAL APÓS DEFESA

Dissertação para obtenção do Grau de Mestre em
Psicologia Clínica e da Saúde
(2º ciclo de estudos)

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agosto 2022

A reserva cognitiva (RC) refere-se à capacidade do cérebro de manter a cognição na presença de alterações cerebrais relacionadas à idade ou neurodegeneração. É definida como a capacidade do cérebro em lidar com disfunção através da otimização e maximização do seu desempenho através de estratégias cognitivas alternativas ; o cérebro compensa a perda através de processos desenvolvidos ao longo dos anos (Álvares-Pereira et al., 2022). Estes processos são determinados por diferenças individuais, que por sua vez são influenciados por diferenças inatas e exposição ao longo da vida (Stern et al., 2020). O treino cognitivo é definido por Bahar-Fuchs, Clare & Woods (2013) como a prática guiada em um conjunto de tarefas padronizadas projetadas para recrutar funções cognitivas específicas, como atenção, memória ou resolução de problemas, apresentadas em papel e lápis, formulário computadorizado ou outros , análoga às tarefas da vida diária.

Ao ter em conta a definição de reserva cognitiva como a capacidade do cérebro em lidar com a disfunção através de estratégias cognitivas alternativas e a definição de treino cognitivo como uma prática que tem o potencial de melhorar ou manter determinada função cognitiva: Esta revisão visou determinar como o treino cognitivo contribui para a reserva cognitiva e como modera a relação entre mudanças e fatores de risco que impactam a cognição.

O presente trabalho consiste numa síntese da produção científica dos últimos 10 anos, partindo da problemática em estudo – treino cognitivo e reserva cognitiva –, através de uma revisão sistemática da literatura. O objetivo principal foi analisar se existe uma relação entre treino cognitivo e reserva cognitiva e a natureza desta relação na população idosa. Este estudo seguiu os princípios do Preferred Reporting Items for Systematic Reviews and MetaAnalyses (PRISMA). Foram consultados três bases de dados: PubMed, Scopus e B-On, utilizando a frase booleana “Cognitive Training” And “Cognitive Reserve”. Após a realização da pesquisa nas respectivas bases de dados, encontrou-se um total de 124 artigos , tendo este número sido reduzido para 5 após aplicar os critérios de elegibilidade e inclusão. A maioria dos estudos demonstraram que o treino cognitivo não constitui em si mesmo um substituto para a reserva cognitiva; ao contrário, estimula mecanismos pré- existentes que constituem a reserva cognitiva que, por sua vez, modula a eficácia do treino cognitivo. Todos os estudos revisados demonstraram uma melhora geral em várias habilidades cognitivas após o treino cognitivo, o que está de acordo com a literatura atual. No entanto, existem vários fatores dos quais a melhora depende, nomeadamente, o estado cognitivo do indivíduo na linha de base antes da intervenção com treino cognitivo.

A reorganização cerebral pode ocorrer no final da idade adulta; destes dois processos intrinsecamente ligados à reserva cognitiva são a neuroplasticidade e a compensação neural.

A neuroplasticidade se manifestará quando um indivíduo experimentar demandas substanciais e sustentadas do seu sistema cognitivo, enquanto a compensação neural é um mecanismo que só aparece quando novos recursos são necessários para manter ou melhorar o desempenho devido a alterações na estrutura cerebral. Em geral é aceite que existe um possível efeito protetor de um indivíduo envolver-se em atividade cognitivamente estimulante; portanto, é possível melhorar o funcionamento cognitivo mais tarde na vida através do treino cognitivo. Portanto é razoável supor que, dada a natureza do treino cognitivo como uma prática guiada em tarefas exigentes que visam funções cognitivas específicas, o treino cognitivo pode estimular tanto a compensação neural em indivíduos com patologia cerebral quanto a neuroplasticidade em idosos saudáveis e aqueles que começam a registrar declínio cognitivo.

A presente revisão encontrou algumas limitações. Nomeadamente: embora a eficácia do treino cognitivo na melhoria da cognição esteja bem documentada, não foi encontrada um grande número de investigações que tenham em conta como o treino cognitivo e a reserva cognitiva se correlacionam entre si, o que constitui a principal limitação do presente estudo. Esta revisão de literatura demonstrou que a eficácia de um programa de treino cognitivo é mais frequentemente relacionada ao nível de reserva cognitiva de uma pessoa. Para melhor compreender as implicações desses resultados, estudos futuros poderão abordar a disparidade de resultados apresentados nos estudos revisados quanto à influência da reserva cognitiva. Futuros estudos podem também ser realizados para determinar que programas de treino cognitivo são os mais adequados para modular melhor os processos cognitivos que constituem reserva cognitiva.

Abstract:

Cognitive reserve (CR) is, considered to be, a mechanism that protects against significant mental decline. It is based on the concept that proxies such as education, complexity of professional occupation and cognitive stimulating activities increases one's resistance to age or disease-related brain changes and cognition. It designates the brain's capacity to adapt and cope with changes related to age or pathology without developing cognitive impairment. (Cheng, 2014; Stern et al., 2020; Tucker and Stern, 2011 as cited by Song, Stern & Gu, 2022).

Conversely, cognitive training is the repeated and structured practice of tasks which aim at improving, maintaining, or restoring mental function (Valenzuela & Sachdev, 2009). Various studies suggest that cognitive training provided later in life can be used as a protective tool against cognitive decline. Different types of cognitive training programs have been shown to have large and durable effects on the cognitive functioning of older adults (Ball et al., 2002).

This systematic review aims to examine the association between cognitive training and cognitive reserve and to determine if the former serves a role as a socio-behavioural proxy for cognitive reserve. Three databases were used: Scopus, B-On and PubMed.

The reviewed literature states that cognitive training is not a Socio-Behavioral proxy for cognitive reserve. Rather, it stimulates pre-existing processes that underlay cognitive reserve which in turn modulates the efficacy of cognitive training in improving certain cognitive functions. However, cognitive reserve was viewed as acquired throughout one's life; the neural dynamics which are intrinsically connected with the concept of cognitive reserve that may have been induced by a cognitive training program in older individuals were not adequately measured nor taken into account in any of the reviewed studies.

Keywords:

Cognitive Reserve; Cognitive Training ;Cognition; Socio-Behavioral Proxy;Systematic Literature Review

Resumo:

A Reserva Cognitiva (RC) é considerada ser um mecanismo que protege contra declínio mental significativo. É baseada no conceito que fatores como educação, complexidade da ocupação profissional e atividades cognitivamente estimulantes aumentam a resistência a mudanças cognitivas e cerebrais relacionadas com a idade ou doença. É a denominação dada à capacidade do cérebro em se adaptar e lidar com mudanças derivadas da idade ou patologia sem o desenvolvimento de deficiência cognitiva (Cheng, 2014; Stern et al., 2020; Tucker and Stern, 2011 citado por Song, Stern & Gu, 2022).

Por outro lado, treino cognitivo é a prática estruturada e repetida de tarefas com o objetivo de melhorar, manter ou restaurar a função cognitiva (Valenzuela & Sachdev, 2009). Vários estudos sugerem que o treino cognitivo fornecido mais tarde na vida pode ser utilizado como uma ferramenta contra o declínio cognitivo. Diferentes tipos de programas de treino cognitivo têm demonstrado ter efeitos significativos e duradouros no funcionamento cognitivo de adultos idosos (Ball et al., 2002).

Esta revisão sistemática de literatura tem como objetivo examinar a associação entre treino cognitivo e reserva cognitiva e determinar se a primeira funciona como um fator socio-comportamental contribuinte para a reserva cognitiva. Três bases de dados foram utilizados: Scopus, B-On e PubMed.

A literatura revista afirma que treino cognitivo não é um fator que contribua para a reserva cognitiva. Mas estimula processos pre-existentes que fundamentam a reserva cognitiva que, por sua vez, modulam a eficácia do treino cognitivo na melhoria de certas funções cognitivas. Contudo, a reserva cognitiva foi vista como uma aquisição ao longo de vida do indivíduo; a dinâmica neural que está intrinsecamente ligada ao conceito de reserva cognitiva que pode ter sido induzida pelo treino cognitivo em indivíduos idosos não foram adequadamente medidos ou tomados em conta em nenhum dos estudos revistos.

Palavras-Chave:

Reserva Cognitiva; Treino Cognitivo; Cognição; Proxy Socio-Comportamental; Systematic Literature Review

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Acronym List

CERAD:	Consortium to Establish a Registry for Alzheimer's Disease
CR:	Cognitive Training
CRI:	Cognitive Reserve Inventory
CT:	Cognitive Training
OG:	Older Group
YG:	Young Group
PRISMA:	The Preferred Reporting Items for Systematic reviews and Meta Analyses
UMAM:	Programa de la Unidad de Memoria del Ayuntamiento de Madrid
MCI:	Mild Cognitive Impairment
MMSE:	Mini-Mental State Examination
RIF:	Retrieval-induced forgetting
SCI:	Subjective Cognitive Impairment
TMT:	Trail Making Test
WM:	Working Memory

Introduction

Cognitive decline is among the most feared aspects of growing old, with cognitive impairment constituting an increasingly widespread and important health and social issue. It is among the costliest, in terms of the personal, financial, and societal burdens (Deary et al., 2009). Although the extent of any cognitive decline is relatively small for most older people, some individuals develop more extensive difficulties and are at greater risk of developing a form of dementia (Martin et al., 2011). This group is described as experiencing 'mild cognitive impairment' (MCI), which display cognitive changes that, although are not severe enough to fulfil diagnostic criteria for dementia, are nevertheless greater than those typically observed in the same age group (Larrieu 2002; Petersen, 2001, as cited in Martin et al., 2011). MCI is assumed to be a precursor of dementia. The prevalence and cost implications of dementia is arguably one of the major impacts set to radically alter the nature of society (Marioni et al., 2012). Presently, around 55 million people worldwide have dementia; this number is expected to rise to 78 million in 2030 and 139 million in 2050 (WHO,2012). Thus, identifying modifiable factors that either reduce the risk of or encourage recovery from cognitive impairment is highly sought after (Marioni et al., 2012).

Cognitive Reserve

The impact of aging on cognitive function has been amply studied, particularly the influence of both biological and environmental factors on cognition. According to Lina et al. (2021), the study of cognitive reserve arises from the discrepancies observed between the degree of dysfunction and the severity of anatomopathological damage of a subject; some people with a significant level of brain atrophy do not show significant dysfunctionality whereas those who have lower levels of atrophy show greater dysfunctionality. This concept is based on the premise that the brain actively attempts to cope with brain damage by using pre-existing cognitive processes or by enlisting compensatory processes (Stern, 2009). Cognitive reserve (CR) therefore refers to the brain's capacity to maintain cognition in the presence of age-related brain changes or neurodegeneration (Anatürk et al., 2020) by adapting and coping with these changes without developing cognitive impairment (Cheng, 2014; Stern et al., 2020; Tucker and Stern, 2011; as cited in Song, Stern & Gu, 2022). It posits that individual differences in the flexibility and adaptability of brain networks underlying cognitive function may explain differential susceptibility of cognitive abilities or day-to-day function to brain aging, pathology, or injury, thereby allowing some people to cope better with brain changes than

others (Steffener & Stern, 2011). Hence, CR is described not only as a factor in understanding individual differences in the progression of neurodegenerative diseases, but as a protective factor (Lina et al., 2021). Cognitive decline may therefore be attenuated through building up CR (Cheng, 2014; as cited in Song, Stern & Gu, 2022). Cognitive Reserve is thus defined as the brain's ability to cope with brain dysfunction through means of optimizing and maximizing performance either through the use of alternative cognitive strategies or the differential recruitment of brain networks; the brain compensates for neural loss through active processes developed over the years (Álvares-Pereira et al., 2022).

These processes are accordingly determined by individual differences, which in turn are influenced by innate differences and lifetime exposures (Stern et al., 2020). Examples of influential lifetime exposures include, but are not limited to, proxies such as education, early-life general cognitive ability, leisure activities, physical exercise, occupation, or social engagement (Stern et al., 2020). Indeed, a wide range of studies have found that a variety of modifiable factors such as dieting, sleep and meditation are beneficial to the cognitive function of older adults as well (Song, Stern & Gu, 2022). CR is therefore not fixed or immutable; and because it is dynamic and influenced by different exposures across the lifespan, each proxy factor may contribute uniquely to CR (Stern Y, Arenaza-Urquijo, Bartrés-Faz D et al, 2020).

Cognitive Training

Cognitive plasticity refers to cognitive changes and adaptations, and especially to the possible performance of people under optimal conditions (Singer 2003). There is evidence of cognitive plasticity in old age as well as a possible protective effect of engaging in cognitively stimulating activity; therefore, it is possible to improve cognitive functioning in later life through cognitive training (Martin et al, 2011).

Neuroplastic mechanisms can be promoted and conserved through complex mental activity into old age (Gates & Valenzuela, 2010). It has been noted that interventions based on expanding complex mental activity represent a new approach to combat age-related cognitive decline and preventing dementia.

Of these interventions, there is ample evidence that states the efficacy of cognitive training on neurological outcomes in both cases (Lampit et al., 2014; Reijnders et al., 2013). Cognitive training (CT) may contribute to delay or to prevent cognitive decline in older adults (Gates et al., 2011).

Bahar-Fuchs, Clare & Woods (2013) define cognitive training as the guided practice on a set of standardised tasks designed to recruit particular cognitive functions

such as attention, memory or problem-solving presented in paper-and-pencil, computerized form or other, analogous of daily living tasks. Gates et al. (2011) define cognitive training to include instruction in and practice of strategies designed to minimise cognitive impairment while enhancing performance (strategy training) as well as cognitive exercise. Cognitive training is based on the premise that practice has the potential to improve or maintain function of a given domain, with the assumption that the effects of practice will generalise beyond the context of training (Martin et al., 2011; Bahar-Fuchs, Clare & Woods ,2013). It is intended to address cognitive impairment and/or cognitive function directly and to produce improvements in performance on standardized measures of the relevant domain (Martin et al., 2011). Cognitive training can differ greatly with regards to the abilities to be trained (e.g. memory and information processing), specificity of training strategies practiced in the training sessions (e.g. imagery training, method of loci), duration of training sessions and overall training period, frequency of training and participant characteristics (Martin et al., 2011).

Objective

According to Álvares-Pereira, Maruta & Silva-Nunes (2022) three components are commonly used to measure and quantify CR:

- socio- behavioral indicators
- residual approach
- functional neuroimaging studies

This review aims to consider all three measurement components of CR to determine if cognitive training constitutes as a CR proxy that moderates the relationship between changes and risk factors that impact cognitive outcomes and whether the proposed CR proxy is associated with cognitive performance above brain change or pathology.

Hence, this systematic review searched for and identified all relevant studies of defined cognitive training and cognitive reserve and their association in individuals to:

- a) Determine the nature of the connection between cognitive reserve and cognitive training; namely if cognitive training constitutes as a proxy for CR
- b) Determine the overall efficacy of cognitive training in at risk individuals and how it relates to CR

Studies considered for this review were randomized controlled trials that described cognitive training interventions targeting specific domains of cognitive functioning such as memory, attention, or processing speed among healthy older people with no diagnosis or older people who meet criteria for mild cognitive impairment.

Methods

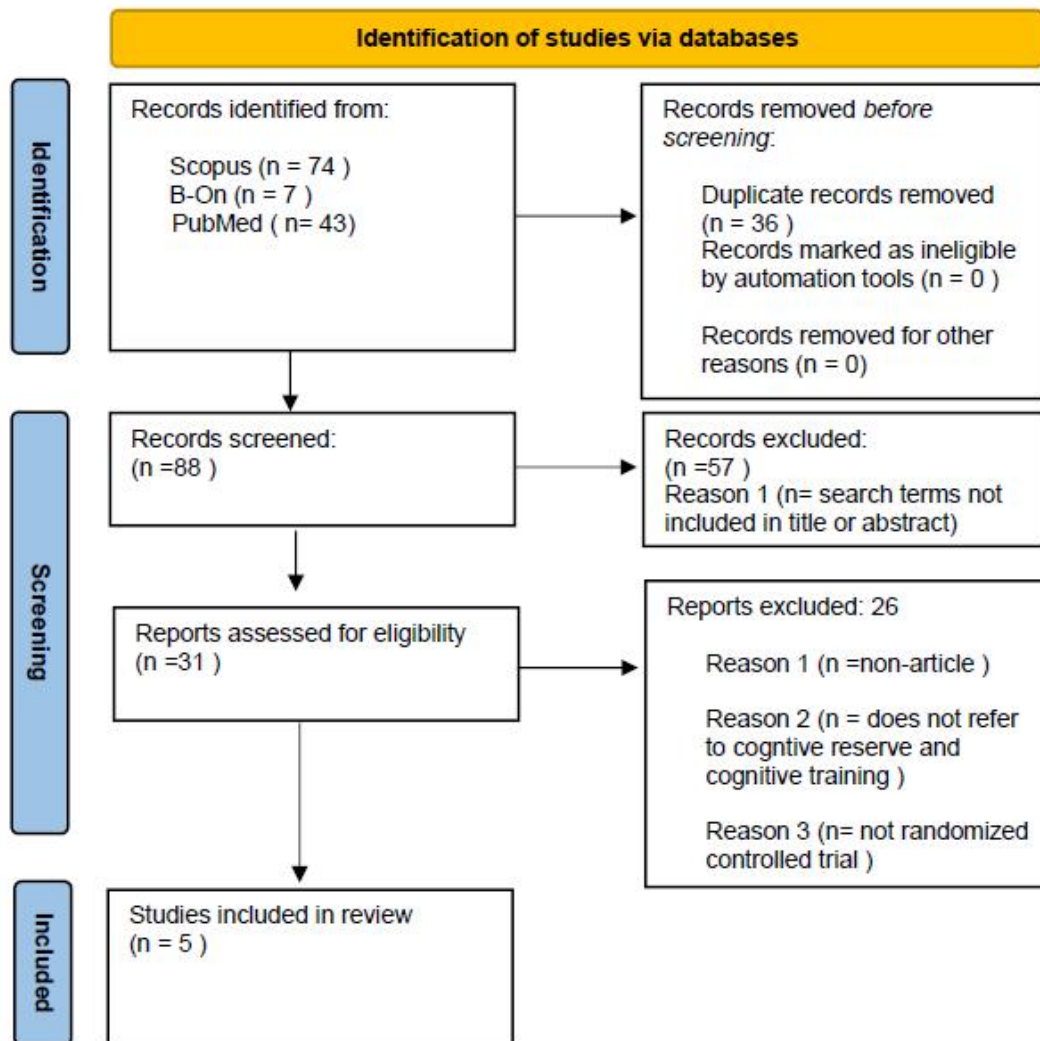
This review was conducted based on the Preferred Reporting Items for Systematic Review and Meta-Analysis Protocols (PRISMA-P) (Moher et al., 2015). It was conducted in the datasets of PubMed, Scopus, and B-On on February 19, 2022, to identify empirical studies that assess the association between cognitive function and cognitive reserve.

The search was limited to articles published between January 2012 and January 2022, using the keywords (“cognitive training”) AND (“cognitive reserve”), with mentioned terms searched through title, abstract and keywords. The search was limited to quantitative and mixed method research articles published in English, Spanish or Portuguese. Studies published in other languages were excluded, as well as non-articles such as book sections, magazine articles, magazine extracts, thesis, case studies and opinion articles. Eligible studies were those that (1) focus on older adults ages 60 and over (2) examined the role of cognitive training and its relationship to cognitive reserve.

Results

This search resulted in a total of 124 articles. A total of 36 duplicate citations were removed prior to screening. The study selection process was conducted in two steps. First, the titles and abstracts of all retrieved citations were reviewed in order to grade each as eligible or not eligible for full review. Eighty eight citations were excluded by not pertaining to the research topic or not meeting the inclusion criteria. Fifty seven citations were left for full review. Of these, five articles directly correlated Cognitive Training and Cognitive Reserve (Table 1).

Figure 1: Diagram of Selection Process. PRISMA Flow Diagram



Bias and Quality of Studies

Based on the Appraisal Checklist Instrument from Joanna Briggs Institute: Checklist for Analytical Cross-Sectional Studies (JBI, 2020), all 5 included studies have been evaluated and found to have high quality.

This checklist scores each study on a scale from 0 to 8, with 8 different questions having three possible answers: yes, no and doesn't apply. The methodological quality of a

study is deemed low with an overall score between 0-2, moderate with an overall score of 3-5, and high with a score of 6-8. All studies reviewed scored high, with individual studies scoring between 6 and 8, as seen in Table 2. The methodological features and main results of each reviewed study is contained in Table 3.

Table 1
Methodological Scores of Selected Studies

Study	Title	Autors	Year	Methodological Quality Score
Study 1	<i>The Impact of Working Memory Training on Cognitive Abilities in Older Adults: The Role of Cognitive Reserve</i>	Mičičl, S., Horvat, M. & Bakracevic, K.	2020	8
Study 2	<i>Age-related changes in inhibition after cognitive training</i>	Razumnikova & Yashanina	2018	6
Study 3	<i>Cognitive Reserve in Dementia: Implications for Cognitive Training</i>	Mondini, S., Madella, I., Zangrossi, A., Bigolin, A., Tomasi, C., Michieletto, M., Villani, D., Di Giovanni, G. & Mapelli D.	2016	6
Study 4	<i>Efficacy of Cognitive Training in Older Adults with and without Subjective Cognitive Decline Is Associated with Inhibition Efficiency and Working Memory Span, Not with Cognitive Reserve</i>	López-Higes, R., Martín-Aragoneses, MT., Rubio-Valdehita S., Delgado-Losada, ML., Montejo, P., Montenegro, M., Prados, JM., de Frutos-Lucas, J. & López-Sanz, D. (2018)	2018	6
Study 5	<i>Cognitive reserve and the effects of virtual reality-based cognitive training on elderly individuals with mild cognitive impairment and normal cognition</i>	Kim, H., Hong, J.P., Kang, J.M., Kim, W., Maeng, S., Cho, S., Na, K., Oh, K., Park, J.W., Cho, S. & Bae, J.N	2021	6

Table 2
Overview of Studies

Study	Authors/Year	Study Design	Population	Dataset	Results	Type of Training
Study 1	Micic et al., 2020	Randomized Controlled Trial	21 healthy older adults aged between 65 and 91 years living in a retirement home, previously screened for cognitive decline	Rey– Osterrieth/Taylor Complex Figure test (ROCF), Digit span, and TMT (part A and part B)	Progress was not statistically significant. No statistically significant transfer of training effects onto tasks of visual-spatial and verbal memory, as well as those related to executive functioning. Statistically significant correlation between cognitive reserve and certain tasks measuring executive functioning and spatial ability	Single n-back task using “Brain Workshop” app. The task required participants to decide if the current stimulus is the same as previous stimulus. The single n-back task presented one visuospatial stimuli. Participants had to decide if the current stimulus is the same as the previous stimulus (n = 1) and n is then increased or decreased depending on accuracy of participant’s performance over the previous three trials.
Study 2	Razumnikova & Yashanina, 2018	Randomized Controlled Trial	131 participants Young group (YG) included 60 university undergraduates (mean age=20; 52 women), and older group (OG) consisted of 51 pensioners (mean age=60.9 years)	RIF	Computerized memory training induces improvement in visual memory in seniors albeit more slowly than in young adults. Cognitive training induced increased memory retrieval with pronounced inhibition function in seniors. Computerized memory training stimulates cognitive reserves due to restored inhibition in older adults, which indicates restructuring of neural systems due to training.	Colored objects from different natural categories were presented in random. From a set of thirty stimuli the any three stimuli appear on the screen, after selecting one of them at the second presentation a stimulus is added in random order. Then, stimuli were presented one after another. Participants of experiment used free choice of items and free association for remembering items.
Study 3	Mondini et al., 2016	Cohort Study	86 participants aged 61–91 years, all community dwelling people with mild to moderate dementia	MMSE COGNITIVE RESERVE QUESTIONNAIRE	A CT rehabilitation program leads to improvement only in subjects with lower level of CR, while patients with higher CR do not similarly benefit from the rehabilitation program. This suggests that in high CR patients the underlying pathology may be more advanced, thus their potential learning ability is reduced	Patients participated in a cycle of CT for a period of 2–4 months, attending 1 or 2 h sessions once or twice a week in small groups (5–6 patients in each group). The specific exercises were designed to stimulate spatial and temporal orientation, memory, attention, language, perception, and visual analysis

Study	Authors/Year	Study Design	Population	Dataset	Results	Type of Training
Study 4	López-Higes et al., 2016	Cohort Study	81 older Spanish-speaking adults with mean age of 70 years who voluntarily participated in study. All recruited from the Center for Cognitive Impairment Prevention (CCIP; Public Health Institute, Madrid City Council),	MMSE	Cognitive training has more positive outcome in lower cognitive reserve patients than in higher cognitive reserve patients. Individuals with a low level of functioning at the baseline would benefit more from CT because they have more room for improvement.	A CT program, called UMAM (Programa de la Unidad de Memoria del Ayuntamiento de Madrid), was implemented in 90 minute sessions, 3 times a week, totalizing 30 sessions in all. It is a multifactorial CT focused on attention and perception, visualization, association, categorization and clustering as well as strategies applied to daily forgetfulness
Study 5	Kim et al., 2021	Randomized Controlled Trial	44 older people mean age 66.8 (22 cognitively normal, 22 with mild cognitive impairment	Neuropsychological Educational Approach to Remediation (NEAR) Consortium to Establish a Registry for Alzheimer's Disease (CERAD)	Patients with MCI and cognitively normal individuals benefited from cognitive training. The cognitively normal individuals with higher CRI-Education showed a greater improvement in their global cognition than did those with lower CRI-Education after cognitive training. Cognitive training led to significant improvement on a measure of working memory and also in processing speed across several assessments.	Both groups underwent a total of eight cognitive training sessions using VR for a period of 4 weeks. They attended 50–60 min sessions twice a week. The VR cognitive training program is designed to train memory, attention, and executive functions. The storyline of each session involves purchasing daily necessities in a supermarket. Participants were briefly shown the list of items to buy at the supermarket; they could then visit seven sections by pushing a button. List of items was evenly and randomly selected from the seven categories of groceries. All virtual environments were fully immersive with increased visuospatial stimulation and presence

Summary of Results

Study 1 aimed to determine whether cognitive reserve plays a role in Working Memory (WM) training and if WM improves the cognitive functioning of older adults. The experimental group received memory training using a single n-back task three times a week during five weeks. Participants had to decide whether the presented visuospatial stimulus was the same as the stimulus presented n places before.

Differences in progress between experimental and control groups on the n-back task were assessed with ANOVA and paired samples t-tests. No statistically significant progress ($\chi^2(14) = 22.50$; $p = .07$) between sessions was found in the experimental group of their performance on the trained task. Neither was there a statistically significant transfer of training effects onto tasks of visual-spatial, verbal memory, and executive functioning. However, there was a statistically significant correlation between cognitive reserve and in tasks measuring executive functioning and spatial ability when including cognitive reserve as a covariate, affecting the results on Taylor complex figure test /marginally/ ($F(1,18) = 4.20$; $p = .05$; $r = .43$) and TMT B task ($F(1,8) = 7.30$; $p = .03$; $r = .69$) in post training performance. Visual-spatial abilities were more successful in Working memory training, than other cognitive abilities that were measured.

Study 2 was based on age-related impairment of memory and executive functions that is commonly associated with a decrease in inhibitory control. Retrieval-induced forgetting (RIF) is a memory phenomenon where remembering causes the forgetting of other information in memory mediated by inhibitory executive-control mechanisms. The aim of this study was to examine how age affects RIF, and whether there was any variation through cognitive training. Two groups were used: Young group (YG) of 60 people with the mean age of 20.3 years, and an older group (OG) consisting of 51 pensioners with the mean age of 60.9 years. After training, memory indices improved in YG by 16% compared to the baseline level, and in OG by 10%.

Differences of RIF dynamics associated with age was revealed between groups, with training inducing the RIF decrease in YG but increasing this effect in OG ($0.01 < p < 0.05$). The results were that computerized memory training stimulates cognitive reserves differently in each group: due to learning effect in young group and through restored inhibition in older adults.

The aim of Study 3 was to evaluate the effect of CR on a cognitive training (CT) for rehabilitation in a group of patients with dementia. The dependent measure taken into consideration when statistically analysing the data was the difference in MMSE scores between T1 and T0. Fifty-seven participants (66.3%) improved the MMSE score between

To and T1 (Mean = 2.67; SD = 1.44), fourteen (16.3%) worsened (Mean = -1.36; SD = 0.49) and fifteen (17.4%) showed no differences. A total of seventeen models were built in order to perform multiple regression analyses to determine dependent variable, age and CR measures. Model 1 included age only, Model 2 included CRI-Total score only and Model 3 included both age and CRI-Total score, after which from Model 4 to 17 the CRI sub-section scores were considered (CRI-Working Activity, CRI-Education, and CRI-Leisure Time) and all combinations of CRI subsections and age as predictors were evaluated. Through regression analyses, all models were significant ($p < 0.05$) apart from Model 1 (with age as predictor) and Model 5 (with age and CRI-Education).

These results show that, taking into account age and level of CR, only CR can predict a significant change in patients' cognitive performance after training. Therefore, CR was a significant factor able to predict changes in cognitive performance after CT. Patients with lower CR benefited from a CT program more than those with high CR.

This result corresponds to the same conclusion reached by Study 4. In this study, the objective was to investigate the role of cognitive reserve, executive functions (cognitive flexibility and inhibition efficacy), and working memory span as factors modulating CT outcomes. There was a significant improvement from pre to post-training MMSE measure across both groups. In the Cognitively Intact (CI) group with mean 28.97 (S.D 1.18) pre-training and 29.14 (S.D 0.83) post-training. In the Subjective Cognitive Decline Group (SCD), mean 28.47 (S.D 1.68) pre-training to 29.22 (S.D 1.04) post-training. There was a very similar MMSE at the baseline between groups (pre-training measure), ($F(1,79) = 3.119, p = 0.81$). Of all models involving selected predictors for each group, the best were: In the cognitively intact group, the lower the digit reordering score at the baseline was, the greater the benefit of training on cognitive status (MMSE). In the SCD group, cognitive reserve and interference were the most influential indicators, with the most influential variable being interference since cognitive reserve did not reach statistical significance. Meaning the lower Stroop's Interference score at the baseline was, the more the benefit of training on MMSE.

The results indicate that cognitive training has a more positive outcome in lower cognitive reserve patients than in higher cognitive reserve patients. The results in both studies contrast with previous ones showing that educational attainment (proxy of cognitive reserve) modulates the effectivity of training in cognitively normal older adults, being participants with low educational level the group in which outcomes after training are better.

Study 5 aimed to explore the associations between CR and the effects of cognitive training using fully immersive virtual reality (VR). At baseline, cognitively normal subjects

had higher Consortium to Establish a Registry for Alzheimer's Disease (CERAD) total scores than patients with MCI (70.41 +/- 5.89 vs 49.68 +/-1137, $P < 0.001$). Regarding CR, CRI-total score and each subdomain score of CRIq showed no significant difference between normal subjects and MCI group, with the exception of CRI Leisure Time.

After cognitive training, (90.9%) of patients with MCI improved the CERAD total score between T0 and T1 and two (9.1%) worsened, with differences ranging from -7 to +20 (mean = 7.73; SD = 6.68). Among the cognitively normal individuals, 18 out of 22 participants (81.8%) displayed improvements in the CERAD total scores between T0 and T1 and four (18.2%) worsened, with differences ranging from -5 to +20 (mean = 4.95; SD = 6.50). There was no significant difference between the two groups for change in the CERAD total score ($p = 0.09$). Multiple linear regression analysis showed that CRI-total score was not associated with changes in the CERAD total score (T0-T1) either in patients with MCI or cognitively normal individuals.

It revealed different impacts of CR on cognitive training according to the participants' cognitive status, in which cognitively normal individuals with higher scores on the Education subdomain of the Cognitive Reserve Questionnaire performed better than those with a lower score. CRI-Education was positively associated with changes in the CERAD total score ($\beta = 0.62$, $P = 0.002$), while CRI-Leisure Time had a negative association ($\beta = -0.52$, $P = 0.02$). Among MCI patients with MCI, there was no association between CR and the outcome of cognitive training.

Discussion

The aim of this systematic literature review was to establish the relationship between cognitive reserve and cognitive training and the efficacy of cognitive training in at risk individuals in improving cognitive performance. It was found that cognitive training provides the conditions under which an individual's cognitive capacity, or cognitive reserve, can be activated (Micic et al.,2022;Kim et al.,2021; Razumnikova & Yashanina,2018).

One measure used in two of the reviewed studies was the effect of cognitive training on Working Memory (WM). Working memory is a cognitive function that is highly sensitive to age (Reuter-Lorenz & Park, 2010; Belleville et al.,2015; cited by Ducharme-Laliberté et al, 2022). It is involved in other cognitive processes, thereby an improvement in working memory function after CT may lead to improvement in other cognitive functions (Micic et al.,2022). After a cognitive training program, cognitively

healthy older individuals showed an improvement in WM (López-Higes et al.,2016). In another, improvement in WM lead to overall improvement of visual-spatial abilities in older individuals (Micic et al.,2022).

These results follow suit in a previous study by Calero and Navarro(2007) that demonstrated a correlation between cognitive reserve and memory training scores. Their findings confirmed a positive association between cognitive reserve and performance on trained tasks, which may explain the immediate and long-term benefits of memory training for older adults (Micic et al., 2020).

On the other hand, Micic et al. found that the capacity for older adults to improve performance on trained tasks is limited and smaller than in young adults. This was also seen by Razamnikova & Yashanina (2018), whose study demonstrated that cognitive training stimulates cognitive reserve differently between young and older adults: the former through forward effect and the latter through restored inhibition. This may be an indication of neural restructuring directly associated with training. In this line, the study by López-Higes et al. (2016) found that a cognitive training program offers more benefits to those that have lower inhibition

Improvement in cognitive function after CT was connected to an individual's measure of selected cognitive capacities at baseline across multiple studies. Lopéz-Higes et al. (2016) found that in adults with subjective cognitive decline, a cognitive training program produced larger benefits for individuals that had shown an overall lower efficiency in inhibition at baseline and for cognitively intact individuals that showed a lower WM at baseline. Therefore, the lower the baseline performance, the greater the benefit in cognition after cognitive training. As a conclusion, the authors did not consider there to be a modulating factor of CR in CT results, since participants with subjective cognitive decline had a lower cognitive reserve at baseline compared for the cognitively intact group. However, this difference was not statistically significant.

Modini et al. (2016) showed that individuals with MCI and with a lower level of CR benefit from CT more than those that had higher CR at baseline. Therefore, a relevant factor modulating CT benefits is the level of functioning at baseline, in which lower-functioning individuals would benefit more from CT than higher functioning individuals.

This contradicts with the study by Kim et al. (2021), which did not establish any association between CR and the outcome of cognitive training in individuals with MCI. However, according to Vuoksima et al. (2013), various studies have shown that individuals with a higher reserve may exhibit more brain pathology and develop dementia later than in individuals with lower levels of CR. Therefore, the lack of benefit from a CT program may be due to the study being focused on patients with dementia, in which a high CR masked a greater extension of cognitive deficit. This would lead to no association

between CR and the outcomes of a cognitive training program. It would also be in line with the results by Modini et al. (2016).

Most studies have shown that cognitive training, therefore, does not constitute in itself a proxy for cognitive reserve; rather it stimulates pre-existing mechanisms that constitute cognitive reserve which in turn modulates the efficacy of cognitive training. All reviewed studies demonstrated an overall improvement in various cognitive abilities after CT training, which is in line with current literature. There are however various factors on which improvement is dependent on, namely the individual's cognitive status at baseline before CT intervention as demonstrated by Kim et al. (2021). This is a common factor found across most of the studies reviewed. Although López-Higes et al. (2016) did not find CR to be a modulating factor in cognitive training, cognitive reserve nevertheless influences both WM and general cognitive function at baseline (Lojo-Seoane et al., 2020), though its influence in WM may be limited, as demonstrated by Facal et al. (2014).

It has been noted that brain reorganization can occur in late adulthood, though the conditions under which healthy older brains reorganize to enhance cognitive function in an adaptive manner are yet to be fully understood (Park & Bischof, 2013). Two studied processes through which changes can occur are neuroplasticity and neural compensation.

The brain's ability to modify, change, and adapt both structure and function throughout life and in response to experience is generally referred to as neuroplasticity (Vos et al., 2017). On the other hand, neural compensation refers to neural activation of additional brain networks that normally are not activated. Unless the task demands exceed the working capacity limit of task-related core networks or if there is damage to said networks, these additional networks typically are not engaged in performing a task (Ji et al., 2018). Both processes are intrinsically connected with the concept of cognitive reserve.

According to Vance et al. (2016) cognitive reserve can be increased or decreased in lieu of activities that either requires adapting to one's environment or to disengage from it in response to lack of stimulation. These processes are referred to as neuroplasticity which create observable morphological changes in response to environmental stimuli which in turn can impact cognition. Such an impact emerges from the development of stronger connections between neurons, and thus improves cognition in order to better meet the challenges of one's environment. According to these authors, this process increases cognitive reserve and is referred to as positive neuroplasticity. Therefore, neuroplasticity will manifest itself when an individual experiences substantial and sustained demands on their cognitive system (Park & Bischof, 2013). Neural compensation on the other hand is a mechanism that only appears when new resources are needed to maintain or improve performance due to changes in the brain structure, in which case brain structures or

networks that are not normally used by individuals with intact brains become activated (Álvares-Pereira, Maruta & Silva-Nunes, 2022).

As previously mentioned, there is a possible protective effect of engaging in cognitively stimulating activity; therefore, it is possible to improve cognitive functioning in later life through cognitive training (Martin et al, 2011). This being said, it is reasonable to assume that, given the nature of cognitive training as a guided practice on often demanding tasks that target specific cognitive functions, cognitive training may stimulate both neural compensation in individuals with brain pathology and neuroplasticity in both healthy older adults and those who start to register cognitive decline.

Throughout the reviewed studies, the success of a cognitive training program in cognitive improvement was often seen as contingent to an individual's level cognitive reserve. The framework of cognitive reserve is based on the premise that certain mechanisms help the brain cope with disease and age related changes. Despite this, there is no operational definition of CR itself nor a clear understanding of its neural bases (Nilsson J, Lövdén, 2018, as cited in Álvares-Pereira, Maruta & Silva-Nunes, 2022). Taking all this into account, it is not unreasonable to consider the possibility that cognitive training may serve as a CR proxy, either as a continuous mental activity through one's life experience, or as a training regimen aimed in increasing CR in old age.

In Study 4, Lopéz-Higes et al. (2016) state that efficacy in cognitive training is associated with inhibition efficiency and working memory span, not cognitive reserve. However, the authors suggest that their results are indicative of neuroplasticity at play, since individuals with lower executive functions benefited more from CT than those with a higher level at baseline. Accordingly, this may be due to a greater mismatch between their own capacity for plasticity and the demands of CT (Lopéz-Higes et al., 2016). Taking into account that cognitive reserve is an active model of Stern's brain reserve hypothesis that enlists compensatory approaches to cope with neural damage and functions as a protective shield against cognitive decline through socio-behavioral proxies, neuroplasticity can speculatively be inferred to as one such compensatory approach. In this case, it is reasonable to hypothesize that CT constitutes a CR proxy itself, since the former stimulates neuroplasticity.

All considered, one can argue that the neural dynamics that may have been induced by cognitive training related to the processes that constitute cognitive reserve were not adequately observed nor measured in any of the reviewed studies; this would have implied neuroimaging to have taken place. Socio-behavioral indicators in most studies were limited to neuropsychological tests used to measure cognitive functions before and after training as a way of measuring impact of cognitive training on cognitive

functions, which did not translate into a measurement of cognitive reserve after cognitive training per se.

Limitations of Existing Research

The main limitation found in the current literature review is the lack of articles found on the relationship between cognitive reserve and cognitive training. This may be due to the nature of the concept behind the cognitive reserve hypothesis. Although the definition of cognitive training in itself is relatively straightforward and has minimum variations in its definition among authors, the concept of cognitive reserve is merely one among others used to address the cognitive pool of resources that protect against age-related cognitive decline.

The concept of the cognitive reserve model that is generally accepted suggests that there are specific experiences and behaviors practiced throughout one's life that confer protection from age-related decline such as education, engaging work, literacy and an overall engaged lifestyle in late adulthood. I speculate that there are few studies that analyse the effect of a cognitive training program on cognitive reserve since the former is commonly used to train certain cognitive abilities in limited moments of time, and the latter is, by its nature, acquired throughout one's life. This leads to the topic of cognitive training and cognitive decline to be underexplored.

The sample sizes in all studies were small, and there was no control group in study 5 to measure for placebo effect (Kim et al., 2021). Study 4 had more females than males in their sample size, all of which could have skewed the data and not allow to identify outliers. Another notable limitation was the variation in methodologies and cognitive measures across the selected articles, which made it difficult to combine homogenous data while considering the heterogeneity of others.

Of all three previously mentioned components used to measure and quantify CR, functional neuroimaging studies were not carried out in any of the reviewed articles. Such a study would clarify whether any brain changes took place after cognitive training, namely any activity that signaled neurocompensation or neuroplasticity. Socio-behavioral indicators were limited to the results given by the Cognitive Reserve Questionnaire, which focuses on measuring known CR proxies in order to attain a person's level of CR. Of these proxies, there is none by which to measure engaging and complex activity that would present the novel environmental press that would be favorable towards neuroplasticity. In other words, activity that would closely resemble CT in terms of focus and cognitive gains is not directly taken into account in the Cognitive Reserve Questionnaire.

Directions for Future Research

Though efficacy of cognitive training in improving cognition is well documented, there has been little focus on how cognitive training and cognitive reserve correlate. Moreover, this literature review has shown that the efficacy of a CT program is more often than not directly related to one's level of cognitive reserve. To better understand the implications of these results, future studies could address the disparity of results shown in the reviewed studies regarding the influence of cognitive reserve. Research can also benefit from long term interventions rather than short ones as performed in the included studies so as to check for any change in pattern.

The present research topic can also be built upon in future studies to focus not only on the relationship between CR and CT, but also to determine what CT training programs are best suited to better modulate the cognitive processes that constitute CR for certain cognitive capacities. Future studies may also focus on how cognitive training may serve as a CR proxy.

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Annex I: Critical Appraisal Checklists for Methodological Quality of Studies

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Study 1: Mičić, S., Horvat, M., & Bakracevic, K. (2020). The Impact of Working Memory Training on Cognitive Abilities in Older Adults: The Role of Cognitive Reserve. *Current Aging Science*, 13(1), 52–61.

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the study subjects and the setting described in detail?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the exposure measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were objective, standard criteria used for measurement of the condition?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were confounding factors identified?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was appropriate statistical analysis used?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Overall Methodological Score: 6

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Study 2: Razumnikova, O., & Yashanina, A. (2018). Age-related changes in inhibition after cognitive training. *2018 11th International Multiconference Bioinformatics of Genome Regulation and Structure\Systems Biology (BGRS\SB)*.

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the study subjects and the setting described in detail?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the exposure measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were objective, standard criteria used for measurement of the condition?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were confounding factors identified?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was appropriate statistical analysis used?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Overall methodological score: 6

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Study 3: Mondini, S., Madella, I., Zangrossi, A., Bigolin, A., Tomasi, C., Michieletto, M., Villani, D., di Giovanni, G., & Mapelli, D. (2016). Cognitive Reserve in Dementia: Implications for Cognitive Training. *Frontiers in Aging Neuroscience*, 8.

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the study subjects and the setting described in detail?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the exposure measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were objective, standard criteria used for measurement of the condition?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were confounding factors identified?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was appropriate statistical analysis used?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Overall methodological score: 6

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Study 4: López-Higes, R., Martín-Aragoneses, M. T., Rubio-Valdehita, S., Delgado-Losada, M. L., Montejo, P., Montenegro, M., Prados, J. M., de Frutos-Lucas, J., & López-Sanz, D. (2018). Efficacy of Cognitive Training in Older Adults with and without Subjective Cognitive Decline Is Associated with Inhibition Efficiency and Working Memory Span, Not with Cognitive Reserve. *Frontiers in Aging Neuroscience, 10*

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the study subjects and the setting described in detail?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the exposure measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were objective, standard criteria used for measurement of the condition?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were confounding factors identified?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was appropriate statistical analysis used?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Overall methodological score: 7

JBI CRITICAL APPRAISAL CHECKLIST FOR ANALYTICAL CROSS SECTIONAL STUDIES

Study 5: Kim, H., Hong, J. P., Kang, J. M., Kim, W., Maeng, S., Cho, S., Na, K., Oh, S. H., Park, J.

W., Cho, S., & Bae, J. N. (2021). Cognitive reserve and the effects of virtual reality-based cognitive training on elderly individuals with mild cognitive impairment and normal cognition. *Psychogeriatrics*, 21(4), 552–559.

	Yes	No	Unclear	Not applicable
1. Were the criteria for inclusion in the sample clearly defined?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
2. Were the study subjects and the setting described in detail?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
3. Was the exposure measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
4. Were objective, standard criteria used for measurement of the condition?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
5. Were confounding factors identified?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
6. Were strategies to deal with confounding factors stated?	<input type="checkbox"/>	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
7. Were the outcomes measured in a valid and reliable way?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
8. Was appropriate statistical analysis used?	<input checked="" type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Overall appraisal: Include Exclude Seek further info

Overall methodological score: 7

